

# HUMAN-NATURE CO-EVOLUTION

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## Introduction

In my *Word of Welcome* I referred to the very long time scales of both the terrestrial and the biological evolutions. Our human species has its roots in the long past evolutionary progress. We can expect that humanity can also participate in the future, slowly progressing evolution of the treasure of high diversities of forms of life and of their natural environments. A scientifically based knowledge of the laws and forces of nature driving the evolutionary progress can help us not to disturb the ongoing evolution and to undertake the appropriate responsibility.

In my presentation I will briefly outline the currently available scientific knowledge on biological evolution and on its systemic aspects. This will lead me to discuss a few conceptual conclusions.

## From the roots of evolutionary biology to molecular Darwinism

It was in the middle of the 19<sup>th</sup> century that Charles Darwin published the theory of natural selection postulating that those organisms dealing best with their encountered natural environments have the best chance for long-term survival as a species. Darwin's theory was based on careful observations of phenotypic traits of some animals. Shortly thereafter, Gregor Mendel started the new discipline of classical genetics on the basis of phenotypic traits of plants. Almost 100 years later, work with bacteria revealed that a major reason for phenotypic traits is specific genetic information carried in filamentous DNA molecules.[1] When the double-helical structure of DNA molecules was determined,[2] it became clear how the linear sequences of nucleotides could carry genetic information and transmit it by replication to the progeny. In the meantime it has become possible to study nucleotide sequence alterations due to spontaneously occurring genetic variations.

The three pillars of Molecular Darwinism are: genetic variation as the driving force of biological evolution, natural selection influencing the direction taken by each step of biological evolution, and both reproductive and geographic isolation which modulates the evolutionary progress.[3] The data on spontaneous genetic variation to be reported below are mainly based on experimental investigations with microorganisms, but there is increasing evidence that the described principals are also valid in eukaryotic organisms.

## **Specific molecular mechanisms can be assigned to three natural strategies of spontaneous genetic variation**

From intensive experimental investigations with *Escherichia coli* bacteria, some of its bacteriophages and a few other microorganisms, it became known that a number of different specific molecular mechanisms serve in nature for the relatively rare spontaneous production of genetic variants.[3] These mechanisms act normally at least to some degree contingently with regard to the site on the DNA and with regard to the time of mutagenesis.[4] It is in general only a minority of novel genetic variants that provide to the organism a selective advantage. Other spontaneous DNA sequence variations may either provide a selective disadvantage or they may not affect any phenotype and remain silent, neutral.

We may classify the various specific molecular mechanisms of spontaneous genetic variation into three natural strategies of genetic variation. Each of these strategies contributes with a different quality to the evolutionary progress:

- (a) One of the natural strategies of genetic variation produces local nucleotide sequence changes, such as a nucleotide substitution, the deletion or the insertion of one or a very few adjacent nucleotides, or a scrambling of a few adjacent nucleotides. By chance, a local nucleotide sequence change can improve already existing genetic information encoding either a specific gene product or a control signal for the expression of a particular gene product.
- (b) A second natural strategy of genetic variation consists in the intragenomic rearrangement of a DNA segment. This can bring about the translocation, a partial duplication, the deletion or the inversion of a DNA segment. By chance, these processes can sometimes result either in the fusion of two different functional domains of genetic information or in the provision of an open reading frame for a gene product with an alternative expression control signal. In the former case, a novel biological function may occasionally result from the fusion, whereas the efficiency of expression of the concerned gene product may be changed in the latter case.
- (c) The third natural strategy of genetic variation resides in the acquisition of foreign genetic information by horizontal gene transfer. This strategy can provide a valuable genetic capacity to an organism in just one single step. We can consider horizontal gene transfer as a sharing in the long-term evolutionary success of another kind of organism. Note that the universal genetic code, i.e. a common language of living beings, facilitates

the success of this strategy.[5] But we have to be aware that the functional harmony of the recipient organism must not be disturbed by the acquisition of additional gene functions.

At any time, novel genetic variants are submitted, together with their parental forms, to the pressure of natural selection. In the longer term, variants with selective advantage may thereby gain over the others. We must be aware, however, that optimal living conditions are neither unique nor absolutely constant for a given kind of living organism. Note that the living conditions depend both on the physico-chemical composition of the environment and on all other living beings present in a given ecosystem.

### **The natural reality takes actively care of biological evolution**

In the living organisms studied so far a number of particular gene products is involved in the occasional production of genetic variants. Some of these enzymes are involved in genetic rearrangements, whereas others contribute to modulate the frequency of genetic variation. Keep in mind that Mother Nature is quite inventive, so that the specific mechanisms of genetically encoded variation generators and variation rate modulators may differ from case to case.

Nature also takes advantage of intrinsic non-genetic elements for spontaneous genetic variation. A good example is the impact of short-living isomeric forms of bioorganic molecules such as nucleotides. The isomeric imino form of the nucleotide adenine does not any longer pair with thymine, but it does so with cytosine.[6] As soon as the adenine reassumes its relatively stable standard form, the shortly before introduced cytosine results in a mispairing. In my opinion, it is wrong to interpret this as a replication error. I rather see in this process a welcome opportunity that can serve nature for the occasional production of a nucleotide substitution. As a matter of fact, the living organisms tested so far also possess so-called repair enzymes with the ability to prevent a stable fixation of the majority of nascent nucleotide mispairings. But their enzymatic prevention is not absolute, which allows to modulate the substitution rates to evolutionarily adequate low levels. In other words, the described process serves the evolutionary progress, it is not an error of the DNA replication fork.

### **Systemic aspects of life and of its biological evolution**

It becomes more and more clear to what degree the living beings interdepend both on contributions provided by a multitude of other living beings and on their variable terrestrial habitats.[7] This insight represents

an important message to all human beings to prevent drastic interventions into the evolutionary progress of the treasure of the encountered biodiversity and of its habitats. We have to be aware that the evolutionary time scale is quite slow, so that we cannot easily perceive the evolutionary progress with our sensory organs. However, taking responsibility for the development at a longer term on our planet Earth, either by a religious mandate or by our own insights into the basic laws of nature, is well anchored in our cultural evolution.

Let me just recall here that the start of agriculture some 10,000 years ago represents an important contribution to improve the living conditions of the human population. Agriculture consists in the domestication of a number of food plants and animals ensuring our food provision. With increasing knowledge of specific values of various gene products we have only very recently started to “domesticate” individual genes, often also from organisms that cannot easily be maintained and propagated as such. But from case to case, a horizontal gene transfer into an appropriate carrier organism can enable us to profit from some products of domesticated genes.[8] This can serve, e.g., for medical and also for nutritional improvements.[9] Since the voluntary translocation of a single gene corresponds to the discussed law of nature of horizontal gene transfer as a driving force of biological evolution, there is no reason to assume risky consequences in all cases of such engineered transfers, in particular if such translocations are made on the basis of an identified and well studied gene product. A good example is golden rice providing a vitamin A precursor to the daily diet.[10]

As human beings we can identify more and more to what degree we interdepend on the rich existing biodiversity and its various habitats. Our microbiome [11] consists of a large diversity of microorganisms which co-habit in and on our bodies. We provide them appropriate habitats and they live with us in symbiosis, contributing mostly to our healthy living. Only relatively rarely we suffer from occasional pathogenic effects.

With these indications it may become clear that for at least two reasons, we have to take good care and not destroy the still rich biodiversity on our planet. As we have seen, spontaneous biological variation can bring about particular gene functions from one organism to another (including the human genome), in particular upon long-term cohabitation. On the other hand, future generations might possibly identify in the rich biodiversity still other useful gene functions which they might like to domesticate and use for their benefit. These long-term aspects should be kept in mind in our considerations on sustainable development. Specific genes are potential renewable resources and should not become lost.

### Additional conceptual aspects of the evolutionary progress

In explaining his drawing of the tree of evolution, Charles Darwin postulated that living organisms must have a common origin. Still today, the sciences cannot explain how life on Earth started nor would we know if there was one or more than one independent start. However, we still use the tree of evolution as a concept. In view of the evolutionary relevance of horizontal gene transfer, I have started to introduce horizontal connectors between branches of the tree in order to symbolize the occasional acquisition of genetic information from another type of organism.[12] Therefore, living beings do not only have a common origin but also a common future. Any living being may, at some forthcoming time, take profit to acquire an additional genetic capacity that had been developed and improved elsewhere.

At least for well-studied bacteria, we can conclude on a duality of the genome. As I have outlined above, some of the genes serve biological evolution, producing variation generators and modulators of the rates of genetic variation. These evolution genes serve for the expansion of life and for providing a rich biodiversity. In contrast, the majority of the genes carried in the bacterial genome serves in the individual for the fulfilment of life from one generation to the next. I assume that this conceptual aspect does also apply to higher organisms.

May I just mention here that we should not assume that lost biodiversity becomes fast reconstituted by the continued evolutionary progress. Rather, we can expect that long-term evolution can bring about an enriched biodiversity again, but not with all the same genetic functions which had been lost before.

From today's point of view, it is important to realize that phenotypic traits do not uniquely depend on specific genetic information. We have to take note also, as already mentioned, of the relevance of symbiotic effects of the microbiome and of effects exerted by any other living organism existing in the same ecosystem. And we also have to consider epigenetic effects [13] of the environment and impacts of nutrition consumed.

In conclusion, life is of a high degree of complexity, which has to be considered in any deeper reflection on the long-term sustainable development of our planet Earth.

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