FRANCISCO J. AYALA: SCIENTIST, PHILOSOPHER, HUMANIST AND FRIEND

Francisco J. Ayala: científico, humanista y amigo

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ABSTRACT: Francisco J. Ayala was a dominant figure in evolutionary biology from the mid 20th through the first two decades of the 21st century. The purpose of this article is to try to place his work into the larger context of evolutionary biology and to briefly consider his important contributions to the philosophy of biology, including reconciling biological evolution and religion and his writings on the evolution of ethics. Another amore personal purpose is to recount his influence on me and on a whole generation of evolutionary geneticists. To achieve these twin purposes, I place his work into the larger historical context with a focus on his early work providing rigorous empirical tests of the hypothesis of neutral gene evolution in 1970s. I try to give some flavor for the human being behind an incredible body of work and to explicate some of the forces that may have influenced his development.
KEYWORDS: Neutral evolution, phylogeny, molecular clock, science and religion, biological ethics.

RESUMEN: Francisco J. Ayala fue una figura destacada en la biología evolutiva desde mediados del siglo XX hasta las dos primeras décadas del siglo XXI. El propósito de este artículo es intentar situar su obra en el contexto más amplio de la biología evolutiva y considerar brevemente sus importantes contribuciones a la filosofía de la biología, incluida la conciliación de la evolución biológica y la religión y sus escritos sobre la evolución de la ética. Otro propósito más personal es relatar su influencia en mí y en toda una generación de genetistas evolutivos. Para lograr estos dos objetivos, sitúo su obra en un contexto histórico más amplio, centrándome en sus primeros trabajos, que proporcionaron pruebas empíricas rigurosas de la hipótesis de la evolución de los genes neutros en la década de 1970. Intento dar una idea del ser humano que existe detrás de una obra increíble, además de explicar algunas de las influencias en su desarrollo.
PALABRAS CLAVE: Evolución neutral, filogenia, reloj molecular, ciencia y religión, ética biológica.

1. **INTRODUCTION**

Francisco J Ayala was gifted with an exceptional intellect, a remarkable work ethic and a high degree of personal generosity. His prodigious scientific output influenced three generations of evolutionary biologists and philosophers and will continue to be influential well into the future. Altogether he published more than 1200 scientific papers, book chapters, book reviews and essays. He also authored or edited 66 books. While he lived and worked in the United States from the early 1960s until his death in 2023, he maintained close connections with the scientific communities of Europe and Latin America and especially with his native Spain. He wrote predominantly in English, but also frequently published in Spanish. He was truly a citizen of the world.

Ayala received his BA in physics from the Complutense University of Madrid in 1955 and entered the seminary shortly thereafter. He was ordained a Dominican priest in 1960, but left the priesthood a few months later. Nevertheless, this experience clearly stimulated his later writings that sought to reconcile evolutionary biology and religion. I was fortunate to count Francisco as a friend for more than 50 years and as such I had the opportunity to observe his remarkable career unfold. I recall once asking Francisco what caused him to choose to study evolution and he replied that Erwin Schrödinger's 1944 book *What is Life* had captivated him as a student and ultimately led him into the field of evolutionary biology. This in turn led him to seek permission for a leave from the Dominican Order to pursue studies in evolutionary biology with Theodosius Dobzhansky at Columbia University in New York City.

Dobzhansky, a Russian/Ukrainian refugee, had joined the laboratory of Thomas Hunt Morgan in 1927 at Columbia University on a Rockefeller fellowship to study the new science of genetics. Dobzhansky became a towering figure in evolutionary genetics, owing to his role as one of the primary architects of the "modern synthesis" of genetics and evolution and owing to his pioneering experimental approaches to the study of evolutionary genetics. By the time Ayala had joined his laboratory, Dobzhansky was celebrated as a leading thinker and writer on evolution and on topics related to the philosophy of evolution. At this time, Dobzhansky's lab was a hothouse of intellectual activity with such notable current and former students as Bruce Wallace, Tim Prout, Richard Lewontin, Wyatt Anderson, Lee Erhman, Lee van Valen and others. Ayala was a natural fit into this stimulating and highly competitive environment.

Back in the 1950s and 60s US universities had mandatory retirement ages and when Dobzhansky reached age 65 he had to retire from Columbia Uni-

versity, but rather than actually retiring he simply moved over the Rockefeller University. By this time Francisco was an assistant professor at Providence College in Providence, Rhode Island, and Dobzhansky arranged to have Francisco join him as an assistant professor at Rockefeller. Around 1970 Dobzhansky moved to UC Davis to take up an honorary faculty position. Part of the deal was that Francisco would also join Dobzhansky in Davis. I was a graduate student in the laboratory of Robert W. Allard, who was chair of the Genetics Department at Davis and who was instrumental (along with Ledyard Stebbins) in recruiting Dobzhansky and Francisco Ayala, so I had a kind of ring side seat on the recruitment. As a consequence, I first met Francisco in 1970 when he visited Davis in connection with negotiating his recruitment and I still vividly recall his striking presence and the masterful seminar he gave to the genetics department.

Francisco moved to Davis in 1971 and immediately established a very active lab and a number of gifted students including Martin Tracey, John MacDonald, Dennis Hedgecock and John Avise quickly joined the Ayala lab. I left Davis in 1972 to take a faculty position at Brown University, but the year of overlap provided a stimulating opportunity for me to interact with the Ayala lab. Francisco became a kind of an academic big brother to me and our paths crossed frequently over the ensuing years. Finally in 2004, Francisco recruited me to join him at UC Irvine where I had the opportunity to engage with Francisco and Hana on a regular basis. I was a beneficiary of their many kindnesses and counted them among my closest friends.

My purpose in this essay is to discuss Ayala's major role in formulating a rigorous empirical approach to population genetics and molecular evolution and to consider his leading role in defending the science of evolution in the face of creationist attacks. Finally, I will briefly consider his interests in human evolution and his seminal contributions to a theory of the evolution of ethics. I will attempt to put his work and ideas into the historical and scientific context of the times and to describe some of currents that influenced research directions and interpretation over the years.

2. **PROLOGUE: EARLY POPULATION GENETICS**

At the time I began to study population genetics in the late 1960s the empirical side of the field was dominated by Dobzhansky's students. Population genetics also had a strong mathematical tradition and Dobzhansky collab-

orated with Sewall Wright, one of the founders of theoretical population genetics, on experiments designed to measure basic parameters of theory. Despite this, the theoretical side of the field was much more advanced and dominated thinking. The tools for empirical study were primitive and/or highly model dependent. But the emerging science of molecular biology and the allied methods of biochemistry were just beginning to shift this balance and Francisco Ayala was one of the principle early figures to seize the opportunity to expand empirical approaches in population genetics.

Theoretical population genetics emerged in the second decade of the 20th century as a mathematical consistency argument to reconcile the seeming paradox of particulate inheritance with natural selection operating on small continuous variations (Provine, 1971). One school, represented by William Bateson (Batson, 1909) argued that mutation was the driving force of evolution while an opposing school, known as the biometricians and represented by Darwin's nephew, Francis Dalton, argued for a kind of continuous inheritance. The final resolution came in 1918 with a seminal article by R. A. Fisher (Fisher, 1918) where he provided a mathematical proof that phenotypic correlations among relatives could be accurately accounted for by the Mendelian transmission of particulate factors (genes).

Fisher went on to prove that not only was evolution by natural selection consistent with particulate inheritance, but that particulate inheritance was in fact a necessary condition for the conservation of genetic variance. Indeed, not only did Fisher prove that Mendelian inheritance conserved genetic variance, but he also argued that it was the simplest system of inheritance with this essential property. In contrast a blending system of inheritance, as postulated by Darwin and some of his contemporaries, would quickly destroy genetic variation rendering natural selection ineffective as an evolutionary force (Fisher, 1930).

The path breaking work by Fisher was soon followed up by the elaboration of mathematical models that considered the dynamics of genes under various patterns of selection, migration, mutation and genetic drift (Fisher, 1930; Haldane, 1932; Wright, 1931). The mathematical approach was to abstract down to single genes without considering possible interactions among genes at different loci and without considering the effects of genetic linkage. This simplification was necessary to make these elementary models mathematically tractable and it was considered a reasonable first approximation to actual evolutionary dynamics. This immediately created a mismatch between empirical work and theoretical work because empiricists had to study the

phenotypic manifestations of entire organisms that were usually the result of many genes.

Despite this, several key empirical questions emerged from these early theoretical considerations. One obvious question was how much genetic variation actually exists in natural populations of typical organisms? Put differently, the question was: of the presumably thousands of genes in the genome, what proportion have two or more mutational forms (alleles) at measurable frequencies in natural populations? Clearly for natural selection to drive evolutionary change, there had to be sufficient preexisting genetic variation in populations to allow an adaptive response to new or changing environmental circumstances. The problem was that at the time there were no good tools to answer this essential question. DNA had not been discovered so geneticists of the 30s and 40s did not know the physical basis of the gene. Even after the discovery that DNA is the physical basis of inheritance in 1953, tools to measure mutational change in the DNA molecule, or its derivative proteins, did not become available for another decade or more.

Early geneticists relied on various indirect techniques to try to measure genetic variation. These included inbreeding (in diploid organisms) to uncover mutations previously masked in heterozygotes. This approach helped reveal a wealth of mostly deleterious phenotypes that segregated as single gene mutations, but it could not assess the general level of genetic variation. Because most of these deleterious phenotypes were recessive and therefore masked in heterozygotes, this led to the recognition that diploid organisms carried a "genetic load" of hidden deleterious mutations (Muller, 1950).

A second approach was to perform long term selection experiments. Populations subjected to several generations of phenotypic selection often showed a substantial response so that after several generations the mean of the resultant population exceeded the distribution of variation in the parental population, demonstrating ample genetic variation underlying the selected trait. But the results were dependent on the selected phenotype and the reference population and so did not allow generalizations about general levels of genetic variation. Another approach was to use the statistical models of quantitative genetics to partition the heritable component of variation into components associated with mechanisms of gene action (additive, dominance or epistatic gene action). Once again, the results were specific to phenotype and reference population and were highly model dependent. While indirect and subject to criticism, the results of numerous selection and quantitative genetic experiments did combine to suggest substantial levels of genetic variation in populations of most organisms investigated (summarized in Lewon-

tin, 1974). Still, it was clear that there was a pressing need for more direct ways to measure general levels of genetic variation.

3. **ISOZYME ERA**

In 1957 Clem Markert and his colleague Robert Hunter (Hunter and Markert, 1957) developed the isozyme method that went on to revolutionize the empirical study of population genetics in the 1960s and 1970s and that began an era of rapid technological change in genetics. Markert had been a post-doctoral student at Cal Tech where he studied the then new field of biochemical genetics under George Beadle, the Nobel Laurate and originator of the one-gene one-enzyme hypothesis. Clem Markert was a veteran of the Abraham Lincoln Brigade of the Spanish Civil War and a strong believer in social justice in the United States. Later, Markert's early academic career was nearly derailed by the infamous House Un American Activities Committee when he was targeted for investigation. He was a remarkable man and perhaps a bit bemused by the impact his technique had on evolutionary genetics.

The Isozyme method allowed the visualization of different forms of enzymatic proteins on a gel. The various protein forms were separated in an electric field and appeared as bands after application of a histochemical stain. Proteins are electrically charged owing to the charge of their constituent amino acids. If a mutation caused an amino acid substitution, especially for the subset of charged amino acids, the net electrical charge of the protein would be altered and hence its mobility in the electric field would change. It was quickly discovered that different alleles of a single genetic locus could be visualized on a gel and so it was possible to detect mutant forms of various enzymatic proteins for a vast range of enzymes, thereby providing a means to estimate genetic variability at the level of individual loci. A locus with two or more forms of a protein was said to be polymorphic and it was a simple matter to calculate the fraction of polymorphic loci.

Looking back, it is interesting that it took population geneticists almost a decade to appreciate that here was an approach to the problem of measuring genetic variation that was direct and based on a more or less random sample of the genome. In 1966 Harry Harris (1966) and Lewontin and Hubby (1966) changed the direction of population genetics by publishing two important papers that used gel electrophoresis to show that levels of poly-

morphism were far higher than had been previously thought. Harris showed that about 30% of human loci, that encoded enzymatic proteins, are polymorphic, based on gel electrophoresis of a sample of ten loci. Lewontin and Hubby produced a strikingly similar estimate from an electrophoretic survey of 18 enzymatic loci in *Drosophila pseudoobscura* sampled across a wide geographic range. The Lewontin and Hubby paper was especially important because the authors presciently spelled out the implications of these findings in population genetic terms.

The most striking implication of the work of Harris and of Lewontin and Hubby was that if 30% of loci are polymorphic then literally thousands or even tens of thousands of genes must have two or more forms segregating in populations. Moreover, this is a serious underestimate because gel electrophoresis only detects a fraction of all amino acid changes (primarily those that induce a charge change). (Synonymous mutations in coding genes and, of course, mutations in non-coding regions of the genome, potentially important in gene regulation, also cannot be detected by the isozyme technique.) Until this time, most population geneticists assumed that polymorphisms were maintained in populations by some form of balancing selection. But the vast levels of genetic variation uncovered by the isozyme method, seemed incompatible with this classical view.

4. **THE NEUTRALITY CONTROVERSY**

Until the introduction of the isozyme method, most studies of genetic polymorphism focused on identifiable traits like wing color patterns in moths (Ford, 1965) or chromosomal inversion polymorphisms in *Drosophila pseudoobscura* (Dobzhansky, 1970). A paradigmatic case of balanced polymorphism of that era was sickle cell anemia where the heterozygote enjoyed significant protection from malaria and didn't suffer the severe anemia of the mutant homozygote (Allison, 1955). The homozygote for the normal allele was susceptible to malaria and suffered higher mortality rates owing to the disease. The geographic distribution of the sickle cell mutant allele mapped very nicely onto the distribution of malaria in Africa and elsewhere which initially suggested an association with disease resistance (Haldane, 1949). These cases and many others were regarded as balanced polymorphisms where selection favored alternative forms depending on ecological circumstances. But the new isozyme results revealed that literally thousands of genes were

polymorphic and it was hard to reconcile this new found variation with classical balancing selection.

Two lines of theoretical argument reinforced the doubts about the role of selection in maintaining molecular variation. The first was based on a famous calculation by J. B. S. Haldane (1957, see also Felsenstein, 1971) on the cost of a gene substitution. Haldane showed that there was an upper bound to the number of genes that could be under selection at any point in time and that the limit was determined by the reproductive potential of the species. In essence differential survival or reproduction required some types be removed, thereby reducing the reproductive potential of the species relative to its maximum. If too many genes are under selection simultaneously, the reduction could be larger than the reproductive potential and the species would decline to extinction. The second closely related argument grew out of the concept of "segregational load" where in diploid organisms balanced polymorphism implied the segregation of less fit homozygous types, as is the case with sickle cell anemia cited above. If literally thousands of loci are under independent balancing selection, implying that fitness is multiplicative over loci, then the reduction in fitness (reproductive potential) would be enormous (Crow and Kimura, 1970).

A resolution to this dilemma was to claim that most molecular variation is neutral to selection. The claim was that most new mutations in DNA (and hence in enzymatic proteins) do not affect phenotype and therefore are not perceived by selection. These new mutations simply drift through populations and in diploids a fraction 1/2N of new mutations will ultimately be fixed (where N is the species effective population size). For the small fraction of new mutations destined to be fixed, it will take 4N generations on average for fixation to occur, which for most species would be a very long time, so at any point in time a sample would reveal neutral mutations at most loci drifting in the population (Kimura, 1968).

The assumption that most new mutations were solely governed by drift simplified theoretical calculations and allowed many important results to be derived such as the ones just cited about expected time to fixation of a new mutation and this led to a rich body of testable theoretical predictions. It also led to some important corollaries such as the molecular clock hypothesis (Crow and Kimura, 1970). The theoretical results were criticized as being too simplistic for not considering so called epistatic selection (interactions among different genetic loci in fitness), or more plausible models of single-locus selection such a frequency dependent selection or temporally varying selection or selection that varied by ecological niche. But ultimately, the question was

an empirical one and required the collection of large data sets to test neutral theory.

Two schools of thought arose almost immediately and could be characterized as the "selectionists" versus the "neutralists." Looking back, it is revealing how tenaciously many of us clung to these contrasting positions. For the "selectionists" the whole Darwinian program seemed at risk, while for the "neutralists" the truth of the theoretical calculations seemed undeniable. (It probably didn't help that the neutral theory came to be known as non-Darwinian evolution!) People became angry and emotional over these contrasting positions and friendships were stressed.

The ensuing controversy lasted for around a decade and consumed a lot of journal pages. Many of the issues that were to define the controversy were explored in 1971 during a symposium at UC Berkeley and later published in 1972 as the Proceedings of the V Berkeley Symposium of Mathematical Statistics and Probability. I was lucky enough to attend the symposium and to hear the leading figures of population genetics debate the issues. These included Dick Lewontin, Jim Crow, Motoo Kimura, Warren Ewens, R. W. Allard and Francisco Ayala among others. It was heady stuff for a graduate student and left an enduring mark on my thinking. At the time, I was just finishing my PhD thesis on geographic patterns of isozyme variation in wild oats in California and the lectures were perfect fodder for my dissertation.

Francisco Ayala represented the empirical side of the field at the Berkeley symposium. Francisco began his career studying the philosophy of biology and was strongly influenced by the work of Karl Popper (1959) that argued that for a scientific theory to be valid its predictions must be subject to falsification by experiment or empirical observations. Francisco had employed the Popperian approach in his 1960s work on competition between species of *Drosophila* to question the competitive exclusion principle in ecology (Ayala, 1969) and he immediately realized that the predictions of neutral theory were ideal for empirical testing.

Following the philosophical framework of Karl Popper, Ayala and his students set out to collect large data sets of isozyme variation from the *Drosophila willistoni* group to test the predictions of neutral theory (Ayala et al., 1970). The sampling design was to collect flies from four different species of the *D. Willistoni* group from a series of islands in the Caribbean. Each fly was assayed for its genotype at 28 different isozyme loci and the allele frequencies within and among populations, islands and species were calculated. From these structured samples a series of statistics were calculated and compared

to expectations based on neutral theory (Ayala and Tracey, 1974). The results of the calculations appeared to provide a clear rejection of neutral theory, because the distribution of locus specific genetic identity among species did not conform to the predictions of theory (e.g. Ayala and Tracey, 1974). Ayala's empirical work testing the neutral theory provided compelling evidence, owing to large sample sizes, large numbers of loci surveyed, the geographically structured nature of the sample and the inclusion of within and between species samples. More importantly it represented a transition to rigorous hypothesis testing in population genetics based on the clear predictions of a well-defined body of theory. This body of work attracted a lot of attention and later contributed to Ayala's election to the US National Academy of Sciences in 1980.

Ultimately the idea of neutral molecular variation came to be an accepted null hypothesis in the field. At the same time, the neutral theory itself was modified to include various selective effects (e.g. associative selection, nearly neutral theory, Ohta, 1971; Kimura and Ohta, 1971), so that the elegant theoretical structure of the neutral theory was expanded while also making it more compatible with empirical observations. This had the effect of rendering the theory less testable, but more realistic.

At about the same time, molecular biology began producing a number of unexpected discoveries about the organization of the eukaryotic genome such as the existence of introns and of multigene families and providing compelling molecular evidence for transposable elements. Each of these new phenomena was entirely outside the postulates of theoretical population genetics and provided a vast stimulus to empirical research. While population genetic models were modified to account for these new phenomena, the research momentum shifted from theoretical to empirical discovery. Empirical research in molecular evolution continued to accelerate with the rapid elaboration of new technologies over the decades since the mid 1970s to the present.

Throughout his career Francisco Ayala was quick to adopt new technologies beginning with isozymes and ending with rapid DNA sequencing. He was also quick to employ new analytical methods and to expand the range of evolutionary questions he investigated, while also emphasizing a rigorous hypothesis testing framework. To amplify on this point I briefly consider his early work utilizing molecular phylogenies and the molecular clock.

5. **PHYLOGENITIC TREES**

An old idea in evolutionary biology is that of an evolutionary tree that depicts the history of branching relationships among species (or other categories of biological diversity), based on their separation over time from common ancestors. In an early use of genetic data for phylogenetic inference, Dobzhansky inferred the branching relationships among inversion polymorphisms in *Drosophila pseudoobscura* in the late 1930s (Dobzhansky, 1970). Ayala was quick to see that the new isozyme data also provided a powerful approach to inferring historical relationships among populations and species. But there are two subtle distinctions between trees derived from inversion polymorphisms and trees derived from many isozyme loci. First, a tree derived from many isozyme loci provides a good representation of average relationships across the entire genome, while one derived from a single character like an inversion type does not necessarily represent the species tree. And second, the temporal ordering of branching events can be inferred in the inversion case, but the individual mutations detected at isozyme loci do not provide information on their temporal ordering. Rather temporal inference is based on some measure of genetic distance averaged over loci and often combined with a molecular clock assumption.

Ayala and colleagues were among the first to use isozyme data to estimate phylogenies, in their case for the *Drosophila willistoni* species complex (Ayala et al., 1974), thus providing a comprehensive picture of the evolutionary relationships among Caribbean island and continental species. This work foreshadowed a large body of later research that projected phylogenies on geography, thereby permitting inferences about the history of interisland migrations and speciation events. In a different, and medically important application of phylogenetic inference, Escalante and Ayala (1994) used small subunit ribosomal DNA sequences to investigate the relationship between malarial parasites with the goal of determining the origin of human malarial parasites. The evolution of human parasites became a major theme of Ayala's later research and contributed importantly to strategies for disease control (e.g., Tibayrenc and Ayala, 2000).

6. **MOLECULAR CLOCKS**

The notion of a molecular clock was first postulated by Zuckerkandl and Pauling (1965) based on their consideration of early sequence data for the

cytochrome c protein. The argument that flows from neutral theory is that if the mutation rate is u and there are 2N copies of a gene in a diploid population then the rate of fixation of a new mutation is u2N(1/2N) = u. That is the rate of fixation of neutral mutations is exactly equal to the mutation rate, a presumed constant, implying a constant rate of molecular divergence between species at any neutral gene.

The molecular clock hypothesis is a powerful idea because it offers a means of estimating the time of divergence between species based solely on measures of genetic distance. Ayala and colleagues (Ayala, 1997; 1999) showed that while important, the molecular clock varied greatly among genes, so its application needed to reflect different rates of molecular evolution among different genes. My own research on chloroplast DNA evolution paralleled these themes during this period (Ritland and Clegg, 1987; Gaut et al., 1992), so I was especially attracted to these results.

7. **HUMAN EVOLUTION**

Research on *Drosophila*, bacteria and viruses dominated the early period of experimental genetics, because these organisms had short generation times and could be cultured in large numbers, rendering them ideal for tracing genetic transmission in the laboratory over several generations. Humans, of course, did not lend themselves to experimental manipulation and have long generation times so the early study of human genetics was mostly limited to cataloging mutant phenotypes. All of this changed with the introduction of molecular techniques and especially with the advent of rapid DNA sequencing and the ability to sequence ancient DNA. Over the last twenty years the study of human evolution has blossomed, both because of molecular technologies and because of an accelerating wealth of new paleontological findings (Seddon, 2022). Here too Francisco Ayala was quick to appreciate the new findings and to interpret the profound implications for our understanding or our human history (Ayala and Cela-Conde, 2017; Cela-Conde and Ayala, 2017a, b).

We now know that over the last 2 million years a wealth of hominin species (or subspecies) walked the earth, although only our own species remains. As of this writing, we can count at least 6 or 7 different *Homo* entities, all of which made tools and operated as cooperative bands. We also know that during the last few million years, the earth has experienced multiple dramatic

changes in climate, having undergone multiple ice ages and alternating dry and humid periods. These climatic changes almost certainly drove the cultural and biological evolution of hominin populations (Seddon, 2022).

Our closest relatives, *H. neanderthalensis* and *H. denisova*, separated from the lineage leading to *H. sapiens* between about 600,000 and 500,000 years ago and then later interbred with our ancestors around 47,000 to 65,000 years ago (Sriram et al., 2016). Recent evidence from Morocco dates the appearance of *Homo sapiens* to about 300,000 years ago (Richter et al., 2017). All three species probably had language and utilized fire. Out of this hominin diversity, only we remain.

Recent analyses estimate that the ancestral species to *Homo sapiens* underwent a severe population bottle neck between about 930,000 and 813,000 years ago that lasted for about 117,000 years, reaching a minimum population size of only around 1280 breeding individuals (Hu et al., 2023). This time frame spans the Early to Middle Pleistocene transition, a period of major climate change. Moreover, there is a major chromosomal fusion that occurs in the human lineage during this time horizon, leading to the speculation that the common ancestor of Neanderthals, Denisovans and *Homo sapiens* may have emerged as a distinct species during this period of extreme demographic stress. Today we would classify a species with an effective population size of 1280 as endangered. It is sobering to reflect on the perilous path we have followed.

Here I'd like to indulge in few speculative thoughts about the role of technology in our collective historical journey. The evolution of spoken language required genetic changes and likely was a prerequisite to later cultural adaptations such as tool making and the utilization of fire. Over the roughly 350,000 years since the appearance of anatomically modern *H. sapiens*, we operated as hunter gather bands for about 95% of our history. It is only in the last 5% of our history that we transitioned to agriculture and more complex societies. Remarkably the transition to agriculture occurred in several parts of the globe more or less contemporaneously, presumably driven by climate change associated with the end of the last period of glaciation. If the climate had been more stable, would we still be hunter gathers?

Over most of the ensuing history since the invention of agriculture, we relied on human or animal labor to meet the needs of ever more complex civilizations. Human slaves were an important part of the economy of many early civilizations (e.g. ancient Rome). The systematic use of the scientific method to investigate our world, and as a source of new technologies, seems to

have begun in earnest with the Renaissance period about 400 years ago. While we have known about other means of harnessing energy to do work since ancient times (e.g., the Library of Alexandria had a model steam engine over 2000 years ago, waterpower has been used for thousands of years), we did not initiate the large-scale use of steam power until the start of the industrial revolution about 250 years ago. Was this transition partly driven by the emancipation movement? In the last 0.07% of human history, we have suddenly created a highly technological world dependent on fossil fuels for work. Associated with this has been a vast increase in scientific knowledge, including a deep understanding of the universe and of our place in the universe, a doubling or more in life expectancies, a roughly ten-fold increase in the human population thereby inducing serious stresses on the global carrying capacity of Earth that threatens our future well-being. What triggered this sudden explosion of technology and can we manage the consequences? Will the computational power of Artificial Intelligence propel us into a new transition akin to the industrial revolution as some speculate? I miss not having Francisco Ayala present to explore these and other speculations about the future of humanity.

8. **THE SCIENCE AND CREATIONISM CONTROVERSIES**

Ever since Darwin there has been a tension between religion and the teaching of evolution. When literally interpreted, the creation stories of many religions conflict with our understanding of human origins based on the modern science of biological evolution. This has set up recurring conflicts between these two domains. In the late 1970s and early 1980s a fight over science curricula emerged, when creationists claimed a kind of "equal time" right to teach religious dogma as a part of science curricula in the United States, masquerading under the misleading appellation of "creation science." The science community viewed this as a serious threat to the integrity of science education and ultimately to the foundations of scientific knowledge.

One of the most important figures in the push back against the demand to use science curricula to propagate religious belief was Francisco Ayala, who became deeply involved in a major court case surrounding an Arkansas law that mandated the teaching of "creation science" in public schools (McLean v. Arkansas, 1982). Ayala testified as an expert witness in the case and his credentials as both a scientist and a former priest carried considerable au-

thority. In 1982 Judge William Overton found against the law ruling that "creation science" was religion and did not satisfy the definition of science.

The US National Academy of Sciences also became concerned about the threat to science posed by "creation science" and by a later derivative argument known as "intelligent design" and appointed an ad hoc committee chaired by Francisco Ayala to craft a white paper explaining the scientific case for evolution (Ayala et al., 1984). The resulting booklet, *Science and Creationism. A View from the National Academy of Sciences,* was sent to virtually every school district in America and proved quite effective in public education (NAS, 1984). I had the privilege of serving on a follow up committee that produced updated editions of the white paper in 1999, also under the chairmanship of Francisco Ayala.

For many years, Ayala remained one of the most active speakers and writers opposing the introduction of religious dogma into school curricula under false premises. In 2007, he wrote a beautifully reasoned book, *Darwin's Gift*, meant to reconcile and explain the separate domains of scientific evidence and religious faith. He later received the Templeton Prize for this book and for his broad efforts to reconcile the two domains of science and religion. Characteristically Ayala donated the one million dollar prize to his university to, in part, support graduate fellowships in ecology and evolution.

9. **ETHICS**

Ethics is fundamental to the practice of science; obviously a truth-seeking process must create a system of practices that put honestly and integrity above all other considerations. An issue for science education, especially at the graduate level, is to transmit this value system to future generations. Often ethical considerations raise hard questions that need careful thought for their resolution. In 1989, the National Academy of Sciences created an ad hoc committee, chaired by Francisco Ayala, to write a report, *On Being a Scientist,* that codified best ethical practices. *On Being a Scientist* explores fundamental ethical questions and addresses critical issues like, how to properly apportion scientific credit, the responsibility that professors and scientific mentors have for their students, issues of data integrity, how to deal with scientific misconduct and a number of related topics. Ayala also served on a later committee that produced an updated version of *On Being a Scientist* in 2009. The booklet *On Being a Scientist* was widely distributed to the scientif-

ic community and still provides the best and most comprehensive source for ethical behavior in science.

Francisco Ayala wrote extensively on ethics over the years. His views are best summarized in a 2017 book chapter (Ayala, 2017) where he argues that moral values and ethics are universal in human society, and he asserts that these values are an indirect product of biological evolution. He claims that ethics are indirectly the result of evolution because they are dependent on advanced intelligence which is itself a direct outcome of natural selection. Ayala identified two preconditions to the acquisition of moral values: (1) abstract reasoning; and (2) the ability to foresee the future consequences of a present action. He then asks the fascinating question of when in the course of hominin evolution did these traits become incorporated into the genetic and cultural endowment of our ancestors? Finally, he concludes that moral codes are a cultural phenomenon and determined by cultural not biological evolution. Ayala then goes on to consider when esthetic values emerged in hominin evolution and he makes a convincing case that at a minimum these values were shared with our Neanderthal cousins.

10. **FRANCISCO AYALA: A REMARKABLE MAN**

I never heard Francisco speak ill of another person. He was always kind and he was particularly generous in advancing the careers of his students and colleagues. I was deeply impressed by his continuous efforts to nominate his colleagues for high honors. Preparing these nominations requires considerable effort and thought and Francisco was the first to step forward to assume these tasks. It was as if he felt an obligation to share his own good fortune as widely as possible. He set a high standard for the rest of us.

For more than sixty years his primary residence was in the United States, yet Francisco remained a European gentleman in his external demeanor. He was always elegantly dressed, even for informal occasions. He was a handsome man but with an open and friendly style who engaged people easily. He was witty and enjoyed sharing a good joke with his colleagues. Despite his prominence, he took considerable pains to make students feel comfortable in his presence. But he was also quite efficient in his use of time. I once asked him how he managed to write so much and he said that he started at 3 am each morning and rarely slept for more than four hours. This iron clad disci-

pline was a likely a consequence of his seminary days, but he maintained it throughout his life and managed to do more than any other two men.

Francisco Ayala received almost every scientific honor afforded by his profession, including the National Medal of Science in 2002. He served on the President's Council of Scientific Advisors during most of the Clinton administration and he was elected President of several scientific societies including the American Association for the Advancement of Science. He believed in service and almost always accepted committee and other assignments.

Amazingly, Francisco managed to be a successful farmer in addition to his academic pursuits. He owned considerable vineyard acreage in the San Joaquin Valley of California and was a major grape producer. He had professional vineyard managers, but he planned daily tasks with them by phone most mornings as he walked to his office at UC Irvine. These operations produced considerable wealth and characteristically, Francisco and Hana dedicated their wealth to philanthropic causes, making a major donation to the university for endowed chairs and the support for graduate students and other generous gifts in support of the arts, prominently to the Pacific Symphony of Orange County.

Francisco had a portion of the highest quality grapes from his farms set aside for his own personal wine and he enjoyed sharing these wonderful vintage wines with his colleagues. Not surprisingly, he was a raconteur who enjoyed excellent food and good conversation. I have many fond memories of dinners in the best local restaurants with Francisco and Hana. We would share one of Francisco's wines while enjoying great food and stimulating talk.

Like his mentor, Th. Dobzhansky, Francisco was a gifted writer in English, despite the fact that English was not his native language. I am told that he wrote quickly and rarely needed to edit. Francisco remained engaged and busy writing almost up until his death in February 2023. I would sometimes run into him walking in our neighborhood during this final year and he would be eager to talk about his latest writing project. He was fortunate to retain his mental acuity until the end.

Francisco J. Ayala left an amazing legacy. He influenced the course of science through his focus of the empirical testing of evolutionary hypotheses. He permanently raised the standard of empirical rigor in population genetics, population ecology, molecular evolution and in evolutionary epidemiology. These fields reached a new level of maturity owing to Ayala's unique combination of empirical science and philosophy. He had a major impact on the

development of the philosophy of biology as a scholarly discipline through his deep reflections on science and religion, on ethics and on the foundations of science.

A measure of one's legacy is the people we have trained, and in this respect Francisco Ayala was also exceptional. All together he trained more than 100 PhD and post-doctoral students. He hosted over 115 scientific visitors in his laboratory and he provided a valued link between the scientific communities of Latin America, Europe and the US. Many of his former students and collaborators are today's scientific leaders in over 20 different countries. His thinking and approach to science will continue to be influential long into the future. Francisco J. Ayala passed away just nine days short of his 89th birthday, a scholar to the end.

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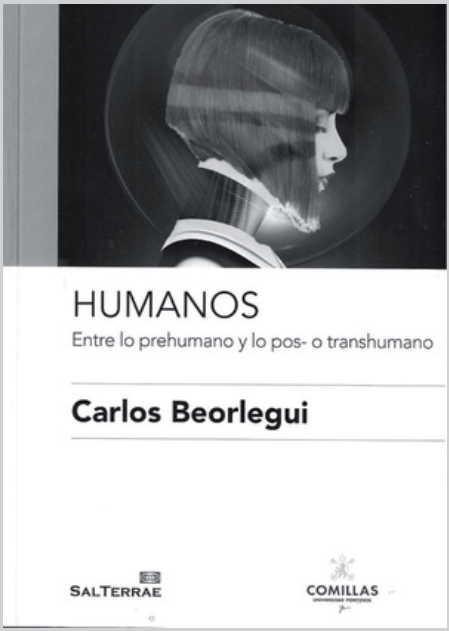
Humanos

Entre lo prehumano y lo pos- o transhumano

Carlos Beorlegui

Un rasgo propio de nuestra especie es la búsqueda de su identidad. En la antigüedad, se de nía en relación a lo divino y, en la actualidad, el elemento de contraste son los animales (lo prehumano) y lo poshumano (cíborgs, androides o robots). Hoy más que nunca, nos hallamos ante la necesidad de ahondar en nuestra propia identidad y defender un renovado humanismo que reivindique nues- tra diferencia cualitativa frente al resto de los animales, a la vez que construi- mos una sociedad futura basada en la defensa de la dignidad e igualdad de todos los humanos.



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