LUIGI LUCA CAVALLI-SFORZA
25 January 1922 — 31 August 2018
LUIGI LUCA CAVALLI-SFORZA

25 January 1922 — 31 August 2018

Elected ForMemRS 1992

BY A. W. F. EDWARDS FRS*

Gonville and Caius College, Cambridge CB2 1TA, UK

Though it was as a bacteriologist that Luca Cavalli-Sforza first flourished scientifically, it was the subject of human population genetics that he dominated for the second half of the twentieth century. He pioneered both genetical demography and the construction of the genetical evolutionary tree of man, initially from gene-frequency data and ultimately from tracing the paths of descent of individual DNA sequences. He was among the first to apply the new computers to the problems he encountered, using his self-taught knowledge of mathematics and statistics. He conducted expeditions to the Pygmies of the African rainforest and studied the spread of agriculture in Europe, demonstrating the similarity between its wave of advance and the contours of population gene frequency. He noted the correspondence between the descent tree of languages and the human evolutionary tree.

Cavalli headed university departments in Pavia and then Stanford, surrounding himself with young colleagues and driving forward research with vigorous discussion and unceasing enthusiasm. His knowledge was spread across medicine and genetics, anthropology and linguistics, archaeology and history, and he expressed himself fluently in speech and writing in Italian, English and French. A true Renaissance man.

His published work in human population genetics and cultural evolution over more than 50 years constituted ‘one long argument’, as Darwin said of The origin of species. The villages of the Parma valley were his Galapagos Islands, and random genetic drift his adjunct to natural selection for the case of man. His demonstration of the importance of drift in recent human evolution informed the model for constructing evolutionary trees from gene-frequency data. On this one long argument he wrote and lectured ceaselessly, not only for other scientists but also for a wider audience, always mindful of a responsibility to promote an understanding of man’s biology and evolutionary history for society’s benefit. In so doing he brought an

* awfe@cam.ac.uk

https://doi.org/10.1098/rsbm.2020.0015 3 Published by the Royal Society
informed and rational approach to the problem of human diversity and the problems of human diversity.

**FAMILY AND EDUCATION**

Luca Cavalli-Sforza died at the age of 96 at his home in Belluno, Italy, on the last day of August 2018. Born in Genoa on 25 January 1922 he was christened Luigi Renato Maria Cavalli, but his preferred name of Luca, a compound of Lu(igi) + Ca(valli), was used not only in the family but throughout his professional life. The omission of Renato Maria and the later addition of Sforza to his surname led finally to the form Luigi Luca Cavalli-Sforza, or L. L. Cavalli-Sforza in most of his books and papers (though L. Luca and Luigi L. also appear). Here we will refer to him when an adult as Cavalli, the customary usage in informal conversation among his academic acquaintances.

Cavalli’s father, Pio Cavalli, was from Peschiera del Garda, but of his father’s ancestry Cavalli could report little. Pio was an advertising agent who travelled extensively, working in Genoa and New York. When Luca was two and his father abroad, his mother, Attilia Manacorda, left Genoa. They lived in various places until settling in Turin when he was four (figure 1). She came from an old family in the Monferrato region of Piedmont, north-west Italy; her father’s brother, Luigi, was mayor of the principal town Casale Monferrato three times over 30 years, and many other Manacordas were notaries, bishops, humanists and mathematicians. Attilia herself was among the first women in Italy to graduate from the University of Turin, with a degree in the humanities. Luca was her only child.

Cavalli’s schooling was initially in the public schools of Turin and included Latin and classical Greek as well as French, English and German, but coming from an intellectually-stimulating family environment he rebelled against the limited scope of school learning under the Fascist regime then controlling Italy. With his family’s support he stopped attending school and, after studying the two-year syllabus in one year at home, took the final exam as a private student. He not only turned out to be the youngest to pass it, aged 16, but also to have the best marks in the whole city.

Compulsorily required to join the Fascist Youth while at school, this did at least provide opportunities for travel to foreign countries and exposure to other ideas. His mother sent him to the University of Exeter in England to improve his English, where, he once remarked, his teachers ‘very kindly took me aside and explained about democracy’.

Immediately after his schooling Cavalli entered the Faculty of Medicine at Turin with a scholarship, but transferred the following year to the University of Pavia, south of Milan, with a scholarship at Collegio Ghislieri, one of the university’s constituent colleges. In 1940 he and his college friend Giovanni Magni went to consult the professor of pathology, Emilio Veratti, about the possibility of measuring the virulence of bacteria by a statistical method. He told them that, as far as he knew, the only person who could help them was Professor Richard Prigge of Frankfurt. However, Veratti lent them a book, *The genetics of microorganisms*, which had been given him by Adriano Buzzati-Traverso—an assistant in zoology, at that time serving as an artillery officer in the Italian army in North Africa—who thought it might be useful for students. It contained papers from a symposium held in the United States just before the war.
In the holidays that year Cavalli and Magni stayed with the children of a friend of Cavalli’s mother at their villa near Como. Magni, himself from Como, had been taking some instruction in microbiology from the director of the Como Province microbiology laboratory. This time Cavalli joined him and every day they took the train into Como to learn about bacteriological laboratory practices. Wanting to study the virulence of bacteria, they reasoned that beyond the simple recording of the death-rate among the infected hosts, recording the times of death would provide extra information. The two students acquired some white mice and inoculated three of them with different concentrations of the *anthrax* bacillus. They found that the time of death was related to the concentration, and concluded that the bacteria were multiplying at a rate determined by this.
Cavalli meets Buzzati-Traverso

Buzzati-Traverso had studied genetics at Iowa State University at Ames in 1934, after two years at the University of Milan, and had brought back with him a number of American books on genetics and statistics besides *The genetics of microorganisms*. Ames had become the centre of the adoption of the modern approach to statistics in the United States, stemming from the work of R. A. Fisher (FRS) at Rothamsted Experimental Station, whose book, *Statistical methods for research workers*, had been published in 1925. By 1930 it was already on its third edition.

The university had the practice of inviting a distinguished scientist as visiting professor for six weeks each summer, and in 1931 George Snedecor, the future founder and director of the Iowa Statistical Laboratory, nominated Fisher. Fisher accepted and, using *Statistical methods* as his textbook, gave three lectures each week. He also gave another three each week on topics from his book *The genetical theory of natural selection*, which had appeared the previous year. Into this atmosphere of advanced statistics and population genetics stepped the young Buzzati-Traverso. Snedecor’s own influential textbook, *Statistical methods*, did not appear until 1937, but Buzzati’s collection of other American books would prove a goldmine for Cavalli, and Buzzati had presumably attended Snedecor’s lectures. Writing to Joshua Lederberg (ForMemRS) in 1986, Cavalli remarked that through Buzzati ‘I managed to have the first books on statistics, Snedecor, and Tippett, which I had longed for, but never had access to’.

Buzzati went to Berlin in 1938, where he had begun a five-year association with Nicolai Timoffief-Ressovsky learning and developing theories and methods of radiation genetics. Italy entered the Second World War in 1940 as an ally of Germany, and Buzzati, now in the army, was posted to North Africa. But he returned to Italy early in 1942 and resumed his work in the Institute of Zoology in Pavia, having been invalided out because of asthma attacks in the desert. He started giving a course in genetics for natural science students, which Cavalli decided to follow when he heard about it as a medical student. Cavalli had enrolled in the medical faculty when he had entered Turin University only because he had been ignorant of the possibility of studying natural science, but genetics was a subject much closer to his heart. One unforeseen beneficial consequence of having chosen medicine was that doctors in training were exempted from military service.

Bacterial genetics

Cavalli and Magni continued to study the virulence of bacteria, and in the summer of 1942 they acted on Emilio Veratti’s suggestion and visited Richard Prigge in Frankfurt. Buzzati fully supported this visit and also suggested a visit to Berlin at the same time, where he would be working with Timoffief-Ressovsky on radiation and population genetics. The two students obtained travel grants and in Frankfurt were able to continue their experiments on mice. Cavalli was overwhelmed by ‘the brilliant personality of Timoffief: “Intelligente, simpatico, ed entusiasta, molto russo”. He convinced me completely that genetics was the best choice I could make, and on my return to Pavia I became a regular “intern” in Adriano’s [Buzzati’s] lab’. There he began to work on the population genetics of *Drosophila*. His work with Magni in Frankfurt resulted in three joint papers in German in *Zentralblatt für Bakteriologie* for
1943 with the general title ‘Quantitative Untersuchungen über die Virulenz’ (1–3)*. These were summarized in English in a paper in Heredity in 1947 (4), which we shall shortly meet as an important element in Fisher’s initial knowledge of Cavalli. Meanwhile Cavalli continued his medical studies, graduating MD in 1944.

In the summer of 1943 Buzzati had invited Cavalli to his family home in Belluno to help with his study of the population genetics of Drosophila. There he met Buzzati’s niece Albamaria Ramazzotti (Alba). Buzzati moved his work with Cavalli from Pavia to the Istituto di idrobiologia in Pallanza, on Lago Maggiore, in the autumn of 1943 to avoid the Allied bombing of northern Italy; when he moved his family from Belluno to live there in early 1944, Cavalli met Alba again. She worked near Cavalli in the laboratory and they were soon engaged, but waited to marry until he had a steady job.

Being unwilling to pursue a medical career, for which he felt himself unsuited, Cavalli learnt that the pharmaceutical company Istituto Sieroterapico Milanese were looking for a young medically-qualified research worker for their immunology laboratory. He was appointed from 1 September 1945. His work there with the bacterium Escherichia coli involved statistical analyses, which increased his interest in the application of statistics to biological problems.

During 1946 C. D. Darlington FRS, at the John Innes Horticultural Institution at Merton, south London, and R. A. Fisher, by then Arthur Balfour Professor of Genetics at Cambridge, were planning a new journal, Heredity, to be published by Oliver and Boyd, publishers of Fisher’s statistical books. There must have been some communication between Buzzati-Traverso and them as editors because the first issue, dated 1 July 1947, contained a paper by Buzzati ‘A bibliography of genetic research published in Italy and Germany, 1939–1945’, marked as received ‘11.xii.46’ from Pallanza (Buzzati-Traverso 1947). Moreover, the journal also received from Pallanza, on ‘13.xii.46’, a paper by Cavalli-Sforza & Magni entitled ‘Methods of analysing the virulence of bacteria and viruses for genetical purposes’ (4). The paper was a summary of the work they had undertaken in Frankfurt and published in Germany in 1943. Whether or not Fisher was the communicating editor, it will have shown him the quality of the statistical thinking of its authors. As to the actual advance they had made during their German visit, they reported that, in addition to the customary measurement of virulence by the percentage survival of host individuals after experimental infection, they had recorded the individual times of death as well. They argued that

This variance and the form of the distribution of death times have both a biological and a genetical meaning. The measurement of individual death times permits the recovery of both extra statistical and extra genetical information. Statistically the precision of the experimental results may be doubled in this way.

Their investigations infecting white mice with Pneumococcus type 1 or Bacillus anthracis had revealed log-linear relationships between the time of death and the initial dose. Independently of the importance of this result, the analysis conveyed to the reader, and no doubt to Fisher, the quality of the statistical thinking of the authors. For Cavalli this was a critical factor in determining the next step in his career.

In July 1948, while he was in the army as a conscript, Cavalli obtained a scholarship from the Italian National Research Council to study the genetics of quantitative characters with

* Numbers in this form refer to the bibliography at the end of the text.
Kenneth Mather (FRS 1949) at the John Innes Horticultural Institution. He managed to get release from the army and to arrange paid leave from his employer. He worked on quantitative characters in *Drosophila* and learnt multivariate analysis. Mather was a friend and former colleague of R. A. Fisher; his book *Statistical analysis in biology* had been published in 1943 (Mather 1943).

**CAMBRIDGE**

In July 1948 Cavalli made the journey to Stockholm for the Eighth International Congress of Genetics, giving a paper on chemical and radiation mutagenesis in *E. coli* (5). The entire population of British geneticists seems to have been present—112 to be precise—including Fisher, Mather and another friend of Fisher’s, the blood-group scientist R. R. Race (FRS 1952), who had met Cavalli in Milan in 1946 when Cavalli introduced himself as a bacteriologist keenly interested in genetics who was studying Fisher’s statistical books. Race duly reported to Fisher how much Cavalli had impressed him.

At the Congress, Cavalli introduced himself to Fisher, ‘and after five minutes of conversation’, he later wrote, ‘he offered me a job at Cambridge in his department for setting up a laboratory to work on crossing-over in bacteria’ (36). Fisher had been among the first to appreciate immediately the significance of the discovery by Lederberg and Tatum in 1946 that certain strains of *E. coli* undergo conjugation, a true sexual process in which genetic recombination can occur. Many bacteriologists were sceptical. In Cambridge ‘Fisher was the only person who was sympathetic and supportive’ (figure 2); he suggested that a virus-like particle might determine sex in bacteria. He wanted to introduce bacterial genetics to his department because the principal studies being undertaken there involved the experimental estimation of linkage in the house mouse and the development of the associated mathematical and statistical theory. The prospect of using *E. coli*, with its comparatively rapid ‘generation’ time, to study linkage beckoned, and Fisher was interested in the theory of crossing-over. ‘He hoped bacteria would provide excellent data to test his theory’ (36). Cavalli accepted, and arrived in Cambridge in October 1948.

Given the trail of events that led to Fisher’s offer, the well-known story of the brevity of this encounter is not so surprising. The role of Buzzati-Traverso had been crucial: first from imbibing the modern Fisherian approach to statistics in Ames, Iowa, in 1934, resulting from Fisher’s Ames lectures in 1931, through to his interaction with Fisher as co-editor of *Heredity* and his presumed guidance in steering Cavalli and Magni towards publication of their English paper describing their war-time work in Germany. Then there were the encomiums of Mather and Race. It is not clear when Buzzati first met Fisher. He did not attend the 1948 Stockholm Congress, but all three—Buzzati, Fisher and Cavalli—were present at the September 1949 conference on Recent Contributions of Human Genetics to Medicine organized by Buzzati in Milan at the Istituto Sieroterpico Milanese.

Fisher offered Cavalli the appropriate university post of assistant director of research and Cavalli accepted on the spot, but Fisher, characteristically, had failed to clear this with the university authorities and had to find other sources of income (which were of a lesser amount) to support him. The following year Fisher asked the university for the junior post of assistant in research for him, and Cavalli was appointed from 1 October 1949 for three years, the very first university appointment Fisher was able to make in his department. In the same year,
after his father’s death, Cavalli, now aged 27, was officially adopted by his childless maternal step-grandfather, Count Francesco Sforza, Governor of the Bank of Italy for Northern Italy at the end of the war, and he adopted the surname Cavalli-Sforza.

Cavalli matriculated in Gonville and Caius College on 23 March 1949, no doubt at Fisher’s instigation. Thus began his life-long membership of the College, for which he retained great affection, reinforced by his election as an honorary fellow in 1982. Cavalli spent two academic years in Cambridge, 1948–1950, lecturing on ‘microbial genetics’ in the Lent terms of both years.

As soon as he had arrived in Cambridge Cavalli had written to Lederberg asking him to send appropriate strains of *E. coli* so that he could attempt to reproduce his and Tatum’s results, which he did successfully. Continuing his research on *E. coli* in 1949 he encountered a mutant strain with a high frequency of recombination ‘Hfr’ while selecting for mutations for resistance to nitrogen mustard (6). This important discovery greatly facilitated subsequent work.

In May 1950 Fisher applied to the university for the more senior post of assistant director of research for Cavalli, but this was not forthcoming. Cavalli then took unpaid leave to return to the Istituto Sieroterapico Milanese for 1950–1951. Finding the work and the conditions satisfactory, and with no prospect of advancement in Cambridge, he became director of research in bacteriology at the Istituto. Thus did Fisher’s attempt to foster bacterial genetics in Cambridge fail.

Sydney Brenner (FRS 1965), at the MRC Laboratory of Molecular Biology at Cambridge, wrote several times to Cavalli some years later, inviting him to join the laboratory, but it was too late. Cavalli realized that if he had been able to stay on in Cambridge, as Fisher had planned, he would have found the colleagues he needed.
In his ‘Recollections of Whittingehame Lodge’ (the name of the house occupied by the Department of Genetics in Cambridge) written for the Fisher centenary in 1990 (36), Cavalli remarked that the most rewarding of Fisher’s papers that he read was ‘The wave of advance of advantageous genes’ (Fisher 1937), which in years to come was to provide the mathematical basis of his work on the advance of agriculture in Europe. He also said ‘Much of my scientific future was forged in those two eventful years in which I worked at Whittingehame Lodge.’ (I can say the same of my three years with Cavalli in Pavia.)

Back in Italy, Cavalli continued his E. coli experiments. Cooperating at a distance with Joshua and Esther Lederberg in Madison, Wisconsin, they discovered and elucidated the complex F-system of sexuality in the bacterium, publishing their results in papers in 1952 (7) and 1953 (8). A year later Cavalli and John Jinks (FRS 1970), visiting Milan from the University of Birmingham, mapped the position of the F factor on the E. coli chromosome, which, when integrated into it, led to the Hfr strain (9), assuming the chromosome to be linear. (It was later discovered to be circular.) Cavalli felt that these collaborative efforts were his best contributions to bacterial genetics, a subject he was soon to leave in favour of forays into human genetics. Some of the results with E. coli, in particular the discovery of the transmissible agent or plasmid—the F factor—were obtained independently at the same time by William Hayes (FRS 1964) at the University of Manchester, whom Cavalli had met in England and to whom he had supplied some strains of the bacterium.

The Lederbergs finally met Cavalli when he was offered a Rockefeller Fellowship to visit them in Madison for three months in 1954. A Rockefeller Foundation ‘talent scout’, visiting Europe and knowledgeable about their joint work at a distance, proposed the visit. Cavalli’s friendship with the Lederbergs would last throughout their lives. In 1993 Cavalli published an account of his work in bacterial genetics in a ‘Perspectives’ in Genetics (39).

When the Orator of the University of Cambridge presented Cavalli to the Chancellor Prince Philip for his honorary doctorate of science in 1992, his peroration carried an apology (in Latin of course, which Cavalli will have appreciated):

Today we right an ancient wrong. For Fisher requested that his pupil should be promoted to the office of Assistant Director of Research. If that request had been granted, we might not have had to share him with so many other nations. But he does not hold it against us, for he is the most generous and warm-hearted of men. And, as he has taught us, we are all in truth one nation.

**Genetical demography**

The decade 1950–1960 saw a major change in Cavalli’s research interests. His duties at the Istituto Sieroterapico Milanese allowed him time to continue research in bacterial genetics, but his interest had begun to wane—partly because of the limited prospects in Italy for this type of work and partly because he was permitted to accept teaching invitations at two nearby universities, Pavia and Parma, in his favourite subjects of statistics and genetics as well as in microbiology. Pavia lies 35 kilometres south of Milan, and Parma 120 kilometres south-east. It was a time of building autostrade in Italy, and wits alleged that it was Cavalli’s influence that led to the first stretches being from Milan, where he lived, to the two cities; and of course Cavalli-Sforza was dubbed Professor Horse-Power (from ‘Cavalli-Sforza’, the Italian for horses and force).
Cavalli’s Pavia lectures in statistics started soon after his return from Cambridge in 1950, encouraged by Buzzati who by then had advanced to the professorial chair of genetics there. Those in Parma, in genetics and microbiology, began in the autumn of 1951 at the invitation of Bruno Schreiber, professor of zoology, who was keen to remedy the pre-war lack of interest in genetics among Italian zoologists. Cavalli’s lectures in Cambridge stood him in good stead. His Parma appointment was as professor with annual tenure, but in 1961 Schreiber succeeded in establishing a permanent professorship intended for Cavalli. However, internal politics meant it was held vacant for a year before he was appointed to it in 1962. He had left the Istituto Sieroterapico in 1957 for the uncertain annual employment at Parma, but no sooner had he secured his permanent professorship than he was offered and accepted the same tenured professorship in Pavia. A happy consequence was that his student friend Giovanni Magni succeeded him in Parma.

One of the best natural scientist students attending Cavalli’s Parma lectures was Don Antonio Moroni, a priest who became a dedicated ecologist. Moroni told Cavalli about the parochial church records of all births, marriages and deaths in the Parma valley since the Council of Trent in 1563. Moreover, all the dispensations for the marriage of near-relatives that church law required were deposited in the archives of the bishop’s palace. Parma was sufficiently far from the Istituto Sieroterapico in Milan to make an overnight stay for Cavalli worthwhile, leading to further discussion with Moroni as they realized what a wonderful resource this would be for studying the genetic architecture of the entire valley population over several centuries.

Soon Cavalli was spending his Parma evenings transcribing all the records of the little upper-valley village of Riana of about 150 souls and taking them home to Milan, where they covered the walls of his study. With these he could reconstruct the genealogy and deduce its various statistical features, such as the level of inbreeding. From this time on, Cavalli’s research interests diverted from bacterial genetics to human genetics, especially human population genetics, where his medical training, his genetical knowledge and his statistical skills could be so effectively deployed. He was quick to report on early results from the Parma valley project with a presentation at the First International Congress of Human Genetics in Copenhagen in 1956: ‘Some notes on the breeding pattern of human populations’ (10). Then in August 1958 he spoke at the Tenth International Congress of Genetics in Montreal on ‘Some data on the genetic structure of human populations’ (11). Cavalli’s open and generous character and his love of travel, coupled with his mastery of European languages, made him many international friends at such congresses and brought his work to the notice of his contemporaries and the funding agencies.

By 1958 Cavalli was directing a research programme in Pavia entitled ‘Mutation rates and mutational loads in man’ supported by the Italian National Council for Nuclear Research, with additional contributions from the Rockefeller Foundation, the US National Science Foundation and the US Atomic Energy Commission. He had quickly come to appreciate that demographic data such as his from the Parma valley could be a rich source of information about mutation rates and the relative importance of selective forces and drift. The granting agencies must have been impressed.

With his appointment as professor of genetics in the University of Pavia in 1962, Cavalli became director of the Istituto di Genetica, but also of the Pavia Section of the Laboratorio Internazionale di Genetica e Biofisica (LIGB), an initiative of Buzzati-Traverso supported by the Italian National Research Council, which was founded on 1 March 1962 with its main base
in Naples. Buzzati had hoped to persuade Cavalli to move there, but failed. Many staff with their equipment did however move from Pavia to Naples, and Cavalli’s task was to revive the depleted Pavia department with the support of the National Research Council. The LIGB Section became the focus of Cavalli’s initiatives in human population genetics, supported by the granting agencies already mentioned.

Thus was born the subject of ‘genetical demography’. By 1960 there was sufficient interest for the World Health Organization to hold an International Symposium of Demography and Genetics in Geneva, at which Cavalli ‘emphasize[d] the need to develop collaboration between demography and genetics to the mutual advantage of both disciplines’ (12).

**EVOLUTIONARY TREES AND GENETIC DRIFT**

With support for his work in human genetics secured, early in 1961 Cavalli visited his old Cambridge department with an offer to me of a position in Pavia to undertake the computer analysis of material emerging from the Parma valley project and other similar investigations. I had been the only undergraduate taken on by Fisher in his retirement year as professor of genetics (1956–1957). After a three-year PhD in the department, I had continued one more year as a ‘post-doc’ until Cavalli’s offer, which I accepted. The offer came as a surprise, like Fisher’s to Cavalli in 1948. Fisher will have been the principal intermediary, but others involved were probably R. R. Race and Kenneth Mather, in whose laboratories I had spent short spells as a student, and Marco Fraccaro, a geneticist from Pavia then at the Swedish State Institute of Human Genetics with whom I had worked during a visit to Uppsala.

One of the attractions of Pavia was the establishment of a computer centre dedicated to Cavalli’s research programme, and the impending delivery of an Olivetti Elea 6001 computer. Late in delivery, it was not installed and working until six months after my arrival, during which time Cavalli invited me to contemplate a project he had conceived while he was in Fisher’s department in Cambridge. As he later described it (38):

> More than 40 years ago, when I was studying bacterial genetics in the laboratory of Sir Ronald A. Fisher of the University of Cambridge, the place was saturated with mathematical theorizing. Thus, it is not surprising that I started thinking about a project so ambitious it seemed almost crazy: the reconstruction of where human populations originated and the paths by which they spread throughout the world. I reasoned that the task could be accomplished by measuring how closely living populations are related to one another and by deducing from this information a comprehensive family tree.

Cavalli’s scheme, as told to me, was straightforward. Using as data the gene frequencies of several blood-group systems for a number of distinct populations, compute a measure of ‘genetic distance’ between each pair of populations. Then choose a reasonable form of ‘evolutionary tree’ uniting the populations and consider the lengths of the segments of the branches. Then estimate these lengths by the method of least squares, comparing each interpopulation genetic distance with the sum of the corresponding segment lengths on the tree. Repeat for other tree forms and find the form for which the overall sum of squares is a minimum. This came to be known as the ‘additive tree’ method.

The Olivetti computer was not provided with a high-level language (FORTRAN II) until 1963, after which progress was rapid. The implementation of Cavalli’s method was reported at the Eleventh International Congress of Genetics in September 1963 (15), where my
algorithmic alternative ‘Method of minimum evolution’ minimizing the total length of the tree was also mentioned, later to be called ‘Parsimony’. The joint paper presented a computed tree for 15 populations based on blood-group gene frequencies using data chosen by Arthur Mourant (FRS 1966), director of the MRC Blood Group Reference Laboratory in London (figure 3). It also pioneered the use of the statistical technique of principal-component analysis in human population genetics, to be much used by Cavalli in his later work for displaying geographical genetic variation.

During the autumn of 1963 the Japanese geneticist Motoo Kimura (ForMemRS 1993) visited Pavia, lectured on mathematical and population genetics and participated in seminars (figure 4). In this atmosphere Cavalli and I quickly came to appreciate that a proper stochastic model for gene-frequency change would enable us to replace our heuristic methods by the method of maximum likelihood in order to estimate the tree. We first proposed this at a meeting
of the Systematics Association early in 1964 (16). It was to become the foundation for the development of the field.

In retrospect, Cavalli’s choice of blood-group gene frequencies to characterize populations was brilliant because geneticists had no clear idea of why these polymorphisms continued to exist, so that it was reasonable to postulate that the variability among the populations was largely a reflection of the phenomenon of drift. Not only did this mean that the project matched the on-going study of drift in the Parma valley, but it justified the stochastic model adopted by Cavalli and me. W. C. Boyd, in his book *Genetics and the races of man* (Boyd 1952), and A. E. Mourant in his *The distribution of the human blood groups* (Mourant 1954), had pioneered the use of blood-group gene frequencies in exploring racial differences, but the new methodology introduced a stochastic model that enabled statistical estimation theory to be applied and evidence from the different blood groups to be combined. Moreover it was a radical departure from the historical anthropological position that inherited characteristics such as skin colour were of importance in population classification, notwithstanding the fact that differentiation was there the result of natural selection.

Meanwhile the analysis of data collected in the Parma valley proceeded apace. Blood samples were taken from villages ranging from the plain to the mountains, and genetic variability computed. The evidence was clear that the variability was higher among the mountain villages and descended towards the plain, as would be expected since the sizes of the villages increased correspondingly. This correlated well with the early results on average consanguinity in the villages. The evidence for the phenomenon of genetic drift as the explanation for the patterns of genetic variation in the Parma valley was substantial, and
the significance of drift in the interpretation of human population genetic variation became an important part of Cavalli’s thinking and a central motif of his writing. The morphological diversity used by anthropologists to deduce population relationships, notably skin colour and body and skeletal form, especially of the skull, was likely to be caused by natural selection responding to different environments, but variation in gene frequencies at polymorphic loci was likely to reflect the existence of drift. From this variation, evolutionary trees could be reconstructed from remarkably small samples of population data. Cavalli liked to think that Kimura’s neutral theory of molecular evolution of 1968 might have had its beginnings in Kimura’s stay in Pavia five years earlier.

In 1963 Cavalli and his colleague Gianna Zei used the Olivetti Elea computer to simulate a population of 5000 individuals spread over 22 villages with demographic characteristics corresponding to those of the upper Parma valley (19). Genotypes for the ABO, Rh and MN blood groups were recorded. Reasonable agreement between the simulated results and the demographic findings was obtained. Debate over the relative importance of drift and natural selection in animals and plants has long been a feature of population genetics, but, taking advantage of the special features presented by a human population of recorded genealogy and known genotypes, Cavalli and his colleagues were able to pinpoint the importance of drift in human evolution.

Following what was to become his usual practice, Cavalli presented much of the work in genetical demography and evolutionary trees at meetings and congresses, including the First International Congress of Human Genetics (Copenhagen, 1956; (10)), the Tenth International Congress of Genetics (Toronto, 1958; (11)), WHO (Geneva, 1960; (12)), Monaco (1962; (13)), the Eleventh International Congress of Genetics (The Hague, 1963; (15)), Systematics Association (Liverpool, 1964; (16)), the Cold Spring Harbor Symposium (1964; (14)), the International Statistical Institute (Belgrade, 1965; (17)), the Royal Society (London, 1966; (18)), the Third International Congress of Human Genetics (Chicago, 1966; (19)), the Twelfth International Congress of Genetics (Tokyo, 1968; (21)), Salt Lake City (1969; (20)), and Mamaia, Romania (1970; (24)). However, the comprehensive account of the work by Cavalli, Moroni and Zei on the population structure of the upper Parma valley did not appear until 2004 in their book Consanguinity, inbreeding, and genetic drift in Italy (44).

**Laboratorio Internazionale di Genetica e Biofisica**

In 1964 LIGB went through a severe crisis as an indirect consequence of the director and the former director of the Higher Health Institute (ISS) in Rome and the president of the National Committee for Nuclear Energy (CNEN) being imprisoned for embezzlement. Scared by these events, the president of the National Research Council (CNR) decided to limit Buzzati-Traverso’s freedom of action, and in so doing reduced the high salaries at LIGB. Buzzati resigned and Cavalli was asked to replace him. Declining repeated requests, he agreed to stand in for a limited period while preparing a report proposing a compromise to the controversy. For seven months he oscillated between Pavia and Naples and negotiated a settlement that enabled Buzzati to return. But in 1968 an even more debilitating crisis hit LIGB, associated with the student revolution that had spread from Berkeley in California to Paris and the rest of Europe: the technicians and some of the research workers took over the running of the laboratory. After a year of this, the resistance by Buzzati finally collapsed and he left. Slowly, under a
new director, the laboratory did recover, but it never realized its early promise (Capocci & Corbellini 2002).

The time Cavalli spent on the problem of LIGB in 1964 meant it was impossible for him to pursue a research project to record the genealogy of the entire population of Iceland on computers in order to study its genetic architecture. However, he later admitted that, given the then stage of computer development, the project was premature. Meanwhile he asked John Edwards (FRS 1979) (my brother) to advise the Icelandic geneticists on such a project.

From 1966 to 1971 Cavalli mounted expeditions to study the structure and genetics of several hunter–gatherer Pygmy populations as exemplars of human evolution before the advent of farming. Further visits were made in 1975, 1976, 1978 and 1980. The detailed results of the investigations were published in 1986 in a book African Pygmies with 34 contributors (34). Edited by Cavalli, he also wrote the 166-page last chapter, ‘African Pygmies: an evaluation of the state of research’. His studies of the Pygmies led him to the hypothesis that the spread of agriculture was not merely a phenomenon of cultural evolution but of migration as the population density grew with the increase in the food supply. He explained this in his paper at the Fourth International Congress of Human Genetics (Paris, 1971; (25)), and was to return to it frequently.

**STANFORD UNIVERSITY**

Lederberg moved from Madison to Stanford in 1959 to set up the Department of Genetics in the Medical School. In the summers of 1960 and 1962 he invited Cavalli to give courses on population genetics. In the latter year Walter Bodmer (FRS 1974) joined him in giving the lectures. Bodmer had arrived in the Stanford department in 1961 from a junior post in Cambridge’s Department of Genetics following his PhD. Like me, he had started in that department in October 1956 in Fisher’s final year as professor of genetics, but was academically one year ahead of me. These joint lectures at Stanford were the origin of Cavalli & Bodmer’s book, The genetics of human populations (26). Cavalli arranged to take the academic year 1968–1969 at Stanford, the principal task being to complete with Bodmer the writing of the 965-page book, eventually published in 1971 (and dedicated ‘to the memory of R. A. Fisher’).

After the 1962 course, Lederberg had offered Cavalli a permanent professorship in his department, which remained open after Cavalli did not accept it immediately. The 1968–1969 sabbatical year at Stanford finally gave Cavalli the experience that persuaded him to leave behind the bureaucratic problems of science in Italy, and in particular those with LIGB, for the opportunities that Stanford afforded. These problems had had a direct impact in Pavia, since the department was partly supported as a Section of LIGB. By 1968 the four Cavalli children had grown up; Matteo was already at Stanford working at the Stanford Linear Accelerator Center, Francesco was a student at nearby Berkeley by the spring of 1969, while Tommaso and Violetta accompanied their parents and completed their schooling in America. Cavalli and Alba moved to California in 1971 and henceforth Cavalli’s career was centred on Stanford, continuing after becoming emeritus in 1992 until he left to go back to Italy in 2008.

The early Stanford years saw the publication of papers derived from the Pavia studies, but also the introduction of the new topics of cultural inheritance (with Marcus Feldman) and the spread of agriculture (with Albert Ammerman). Collaboration with Bodmer continued with
the writing of another large book (782 pages) *Genetics, evolution and man* (30), more of a text for students than its predecessor, published in 1976. At this time Cavalli also began to publish general papers about human population genetics for wider audiences, as for example his ‘Analytic review: Some current problems of human population genetics’ in *The American Journal of Human Genetics* in 1973 (28) and ‘The genetics of human populations’ in *Scientific American* in 1974 (29). The latter was given a subtitle, ‘The differences between populations are less than those within populations’, which was an influential over-simplification of the multivariate genetical data.

In 1972 Marcus Feldman, an Australian mathematician and population geneticist, was appointed to an assistant professorship at Stanford after completing his PhD. He and Cavalli found a common interest in the parallels between biological evolution and cultural evolution and started to explore the extent to which the similarities could be studied mathematically by borrowing from theoretical population genetics. Cavalli’s initial interest, as recalled in his paper ‘Similarities and dissimilarities of sociocultural and biological evolution’ at the 1970 Mamaia conference mentioned above (24), stemmed from Mather’s (1964) book *Human diversity*, itself based on his 1960 Ballard–Matthews lectures. A series of joint papers by Cavalli and Feldman in the 1970s culminated in their 1981 book *Cultural transmission and evolution: a quantitative approach* (31). Anthropologists found its mathematical basis difficult to handle. Cavalli remarked that economists found it interesting, having no fear of mathematics, but that it was the anthropologists who should have found it useful. Nevertheless, it came to be seen as one of the founding texts of the subject.

**Race**

In 1969, just before Bodmer left Stanford the following year to become professor of genetics at Oxford, a controversy broke out about a paper by Arthur Jensen, which maintained that the difference in mean IQ between white and black people in the United States was largely genetic in origin. William Shockley, a Nobel-Laureate physicist at Stanford, was promoting Jensen’s views, and Lederberg and other members of the Department of Genetics, including Bodmer, signed a letter criticizing them. This led to a meeting with Shockley, who brought along Jensen. Bodmer then joined with Cavalli, by now back in Italy, in writing an influential article, ‘Intelligence and race’, for *Scientific American* in 1970 (22), in which they carefully examined the basis of the claims that had been made and concluded that

> We do not by any means exclude the possibility that there could be a genetic component in the mean difference in IQ between races. We simply maintain that currently available data are inadequate to resolve this question in either direction.

They took the view that ‘there are many more useful biological problems for the scientist to attack’ and in any case ‘Innate differences in ability . . . must be judged on the basis of the individual and not on the basis of race’.

Cavalli maintained these and similar sentiments throughout his many writings, establishing him as a calming influence in a sometimes torrid debate. His and Bodmer’s views expressed in the paper were just in time to be included in *The genetics of human populations* in 1971 (26), and were reinforced in *Genetics, evolution and man* in 1976 (30). A later perspective is in the book by Cavalli and his son Francesco, *Chi siamo* (‘Who we are’), published in Italian
in 1993 (40) and in English as *The great human diasporas* in 1995 (42). The English edition contains a ‘Postscript’ by Cavalli devoted to the controversy and giving his perspective of it from the age of 73.

### Archaeology and the Spread of Farming

Passing reference has already been made to a conference in Mamaia, Romania, in 1970. Entitled ‘Mathematics in the archaeological and historical sciences’, it was organized by the Royal Society and the Academy of Romania. As well as the subjects of its title, genetics was well-represented, particularly by Cavalli and members of his Pavia group.

Also present was an American, Albert Ammerman, who spoke on ‘A computer analysis of epipalaeolithic assemblages [of flint tools] in Italy’ using multi-dimensional scaling (Ammerman 1970). Ammerman had been studying for a PhD at the Institute of Archaeology using the University of London’s Atlas Computer. Cavalli invited Ammerman to Pavia. Cavalli’s genetical knowledge and Ammerman’s archaeological knowledge complemented each other nicely. In 1971 they published a computer-generated map (23) showing the spread of early farming in Europe in the form of a wave-front advancing from the south-east towards the British Isles, with the dates of its passage. From the low rate observed, about one kilometre a year, they then argued that it was likely that this spread of farming was a result of an advancing population wave caused by the increased growth associated with the new agriculture—‘demic diffusion’—rather than cultural diffusion, as had often been supposed. In 1973 (27) they introduced Fisher’s ‘wave of advance’ mathematical theory, which Cavalli had read about in his Cambridge days (36). Their conclusions were summarized in *The Neolithic transition and the genetics of populations in Europe* (33) and by Cavalli in *Genes, peoples and languages* in 2000 (43), in which he reported that the demic theory was becoming accepted by archaeologists.

### The History and Geography of Human Genes

In 1977 Cavalli started a project at Stanford in collaboration with Paolo Menozzi, of the University of Parma, and Alberto Piazza, of the University of Turin, to construct a genetic European map from blood-group, enzyme and HLA gene-frequency data parallel to the one for the spread of farming. Using the combined data from modern populations they plotted the first principal component and noted the close correspondence of the two maps. But they also prepared similar maps using the second and higher principal components from the same data. The interpretation of higher components naturally becomes more and more uncertain, but known relatively-isolated populations such as the Basques and the Lapps stood out. This is to be expected in a principal-component analysis because each component reflects a linear trend and leaves local variation to be revealed in higher-order components.

Over the next eight years the team of Cavalli, Menozzi and Piazza (figure 5) extended their work to cover the whole world, marshalling the data by 1986 and finally publishing their analysis in the magisterial volume *The history and geography of human genes* in 1994 (41). It replaced and greatly extended the 1976 comparable volume *The distribution of the human blood groups and other polymorphisms* by Mourant, Kopeć and Domaniewska-Sobczak (Mourant *et al*. 1976), while incorporating some of its data. A paperback edition
without the tables was published in 1996. In the 1980s the ‘out of Africa’ hypothesis of the root of the evolutionary tree of humans had been promoted by archaeological and palaeontological discoveries, and *The history and geography of human genes* displayed results that were compatible with this hypothesis.

Further evidence came from linguistics, the prime example of cultural transmission, as emphasized by Cavalli and Feldman in their book *Cultural transmission and evolution* (31). Cavalli attributed his love of languages to a combination of his mother’s cultural influence and his father’s genes for ease of understanding them, a nice compliment to his parental inheritance both cultural and genetic. In Stanford he had the benefit of knowing the linguist Joseph Greenberg and his pupil Merritt Ruhlen. Ruhlen was working on a new classification of world languages and allowed Cavalli access to it. In 1988 *The history and geography of human genes* was still six years from publication and Cavalli, along with Piazza and Menozzi, were anxious to publish a preliminary account of the ‘Reconstruction of human evolution: bringing together genetic, archaeological and linguistic data’; fortunately, Lederberg had recently and successfully proposed Cavalli for membership of the National Academy of Sciences, and so he communicated this paper (35). A fourth author was Joanna Mountain, who helped to carry out the general analysis and in particular the matching of the linguistic ‘tree’ to the genetical one. The paper was not without its critics in linguistics and palaeontology, some of whom disputed the statistical significance of the match. In a rare acid remark (46), Cavalli wrote that he had never had ‘occasion to discover’ whether that group had admitted their mistake.

In *The history and geography of human genes*, Cavalli and his co-authors comprehensively surveyed the field that Cavalli had made his own. He had brought together demographic genetics, mathematical population genetics, archaeology, linguistics, anthropology, the latest statistical methods and the use of the novel electronic computers. He became expert in each of these fields. The book, with its extensive tables, was an exhaustive account of what had been learnt about human evolution by the early 1990s. It formed a firm basis for the information to come from the imminent DNA revolution involving single nucleotide polymorphisms,
mitochondrial DNA and the Y-chromosome, which, it may be said, confirmed and filled out the picture.

DNA

The revolution in the 1980s that led to the sequencing of DNA opened up possibilities for the study of human phylogeny that Cavalli was quick to embrace. Already it was known that mitochondrial DNA (mtDNA) was maternally inherited, and it followed that by itself the variability of its sequences would be a source of phylogenetic information enabling the construction of a female-based evolutionary tree. Cavalli’s laboratory began to study population differences in mtDNA. He already had blood stored from his Pygmy expeditions and was fortunate to be able to extend a conference visit to South Africa to obtain samples from the Bushmen of Botswana as well. The result was a 1983 paper, with Cavalli as the last of the five authors (32), in which an evolutionary tree was depicted for five groups, complete with genetic distances assuming a constant rate of evolution. Oriental, American Indian and Caucasian were closely grouped while Bantu separated earlier and Bushmen much earlier still at a point indicating the root of the tree. (It seems that, in the event, the Pygmies were not included.) The figure also showed where the root would have been estimated to be on the basis of the three ‘central’ mtDNA types. Twenty years earlier, Cavalli and I had rooted our tree arbitrarily at a similar central point, but here was a tree that suggested an African origin. Cavalli later remarked that he did not like to publish the suggestion on such modest data: ‘I don’t regret being prudent: I have always preferred to be prudent rather than to have to eat my words [rimangiare le conclusioni]’ (46). In any case, he thought it was Masatoshi Nei who had first speculated that it might be the case, based on the best pre-DNA evolutionary trees. (But we should not forget Darwin in The descent of man (Darwin 1871, p. 199): ‘it is somewhat more probable that our early progenitors lived on the African continent than elsewhere’.)

It was a time when archaeological and palaeontological investigations in East Africa were beginning to point to an African origin, but the breakthrough really came from the laboratory of Allan Wilson (FRS 1985) in Berkeley, who, with Rebecca Cann, was studying mtDNA using a more efficient technique and larger samples—unknown to Cavalli and his group just 50 miles away across San Francisco Bay. But what is sauce for the goose is sauce for the gander, and the Y-chromosome, if DNA polymorphisms on it could be found, would enable male-based evolutionary trees to be computed and compared with the female-based trees from mtDNA.

Before turning to the Y-chromosome, however, Cavalli’s laboratory worked with autosomal microsatellite and single nucleotide polymorphisms (SNPs), initially studying 100 SNPs from populations in Europe, China, Melanesia and Africa (Pygmies). This time (1991) Cavalli was the last of seven authors (37). The results matched existing trees well except for a suggestion that the European population might have included a late contribution from Asian and African admixture. The opportunity was taken of pursuing Cavalli’s particular interest of genetic drift. Computer simulation enabled the extent to which the DNA variability could be explained by drift, and it was concluded that at least two-thirds of the polymorphisms seemed to be selectively neutral. Later work based on microsatellites showed how it was possible to construct phylogenetic trees right down to the level of individuals, foreshadowing how it would become possible to trace evolutionary paths through the movement of specific markers.
The use of the Y-chromosome required the discovery of polymorphic loci on its non-recombining part. By the early 1990s only one such polymorphism was known, so the challenge Cavalli set his laboratory was to find more. The search started in 1994, using the slow sequencing machines then available. Peter Underhill, who had joined the laboratory in 1991, was responsible, assisted by Joan Herbert as technician. It took a year of repetitive work before Herbert found the first mutation.

A fortunate meeting between Underhill and Peter Oefner, an Austrian working at Stanford on ways to improve DNA sequencing, resulted in 1995 in the development of a vastly-improved technique for discovering Y-chromosome variants differing in single bases. Soon there was an abundance of data, including discoveries made in other laboratories. Cavalli’s group, with an ever-changing membership, published a sequence of papers in the next 10 years that refined the conclusions from the microsatellite and mtDNA data, in particular improving the dating of migrations across the globe. Differences between the spread of mtDNA variants and Y variants reflected different migration patterns of men and women. Soon the advent of whole-genome analysis would open up a new level of detail in the story of human evolution, and the ability to sequence DNA from ancient material would add a new perspective.

**Human Genome Diversity Project**

In 1991 Bodmer, by now director of the Imperial Cancer Research Fund in London, was the second president of the Human Genome Organisation (HUGO), having succeeded Victor McKusick. That organization had been set up to foster cooperation among geneticists involved in the project to sequence the human genome. Bodmer had been one of the initiators of HUGO in 1988, and in 1991 he invited Cavalli to chair a committee on genome diversity, leading to what came to be called the Human Genome Diversity Project (HGDP). The first meeting was held at Stanford involving mainly population geneticists. Subsequent meetings were held in Sardinia, Pittsburgh, and finally at the National Institutes of Health in Bethesda, Maryland.

Discussion revolved around the primary task of surveying the human genome worldwide, with special reference to aboriginal populations as a source of information about human evolutionary history. But it soon became apparent that this was one of those types of scientific investigation that could be challenged on the grounds that it might lead to information that ought not to be sought, and which might be used for commercial gain. It could also lead to conclusions that were alien to the beliefs of certain population groups such as the Native Americans. Such considerations had hitherto been alien to science, though occasionally voiced retrospectively, as in the case of atomic physics. In the case of recording human genetic diversity, objections were raised that it might differentiate populations in unfortunate ways, even though there might be some positive medical advantages for those with higher frequencies of particular inherited diseases. Critics feared ‘racist’ consequences and wanted to know what was meant by a ‘race’; they doubted the ethics of taking blood from aboriginal populations and worried about how to achieve consent; but mostly their hostility was based on the rising cultural phenomenon of ‘identity politics’ and ignorance or even denial of the existing knowledge of human genetic variability.

Cavalli bore the brunt of the attack and in his customary courteous, sympathetic and informed way worked tirelessly in meetings, by discussion with native groups and in his writings, to counter it. But he was not by nature a politician. His successful interactions with
fellow scientists were founded on a life-long passion for science and scientific objectivity, mutual respect and his deep humanity. Confronting people with fixed views and political agendas was not easy for him. In their authorized biography of Cavalli, *A genetic and cultural odyssey: the life and work of L. Luca Cavalli-Sforza* (Stone & Lurquin 2005), Linda Stone, anthropologist, and Paul Lurquin, geneticist, included a chapter on the HGDP, which Cavalli read in draft and said it was the most difficult one for him. They wrote: ‘We consider this is because the HGDP became such a difficult chapter in his life.’ For a discussion of the controversies surrounding the HGDP, see Reardon (2005).

In 2005 *Nature Reviews, Genetics* published a ‘Perspectives’ article by Cavalli (45), who was by then 83, describing the origin of the Project, the mounting criticism of it that had had to be countered, the means by which this was achieved and, finally, the establishment of the collection of cell lines at Centre d’Etude du Polymorphisme Humain (CEPH) in Paris and their subsequent distribution. In addition, the paper contained much information about the earlier work in which Cavalli had been the leading figure for so many years.

**Books**

Central to Cavalli’s scientific activity was his sense of obligation to make its results known not only through conferences and journals but also in books addressed to a wider public. He was the author or one of the co-authors of almost 600 scientific papers and around 20 books (some as editor). Not all the books related to his scientific work, but those that did were an integral part of it. It is worthwhile considering them in sequence.

The first, in 1971, was the magnificent volume with Bodmer *The genetics of human populations* (26). It not only encompassed all that was then known of human genetics, but continued with human population genetics and evolution, including the latest advances made by the authors themselves. Questions of eugenics and race were not avoided. Three statistical appendices covered in 100 pages the whole of statistics as applied to human genetics, a textbook in itself. A paperback edition was issued in 1977 and the accolade of a Dover Books reprint in 1999. A subsequent book, *Genetics, evolution and man* (30), with Bodmer as the senior author, was a little shorter and intended more for a student readership. Appearing in 1976, it included recent research on the construction of evolutionary trees from the amino-acid sequences of proteins as well as on the evolution of modern man, incorporating archaeological information and the map showing the ‘wave of advance’ of early farming in Europe.

In 1981 *Cultural transmission and evolution: a quantitative approach* came out (31), jointly authored with Feldman and the first of Cavalli’s books to summarize a research field, as already mentioned. Similar in its purpose was Ammerman & Cavalli’s 1984 *The Neolithic transition and the genetics of populations in Europe* (33). Then in 1986 came *African Pygmies* edited by Cavalli (34), with the Introduction and seven of the chapters by him or jointly with him, including the long final chapter ‘An evaluation of the state of research’.

Next, in 1993, was the first of the books aimed at a wider audience (albeit initially an Italian one): *Chi siamo: la storia della diversità umana* (40) with Francesco Cavalli-Sforza (‘Who we are: the history of human diversity’). Francesco, the Cavallis’ second son (born during their time in Cambridge), graduated in philosophy and is a writer and film and television producer in educational fields, particularly for the younger generation. *Chi siamo* was published in English translation in 1995 as *The great human diasporas* (42). The Italian title is reflected in
David Reich’s *Who we are and how we got here* (Reich 2018), a recent update of the field, which opens with ‘This book is inspired by a visionary, Luca Cavalli-Sforza, the founder of genetic studies of our past. I was trained by one of his students, and so it is that I am part of his school, inspired by his vision of the genome as a prism for understanding the history of our species’. *The great human diasporas* is a mixture of the history of humans as revealed by the latest research, including linguistics, combined with reflections on cultural inheritance, race and racism, and eugenics.

Reich (2018) continued: ‘The high-water mark of Cavalli-Sforza’s career came in 1994 when he published *The History and Geography of Human Genes* ([41]), which synthesized what was then known from archaeology, linguistics, history, and genetics to tell a grand story about how the world’s peoples got to be the way they are today.’

In 1996 Cavalli published *Gènes, peuples et langues*, originating from lectures given at the Collège de France. An Italian edition followed, and in 2000 an English one ‘Genes, peoples and languages’ (43). In half as many words as *The great human diasporas*, it covers much the same ground in a lighter style, written in the first person. Finally, in 2004, came the last of his scientific books (44), already mentioned.

Then in 2005, aged 83, Cavalli published his scientific autobiography, *Perché la scienza: l’avventura di un ricercatore* (‘The why of science: the adventure of a research scientist’; (46)), jointly with Francesco, who also wrote the long introduction. It is a wonderful account of Cavalli’s scientific journey, with many personal memories and ending with three philosophical problems drawing on his long experience: Why do science? The fear of science and other fears. To become a scientist? The book was a major source of information for this memoir.

This does not complete the list of Cavalli’s books. Others, mostly in Italian and often with Francesco, deal with themes always related to the culture and evolution of man. In 2009 the 12-volume encyclopaedia *La cultura italiana* appeared, which he edited.

From 1992 Alba and Luca had begun to spend half each year in Italy, and in 2008 they moved back permanently: to their Milan flat for the winter and the house in Belluno in the summer. Alba died in 2015, after which Cavalli remained in Belluno until his death in August 2018. They are survived by their four children Matteo, Francesco, Tomasso and Violetta. Alba’s uncle, Adriano Buzzati-Traverso, had died in 1983.

**AWARDS, HONOURS AND APPOINTMENTS**

_Awards_

Honorary degrees of Italian universities: Parma, Torino, Bologna, Viterbo, Roma, Sassari, Cagliari, Calabria, Palermo
Honorary degrees of other universities: Columbia University NY, University of Cambridge, University of Marseille
1982 Honorary Fellow of Gonville and Caius College, Cambridge

_Honours_

1978 Weldon Medal in Biometry, University of Oxford
1987 Allen Award, American Society of Human Genetics
1990 Gold Medal of the Italian National Research Council
1994 Fondation Fyssen International Award, France
Biographical Memoirs

1999  Balzan Prize for the Science of Human Origins, Italy
2011  Gold Medal of the Telesio Galilei Academy

Appointments

1967  President of the Biometric Society
1968  Vice-President of the Twelfth International Congress of Genetics, Tokyo
1972  Huxley Lecture, Royal Anthropological Institute of Great Britain and Ireland
1974  R. A. Fisher Memorial Lecture, London
1978  Foreign Associate of the National Academy of Sciences, Washington
1989  President of the American Society of Human Genetics
1991  Member of the Accademia dei Lincei, Rome
1992  Foreign Member of the Royal Society of London
1992  Member of the Académie des Sciences, Paris
1994  Member of the Pontifical Academy of Sciences
2000  Cavaliere di Gran Croce Ordine al Merito della Repubblica Italiana
2002  Mendel Lecturer, Genetics Society, London

ACKNOWLEDGEMENTS

Of the many to whom I have been indebted during the drafting of this memoir, particular thanks are due to Francesco Cavalli-Sforza for his help throughout. Francesco is Cavalli’s second son, and co-author with his father of several books, including the invaluable source of information for this memoir, *Perché la scienza: l’avventura di un recercatore* (46) [The why of science: the adventure of a research scientist].

The portrait photograph was taken in 1993 by A. C. Cooper and is © The Royal Society. Unless otherwise credited, other photographs were kindly provided by the Cavalli-Sforza family.

AUTHOR PROFILE

Anthony Edwards

Anthony Edwards is Emeritus Professor of Biometry, University of Cambridge. In 1956 he was the only undergraduate to ask to take Genetics in R. A. Fisher’s retirement year as Arthur Balfour Professor of Genetics. In 1961 he accepted Luca Cavalli-Sforza’s invitation to join his group in the University of Pavia, whence sprang his involvement in Cavalli’s idea of estimating evolutionary trees from blood-group gene-frequency data. After three years, and a year at Stanford with Walter Bodmer in Joshua Lederberg’s department, he was senior lecturer in statistics in Aberdeen with David Finney before returning to Cambridge as a Bye-Fellow of Gonville and Caius College and subsequent appointments to university posts. His work has spanned statistical inference and population genetics, leading to the books *Likelihood* (1972) and *Foundations of mathematical genetics* (1977). Among his other books are two in the history of mathematics, *Pascal’s arithmetical triangle* (1987) and *Cogwheels of the mind: the story of Venn diagrams* (2004). *Phylogenetic inference, selection theory and history of science* (Winther 2018) includes eight of his papers jointly with Cavalli-Sforza, to whom the book is dedicated: ‘Pioneer of phylogenetic inference’.

REFERENCES TO OTHER AUTHORS

Ammerman, A. J. 1970 A computer analysis of epipalaeolithic assemblages in Italy. In *Mathematics in the archaeological and historical sciences* (ed. F. R. Hodson, D. G. Kendall & P. Tăutu), pp. 133–137. Edinburgh, UK: Edinburgh University Press.
Boyd, W. C. 1952 *Genetics and the races of man: an introduction to modern physical anthropology*. London, UK: Little, Brown & Co.

Buzzati-Traverso, A. 1947 A bibliography of genetic research published in Italy and Germany, 1939–1945. *Heredity* 1, 19–52. (doi:10.1038/hdy.1947.2)

Capocci M. & Corbellini G. 2002 Adriano Buzzati-Traverso and the foundation of the International Laboratory of Genetics and Biophysics in Naples (1962–1969). *Stud. Hist. Philos. Sci. C: Biol. Biomed. Sci.* 33, 489–513. (doi:10.1016/S1369-8486(02)00007-9)

Darwin, C. 1871 *The descent of man, and selection in relation to sex*. London, UK: John Murray.

Fisher, R. A. 1937 The wave of advance of advantageous genes. *Ann. Eugen.* 7, 355–369. (doi:10.1111/j.1469-1809.1937.tb02153.x)

Mather, K. 1943 *Statistical analysis in biology*. London, UK: Methuen.

Mather, K. 1964 *Human diversity*. Edinburgh, UK: Oliver and Boyd.

Mourant, A. E. 1954 *The distribution of the human blood groups*. London, UK: Blackwell Scientific Publications.

Mourant, A. E., Kopeč, A. C. & Domaniewska-Sobczak, K. 1976 *The distribution of the human blood groups and other polymorphisms*. London, UK: Oxford University Press.

Reardon, J. 2005 *Race to the finish*. Princeton, NJ: Princeton University Press.

Reich, D. 2018 *Who we are and how we got here*. Oxford, UK: Oxford University Press.

Stone, L. & Lurquin, P. F. 2005 *A genetic and cultural odyssey: the life and work of L. Luca Cavalli-Sforza*. New York, NY: Columbia University Press.

Winther, R. G. (ed.). 2018 *Phylogenetic inference, selection theory and history of science: selected papers of A. W. F. Edwards with commentaries*. Cambridge, UK: Cambridge University Press.

---

**BIBLIOGRAPHY**

The following publications are those referred to directly in the text. A full bibliography is available as electronic supplementary material at https://doi.org/10.6084/m9.figshare.c.5322639.

(1) 1943 (With G. Bonezzi & G. Magni) Quantitative Untersuchungen über die Virulenz. I. Mitt.: eine Virulenzgleichung und ihre biologische Deutung. *Zbl. Bakt. I Orig. Bd.* 150, 17–25.

(2) 1944 (With G. Magni) Quantitative Untersuchungen über die Virulenz. II. Mitt.: die bakteriostatische Wirkung der sulfanilamide in vivo. *Zbl. Bakt. I Orig. Bd.* 150, 25–32.

(3) 1947 (With G. Magni) Quantitative Untersuchungen über die Virulenz. III Mitt.: analyse der Häufigkeitsverteilung der Absterbezeiten von infizierten Mäusen. *Zbl. Bakt. I Orig. Bd.* 150, 353–371.

(4) 1947 (With G. Magni) Methods of analysing the virulence of bacteria and viruses for genetical purposes. *Heredity* 1, 127–132. (doi:10.1038/hdy.1947.8)

(5) 1948 (With N. Visconti di Modrone) Bacterial mutations for resistance to radiations and to nitrogen mustard. (Abstract.) In *Proc. 8th Int. Congr. Genet.*, pp. 550–551.

(6) 1949 (With H. Heslot) Recombination in bacteria: outcrossing *Escherichia coli* K 12. *Nature* 164, 1057. (doi:10.1038/1641057c0)

(7) 1952 (With J. Lederberg & E. M. Lederberg) Sex compatibility in *Escherichia coli*. *Genetics* 37, 720–730.

(8) 1953 (With J. Lederberg & E. M. Lederberg) An infective factor controlling sex compatibility in *Bacterium coli*. *J. Gen. Microbiol.* 8, 89–98. (doi:10.1099/00221287-8-1-89)

(9) 1956 (With J. L. Jinks) Studies on the genetic system of *Escherichia coli* K-12. *J. Genet.* 54, 87–112. (doi:10.1007/BF02981705)

(10) 1957 Some notes on the breeding patterns of human populations. *Acta Genet. Statist. Med.* 6, 395–399. (doi:10.1159/000150858)

(11) 1958 Some data on the genetic structure of human populations. In *Proc. X Int. Congr. Genet.*, vol. 1, pp. 388–407.

(12) 1960 Demographic attacks on genetic problems: some possibilities and results. In *UN WHO Seminar*, pp. 221–233.
Biographical Memoirs

(13) 1962 The distribution of migration distances: models, and applications to genetics. In *Entretien de Monaco en Sciences Humaines: Première Session Human Displacements*, pp. 139–158.

(14) 1964 (With I. Barrai & A. W. F. Edwards) Analysis of human evolution under random genetic drift. *Cold Spring Harb. Symp. Quant. Biol.* 24, 9–20. (doi:10.1101/SQB.1964.029.01.006)

(15) (With A. W. F. Edwards) Analysis of human evolution. *Genet. Today, Proc. XI Int. Congr. Genet.*, vol. 2, 923–933.

(16) (With A. W. F. Edwards) Reconstruction of evolutionary trees. *System. Assoc. Publ.* 6, 67–76.

(17) 1965 (With A. W. F. Edwards) Estimation procedures for evolutionary branching processes. *Bull. Int. Statist. Inst., Proc. 35th Sess.*, 803–808.

(18) 1966 Population structure and human evolution. *Proc. R. Soc. Lond. B* 164, 362–379. (doi:10.1098/rspb.1966.0038)

(19) 1967 (With G. Zei) Experiments with an artificial population. In *Proc. III Int. Congr. Hum. Genet.*, pp. 473–478. Baltimore, MD: Johns Hopkins Press.

(20) 1969 (With I. Barrai & A. Moroni) Demography and genealogy: I. Family reconstitution by computer. In *World Conference on Records and Genealogical Seminar, Salt Lake City, Utah, August 1969*, pp. 1–7. Salt Lake City, UT: Corporation of the President of the Church of Jesus Christ of Latter-Day Saints.

(21) Human diversity. In *Proc. XII Int. Congr. Hum. Genet.*, Tokyo, Japan, 1968, vol. 3, pp. 405–416.

(22) 1970 (With W. Bodmer) Intelligence and race. *Sci. Am.* 223, 19–29. (doi:10.1038/scientificamerican1070-19)

(23) 1971 (With A. Ammerman) Measuring the rate of spread of early farming in Europe. *Man* 6, 674–688. (doi:10.2307/2799190)

(24) Similarities and dissimilarities of sociocultural and biological evolution. In *Mathematics in the archaeological and historical sciences* (ed. F. R. Hodson, D. G. Kendall & P. T’autu), pp. 535–541. Edinburgh, UK: Edinburgh University Press.

(25) Pygmies, an example of hunters-gatherers, and genetic consequences for man of domestication of plants and animals. In *Human genetics: Proc. IV Int. Congr. Hum. Genet., Paris, September 1971*, pp. 79–95. Amsterdam, The Netherlands: Excerpta Medica.

(26) (With W. F. Bodmer) *The genetics of human populations*. San Francisco, CA: W. H. Freeman & Co.

(27) 1973 (With A. J. Ammerman) A population model for the diffusion of early farming in Europe. In *The explanation of culture change* (ed. C. Renfrew), pp. 343–357. London, UK: G. Duckworth & Co.

(28) Some current problems of human population genetics. *Am. J. Hum. Genet.* 25, 82–104.

(29) 1974 The genetics of human populations. *Sci. Am.* 231, 81–89.

(30) 1976 (With W. F. Bodmer) *Genetics, evolution and man*. San Francisco, CA: W. H. Freeman & Co.

(31) 1981 (With M. Feldman) *Cultural transmission and evolution: a quantitative approach*. Princeton, NJ: Princeton University Press.

(32) 1983 (With M. J. Johnson, D. W. Wallace, S. D. Ferris & M. C. Rattazzi) Radiation of human mitochondria DNA types analyzed by restriction endonuclease cleavage patterns. *J. Mol. Evol.* 19, 255–271. (doi:10.1007/BF02099973)

(33) 1984 (With A. J. Ammerman) *The Neolithic transition and the genetics of populations in Europe*. Princeton, NJ: Princeton University Press.

(34) 1986 *African Pygmies*. Orlando, FL: Academic Press.

(35) 1988 (With A. Piazza, P. Menozzi & J. L. Mountain) Reconstruction of human evolution: bringing together genetic, archeological and linguistic data. *Proc. Natl Acad. Sci. USA* 85, 6002–6006. (doi:10.1073/pnas.85.16.6002)

(36) 1990 Recollections of Whittingehame Lodge. *Theor. Pop. Biol.* 38, 301–305. (doi:10.1016/0040-5809(90)90016-O)

(37) 1991 (With A. M. Bowcock, J. M. Hebert, J. L. Mountain, J. R. Kidd, J. Rogers & K. K. Kidd) Study of additional 58 DNA markers in five human populations from four continents. *Gene Geogr.* 5, 151–173.

(38) Genes, peoples and languages. *Sci. Am.* 265, 104–110. (doi:10.1038/scientificamerican1191-104)

(39) 1993 Forty years ago in genetics: the unorthodox mating behavior of bacteria. *Genetics* 132, 635–637. (doi:10.1093/genetics/132.3.635)

(40) (With F. Cavalli-Sforza) *Chi siamo: la storia della diversità umana*. Milano, Italy: A. Mondadori.
Luigi Luca Cavalli-Sforza

(41) 1994 (With P. Menozzi & A. Piazza) *The history and geography of human genes*. Princeton, NJ: Princeton University Press.

(42) 1995 (With F. Cavalli-Sforza) *The great human diasporas*. Reading, MA: Addison-Wesley.

(43) 2000 *Genes, peoples and languages*. New York, NY: Farrar Straus & Giroux.

(44) 2004 (With A. Moroni & G. Zei) *Consanguinity, inbreeding and genetic drift in Italy*. Princeton, NJ: Princeton University Press.

(45) 2005 The human genome diversity project: past, present and future. *Nature Rev. Genet.* 6, 333–340. (doi:10.1038/nrg1579)

(46) 2005 (With F. Cavalli-Sforza) *Perché la scienza : l’avventura di un ricercatore*. Milano, Italy: Mondadori.