

## The Legacy of Charles Darwin

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#### Agrociencia Uruguay

Universidad de la República, Uruguay

ISSN-e: 2730-5066

Periodicity: Bilingual

vol. 27, e1200, 2023

agrociencia@fagro.edu.uy

Received: 22 May 2023

Accepted: 24 May 2023

Published: 29 May 2023

URL: <http://portal.amelica.org/ameli/journal/506/5063857010/>

DOI: <https://doi.org/10.31285/AGRO.27.1200>

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Agrociencia Uruguay, 2023



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Since the advent of agriculture approximately 12000 years ago, human life and survival have undergone a profound transformation. The deliberate improvement of plants and animals through selective crossbreeding of desirable variants has enabled humankind to achieve significant modifications relatively quickly. Despite the availability of this empirical knowledge, it was not linked to the biological processes of change occurring in nature as Charles Darwin did 165 years ago.

Almost fortuitously, his 5-year journey aboard the *HS Beagle*, a British Navy ship whose mission was to survey the coast of South America, significantly influenced his ideas on the transformation of species.

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#### AUTHOR NOTES

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Upon his return to England in 1836, he dedicated several years to conducting experiments and gathering information to substantiate his groundbreaking ideas. He foresaw that his concepts would revolutionize the scientific community. However, it wasn't until 1858 that a letter from Alfred Wallace, a young researcher who had independently arrived at the same conclusions, spurred him to publish a note describing their findings jointly<sup>(1)</sup>. The following year, Darwin published his famous book *On the Origin of Species*. In this influential book, Darwin presented his central idea of evolution through natural selection, supported by a wealth of empirical evidence. He also anticipated the possible criticism that could be made by answering them. He was not the first to speak about biological evolution, but he proposed an effective mechanism in which species could adapt to the environment without invoking a divine creator.

Darwin introduced the concept of evolution through natural selection, which mirrors the process of artificial selection undertaken by humans when modifying animal and plant species to suit our preferences. The same principle applies in nature, but the modifications occur in response to environmental pressures. Darwin wrote:

“If during the long course of ages and under varying conditions of life, organic beings vary at all in the several parts of their organization, [...] if there be, owing to the high geometrical powers of increase of each species, [...] a severe struggle for life, [...] if variations useful to any organic being do occur, assuredly individuals thus characterized will have the best chance of being preserved in the struggle for life; and from the strong principle of inheritance they will tend to produce offspring similarly characterized”<sup>(2)</sup>.

Thus, Darwin's theory states that certain organisms with inheritable advantageous traits tend to leave more offspring in each generation on average. As a result, the favorable characteristics progressively become more prevalent within populations over time. Therefore, a mechanism that occurs at the individual level (natural selection) produces changes in populations as the frequency of different variants appearing over time is modified (evolution). Additionally, Darwin explored how certain organisms, generally males, possess conspicuous features that may be seen as disadvantageous for their survival, such as the vibrant plumage of birds or exaggerated structures in mammals. To explain this phenomenon, Darwin introduced a complementary form of natural selection he termed *sexual selection*: competition and choice for mates play a crucial role in the origin and maintenance of sexual dimorphism.

Another groundbreaking contribution was his recognition that population variability is the fundamental basis for natural selection. He understood that individuals with diverse traits possess varying opportunities for survival and reproduction. By acknowledging the significance of variation as “raw material” for natural selection, Darwin emphasized how the interplay between inherited traits and the environment determines the success or failure of individuals in a population. Thus, he broke with the prevailing concept of essentialism, which held that species were fixed, unchanging entities with a set of inherent, unalterable characteristics or “essences”.

In addition to explaining the emergence of adaptations with a simple and contrastable mechanism, Darwin explained the differentiation of all life forms on earth and their possible “improvement” from a common ancestor. Implicitly, this encompassed our species, humans. This had profound implications, removing the notion of human exceptionalism: the same mechanism responsible for shaping human characteristics also played a role in developing other life forms. In 1871 Darwin courageously released a new book: *The descent of man, and selection in relation to sex*, delving into his ideas on human evolution. Despite having limited information available, Darwin puts forth four fundamental concepts that have been extensively supported by subsequent evidence.

Firstly, he proposes that our closest living relatives are chimpanzees and gorillas, as our skeletal structures share common characteristics inherited from a primate-shared ancestor. Secondly, Darwin suggests that the geographic origin of our species is Africa, considering that chimpanzees and gorillas are exclusively found on that continent. Therefore, it is reasonable to conclude that the ancestor of all three species likely

originated there. Thirdly, he identifies a crucial milestone in our lineage's differentiation: the adoption of upright walking, which freed arms from locomotion<sup>(3)</sup>. This enabled the development of more sensitive hands and refined motor skills, as the hands were no longer subjected to calluses resulting from constant weight-bearing. Lastly, Darwin posits that the evolution of the brain and its associated cognitive abilities would be a subsequent advancement in our species' development. Although initially proposed with limited information, these ideas have gained significant support from subsequent scientific research and continue to shape our understanding of human evolution.

Since then, significant scientific advancements have further bolstered Darwin's claims, particularly in genetics. The understanding of variation, an unknown aspect in Darwin's time and considered a weak point in his theory, has been significantly illuminated. Notable landmarks include the rediscovery of Mendel's laws of genetics, the identification of DNA as the hereditary material with its double helix structure, and the development of DNA sequencing and analysis techniques. Empirical evidence, spanning phenotypic, genetic, and genome levels, has demonstrated the existence of natural selection, including the intricacies of sexual selection. The concept of a single origin of life is now widely accepted scientifically. A compelling example of this unity is the shared genetic code among all living organisms, with minor variations that are difficult to explain if diverse origins were considered.

Moreover, through comparative analysis of shared genetic sequences, such as those involved in primary metabolism, it is possible to reconstruct the evolutionary history of life on Earth, as evidenced by the "Tree of Life" project (<http://tolweb.org/tree/>). Detailed anatomical and genomic comparisons leave no doubt that our closest living relatives are chimpanzees, and the fossil record of our lineage, until approximately 1.5 million years ago, is exclusively found in Africa. Within our lineage, the adoption of upright posture emerged at least 3.5 million years ago in the genus *Australopithecus*, considered the most likely ancestor of the genus *Homo* to which our species belongs. Notably, cranial capacity began to increase much later, in the genus *Homo* about 2 million years ago, and after the development of upright posture.

## DARWINISM TODAY

The current evolutionary theory, built upon the foundation of Darwinism, continues to evolve with discoveries and insights. An illustrative example lies in our current comprehension of molecular evolution, where chance plays a relevant role, a mechanism known as genetic drift. It is now understood that many DNA changes do not impact organisms, and these mutations can persist, be eliminated, or randomly replace previous versions. This concept was unimaginable in the early 20<sup>th</sup> century and has expanded our understanding of the complexities of evolution.

Some authors argue that Darwin's ideas were instrumental in establishing Biology as a distinct scientific discipline<sup>(4)</sup>. The concept of a common ancestor for all living beings has broken down the barriers between different branches of biology, creating a unifying framework. By exploring what we share, such as the genetic code, how we differ from our ancestors, and the advantages conferred by environmental changes, we gain insights into the vast biological diversity present in the world. This holistic approach to studying biology allows us to uncover the intricate interconnectedness of life and better comprehend the processes that have shaped the diversity of organisms we observe today. It highlights the importance of understanding the similarities and differences across species, offering valuable insights into the mechanism underlying evolutionary change.

Many of the challenges humanity faces today can be analyzed through an evolutionary lens, and the most effective strategies to address them often draw upon applications of evolutionary theory in various fields. For example, the emergence of novel viruses, such as SARS-CoV-2 and influenza, are "zoonotic spillovers", like approximately 60-75% of human infectious diseases. These viruses were transmitted from wild animals to

humans and between non-human species, exemplified by avian influenza. Through the lens of evolutionary theory, we can gain insights about the most probable patterns of their evolution and thus somehow predict the change. Molecular evolution analyses have become routine in vaccine design, helping to identify changes in specific regions of the virus genome by analyzing patterns of DNA sequence variation.

The overuse of antibiotics and pesticides has created selection pressures that favor the emergence of drug-resistant organisms. As a long-term and sustainable solution, efforts are being made to transition towards a less aggressive and more diverse intervention. The susceptibility of certain animal and plant breeds is a consequence of artificial human selection. Like natural selection, this process reduces genetic variation around the selected DNA sites responsible for the desired traits, which enables the identification of the genetic basis of the adaptations. However, unlike natural selection, artificial selection, influenced by human-controlled environments and small population size, can result in the accumulation of deleterious double recessive traits through crossbreeding and a lack of population variation to respond to new environmental challenges.

Integrating an evolutionary and holistic perspective, the concept of “One Health” has emerged, recognized for over a century. This concept emphasizes the interconnectedness and interdependence of human health, domestic and wild animals, plants, and the broader environment, including ecosystems. In other words, effectively understanding, anticipating, and addressing global health risks necessitate a collaborative and interdisciplinary approach involving academia, society, and governments.

The impact of evolutionary theory on the fields of medicine and veterinary science is made evident in the recent recognition of Svante Pääbo, who was awarded the Nobel Prize in Medicine and Physiology last year. Pääbo, a paleoanthropologist, dedicated much of his academic career to sequencing the genomes of extinct species within our genus *Homo*, including the Neanderthals. Eventually, he achieved this feat and even uncovered an unexpected *Homo* species, the Denisovans. Neanderthals and Denisovans were discovered in the Denisova Cave in Asia, where our *Homo sapiens* ancestors also resided. This evidence indicates that past humans coexisted and interbred with other hominid species. The genomic and fossil records demonstrate hybridization between the three species. Consequently, parts of the Denisovan and Neanderthal genomes are present in the genomes of some present-day humans. These genetic segments have implications, such as adaptations to altitude (cold and hypoxic environments)<sup>(5)</sup> and susceptibility to COVID-19<sup>(6)</sup>. In a recent special issue of *Science* magazine, the results of genome comparison among 240 mammalian species were published. While seemingly unrelated to immediate human concerns, this project provides insights into the deep relationships between mammalian lineages and their common ancestors. Additionally, it sheds light on which genomic regions are conserved across mammals, indicating their essential functions. If a specific DNA position remains unchanged across all mammals, it suggests that any alteration in that region was eliminated due to negative consequences for the organism carrying them. This knowledge becomes invaluable in deciphering the genetic causes of certain diseases<sup>(7)</sup>.

In summary, today’s biological diversity and the intricate interactions between organisms and their environment result from evolution. Despite the vast amount of information we have acquired and the details we can now access, the fundamental principles proposed by Darwin 160 years ago remain the cornerstone of our understanding of life's complexities.

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