Flegr, J. (2023). Constructive Neutral Evolution. In: Shackelford, T.K. (eds) Encyclopedia of Sexual Psychology and Behavior. Springer, Cham. https://doi.org/10.1007/978-3-031-08956-5_1746-1

Constructive Neutral Evolution

Jaroslav Flegr

Department of Philosophy and History of Science, Faculty of Science, Charles University, Prague, Czech Republic. E-mail: flegr@cesnet.cz

Synonyms
Passive evolution or passive selection (both rarely).

Definition
Constructive neutral evolution (CNE) is a process in which complex, potentially detrimental structures and features in organisms arise through the interplay of neutral evolutionary forces and natural selection.

1. The Concept of Constructive Neutral Evolution
Constructive neutral evolution is a concept in evolutionary biology that offers an explanation for the emergence of complex features and structures in organisms without relying exclusively on natural selection. During constructive neutral evolution, selection does not directly increase an organism's functionality (viability or fertility); instead, it acts on secondary elements that compensate for the detrimental effects of primary elements produced by selectively neutral or detrimental evolutionary changes (Covello & Gray, 1993; Gray, et al., 2010; Stoltzfus, 1999).

During constructive neutral evolution, selectively neutral evolutionary processes and selection work together to create sophisticated and complex structures or behavioral patterns. Neutral evolutionary processes produce primary elements that are either useless or detrimental, while natural selection generates secondary elements that mitigate the negative impacts of primary elements on an organism's functionality. The complexity of structures, originally arising in their simple form due to selectively neutral evolutionary processes, gradually increases as original primary elements are supplemented with new secondary elements that neutralize the adverse effects of primary elements to maintain the organism's functional state. The emergence of these secondary elements can create an *evolutionary trap*—once they arise, they increase the likelihood that additional primary elements will accumulate through the action of neutral evolutionary processes, e.g., mutagenesis, since their negative effects are immediately neutralized. This will generate selection pressure for the development of further secondary elements that remove other negative consequences of new elements produced by neutral evolutionary processes. As a result, the entire system becomes increasingly complex, and the emerging structures composed of both types of elements may pose a growing burden for the organism, both energetically and evolutionarily. For the building up and smooth functioning of the entire system, the organism must provide not only resources, such as energy but also maintain the functionality of many genes that would otherwise be unnecessary. *Loss-of-function mutations* continuously arise in these genes, reducing the viability of an individual or leading to its death. The resulting number of *genetic deaths* necessary for keeping the whole structure functional, i.e., the number of individuals eliminated by selection against mutants, i.e. mutation load, may be so high that it threatens the very existence of a given species. Consequently, a species with structures formed by constructive neutral evolution functions worse than it would without these structures. It should be noted, however, that the structures created by constructive neutral evolution may, in some cases, positively influence a species' future evolution. Like *spandrels*, they can act as a starting point for the emergence of new adaptive structures capable of performing a specific new function.

2. Examples of Systems Possibly Originated by Constructive Neutral Evolution
The quintessential example of a product arising from constructive neutral evolution is the *RNA editing* system in trypanosomes, as discussed below. Nevertheless, numerous other molecular systems have been identified as potentially having evolved through constructive neutral evolution (Stoltzfus, 1999). Some instances are relatively straightforward, like the emergence of alternative genetic codes in mitochondria, while others are considerably more intricate albeit much more widespread. One such example involves the evolution of the contemporary spliceosome-based splicing apparatus in eukaryotic cells, which originated from a primordial form of splicing reliant on the activity of self-splicing group II introns (Covello & Gray, 1993).

2.1. Example: RNA Editing in Trypanosomatids
The RNA editing mechanism in trypanosomes (Kinetoplastida) exemplifies a system that may have evolved into its present-day complex form by constructive neutral evolution (Lukes, Kaur, & Speijer, 2021; Stoltzfus, 1999). Many species within this taxon share a very interesting and complex method of managing genetic information (Benne, 1992). Their modified mitochondria contain numerous genes stored in DNA in a strangely encrypted form, requiring editing at the RNA level before translation into proteins.

The editing process involves molecules of guide RNA (gRNA) directing the special enzymes of the editing apparatus to insert or remove individual nucleotides at specific sites on the immature messenger RNA (pre-mRNA). Many specific gRNAs for a particular gene, coded at different locations in the trypanosome mitochondrial genome, participate in a specific order to edit one mRNA.

It has been repeatedly suggested that this intricate and energetically demanding system did not have any functional importance for trypanosomes, and its formation was a result of constructive neutral evolution. When a mutation occurs in the DNA, such as a nucleotide deletion that reduces an organism's biological fitness, selection pressure begins to act on the mutant and its progeny. Over time, mutants carrying reverse mutation or mutants carrying mutations capable of compensating for the negative manifestations of the mutation will predominate in the population. One way to compensate for the negative manifestations of the mutation involves the emergence of an editing apparatus that repairs the change at the mRNA level. The DNA error (i.e., an element created by neutral evolution, e.g., deletion of some nucleotide) remains still present, but the sophisticated editing apparatus consistently repairs corresponding RNA molecules, preventing the mutation from reducing the carrier's viability. Once emerged, the RNA editing apparatus can evolve through constructive neutral evolution to compensate for a broader range of mutations, with its complexity gradually increasing, for example, through the addition of different types of gRNA. As a result, more and more mutations can accumulate in the mitochondrial genes of trypanosomes. As the accumulation of primary elements continues, the editing process becomes increasingly vital for the organism, which now depends on the consistent repair of its mRNA. This mRNA editing-based repairing mechanism is especially effective for genes located in many identical copies within a cell, such as genes coded in mitochondrial or plastid DNA. Here, it

Flegr, J. (2023). Constructive Neutral Evolution. In: Shackelford, T.K. (eds) Encyclopedia of Sexual Psychology and Behavior. Springer, Cham. https://doi.org/10.1007/978-3-031-08956-5_1746-1

is not possible to remove the same mutation by reverse mutations in all copies of a particular gene on all copies of mitochondrial DNA; however, it is possible to correct all molecules of RNA by RNA editing.

3. Constructive Neutral Evolution at the Organismal Level

At the organismal level, structures or behavioral patterns influenced by constructive neutral evolution may not have been extensively identified or described. While some examples might hint at the involvement of constructive neutral evolution, a comprehensive understanding of its role in shaping organismal traits remains to be fully explored. As research into constructive neutral evolution progresses, it is likely that more examples will be discovered, which will contribute to a deeper understanding of its impact on the evolution of various complex structures and behavioral patterns.

On the other hand, it can be hypothesized that numerous phenomena in cultural evolution are driven by constructive neutral evolution. For instance, the complex and elaborate structure of languages, encompassing various grammatical rules, redundancies, and irregularities, could be a result of *constructive neutral cultural evolution*. These intricacies might not necessarily offer a communicative advantage, but they have emerged and persisted due to neutral evolutionary processes. Similarly, some rituals and customs may have evolved to become more complex and elaborate over time, owing to constructive neutral cultural evolution. The accumulation of specific practices or symbols might not necessarily provide a direct adaptive advantage, but they persist and become more intricate through neutral evolutionary processes.

3.1. Healthcare and the Implications of Constructive Neutral Evolution

It can also be speculated that some sectors of modern medical care are, or will soon become, complex systems shaped by constructive neutral evolution, exhibiting all the peculiarities and disadvantages of such systems (Flegr, 2022). With advancements in healthcare, particularly assisted reproduction methods, genes associated with semi-lethal traits or sterility might increasingly accumulate in the human gene pool without any negative consequences. The presence of such alleles may eventually render most humans reliant on these techniques, necessitating the development of more sophisticated methods. This cycle could, in turn, accelerate the accumulation of other detrimental alleles. Without the capability and willingness to correct these alleles in the germinal cell line, this positive feedback loop could lead to a situation where human reproduction drastically differs from the reproduction of all other species, becoming absolutely dependent on medical technology.

Conclusions

In conclusion, constructive neutral evolution offers a complementary explanation for the emergence of complex structures and features in organisms, highlighting the interactions between neutral evolutionary processes and natural selection. By emphasizing the role of random processes in the evolution of complexity, and the compensatory nature of secondary elements that counteract the negative impacts of primary elements, this concept broadens our understanding of how complexity arises. Although constructive evolution examples in current scientific literature predominantly involve molecular structures and processes, such as the RNA editing mechanism in trypanosomes, it is plausible that constructive neutral evolution may also influence the emergence of diverse morphological structures and behavioral patterns at the organismal level. As our knowledge of constructive neutral evolution expands, we can anticipate to gain further insights into the evolution of complexity in diverse biological and cultural systems, and their potential consequences for the future of various species, including our own.

Cross-References

None

References

Benne, R. (1992). Review - RNA editing in trypanosomes - The us(e) of guide RNAs. *Molecular Biology Reports, 16*, 217-227.

Covello, P. S., & Gray, M. W. (1993). On the evolution of RNA editing. *Trends in Genetics, 9*, 265-268.

Flegr, J. (2022). Adaptations, By-products, and Spandrels. In T. K. Shackelford (Ed.), *Cambridge Handbook of Evolutionary Perspectives on Sexual Psychology: Volume 1, Foundations* (Vol. 1, pp. 87-113). Cambridge: Cambridge University Press.

Gray, M. W., Lukes, J., Archibald, J. M., Keeling, P. J., & Doolittle, W. F. (2010). Cell biology. Irremediable complexity? *Science, 330*(6006), 920-921. doi:10.1126/science.1198594

Lukes, J., Kaur, B., & Speijer, D. (2021). RNA editing in mitochondria and plastids: Weird and widespread. *Trends in Genetics, 37*(2), 99-102. doi:10.1016/j.tig.2020.10.004

Stoltzfus, A. (1999). On the possibility of constructive neutral evolution. *Journal of Molecular Evolution, 49*(2), 169-181.