OBITUARY

C. C. Li (1912–2003): his science and his spirit

Ching Chun Li passed away on 20 October 2003, in Pittsburgh. He was an outstanding population geneticist, a wonderful teacher, and above all, a great human being. Devotion to work and humility were the hallmarks of C. C. Li, who was known as C.C. to his contemporaries and colleagues, and as Dr Li to his students. In the United States, he stayed with the same University (the University of Pittsburgh) from 1951 until his death. He formally retired in 1982, but continued to come to work regularly for two decades after his retirement. "I go to my office because there is nothing else better to do." He published over 25 papers after his "retirement;" he wrote his last scientific paper when he was 88 years of age. In 2002, Dr Li and his wife, Clara, established an Endowed Research and Education Fund in Human Genetics through a generous gift of $ 1 million to ensure that human genetics education and research play an important role at the University of Pittsburgh. "This is not about what I'm giving to the University; it's about what the University has given me."

Dr Li was a very courageous, kind, and relaxed person, with a strong sense of humor. If you walked into his office, he was always reading, writing, or calculating something. However, he always had time for you. If you gave him a manuscript, you could be sure of receiving his thoughtful comments in a short time. His style of work was amusing to many of us. Even if he had derived an equation algebraically, he had to work out some numerical examples to verify that the equation was correct. Sometimes, of course, such numerical exercises provided further insights for him. Thus, he would spend hours in his office working on his desk calculator that had a large red LED display—his eyesight was poor. And, of course, he always used the white backsides of discarded pages for such purposes. You could also discuss your personal problems with him; you could be sure of receiving his wise counsel. He was very affectionate to everyone.

C. C. Li supervised the work of 12 Ph.D. students. He was elected a Fellow of the American Statistical Association and of the American Association for the Advancement of Science, President (1960) of the American Society of Human Genetics (ASHG), and Member of the International Statistical Institute and the Academia Sinica (Chinese Academy). In 1970, he was elected "Pittsburgh Statistician of the Year" by the American Statistical Association. In 1998, the ASHG honored him with their "Award for Excellence in Education."

Throughout his life, C. C. Li steadfastly strove to uphold the autonomy of science and the freedom of scientists. In his speech delivered during the ASHG award ceremony in 1998, Dr Li said, "If one insists that science itself has also its own ideology, then I shall say: let that ideology be the autonomy of science, although I personally feel that autonomy is an essential property of science, not its guiding ideology. If there were no autonomy, there would be no science to speak of." He was also acutely aware of the social responsibility of scientists. "They must look after the social consequences" of their science, he said.

C. C. Li wrote 10 books. These were on population genetics, human genetics, the design of experiments, and path analysis. Two of these books were his Chinese translations of books by T. D. Lysenko (*Heredity and its Variability*) and Julian Huxley (*Soviet Genetics and World Science*). He published over 100 papers in peer-reviewed journals; he was the sole author on about 60% of these.

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"I have written no outstanding papers, but I like the ito paper"

Having heard that the probabilist William Feller had included many examples from population genetics in his book *An Introduction to Probability Theory and Its Applications, Volume 1* [Feller 1950], C. C. Li acquired a copy. One of the problems Feller [1950] dealt with was to find the probability that an individual will be of a specific genotype conditional on a given genotype of a sibling (or another relative), i.e., share 0, 1, or 2 alleles identical by descent. Feller [1950] provided a solution using the concept of transition matrices, but to Dr Li's intuition and knowledge, the result did not seem correct. He started thinking about the problem in general terms, but his limited knowledge of matrix algebra turned out to be a handicap. So he began discussions with a mathematician, Dr Louis Sacks, and they wrote the "ITO paper" [Li and Sacks 1954]. In this paper, they showed that the results by Feller [1950] for a pair of siblings were incorrect, and they provided a general method for obtaining these conditional probabilities for any pair of relatives. Actually, R. A. Fisher in his famous 1918 paper had also dealt with the same problem, and obtained correct results for some specific pairs of relatives (e.g., double first cousins). But the algebraic methods used by Fisher [1918] were inelegant. Later, in 1966, when P. A. P. Moran and C. A. B. Smith wrote their commentary on Fisher's paper, they noted that the results are "more easily obtained by the Li and Sacks method" [Moran and Smith 1966]. Dr Li said that "Feller amended his statement in a later edition of his book and stated that his original solution T^2 for sibs was actually for half-sibs, which is correct. He referred to my paper, but the citation was *Biometrika*, when it should have been Biometrics. I think Feller actually didn't read my paper. Even after the amendment, he didn't talk about the I matrix."

The ITO method was generalized for multiple loci [Campbell and Elston 1971], and has been widely used in solving various problems in human population genetics that involve derivation of probabilities of identity-by-descent. However, Dr Li lamented that "Many of the young workers do not know about the ITO method. I think one of the reasons is that the following two powerful books do not mention ITO at all: Crow and Kimura [1970], Hartl and Clark [1989]."

"I am of the same age as the Chinese Republic"

C. C. Li was born on 27 October 1912, in a village called Taku, near Tientsin in northeastern China. (1911 was the final year of China's last emperor; 1912 witnessed the birth of the Chinese Republic.) His father, a successful businessman in Tung oil, was among the first generation of Chinese who had a missionary education and learned English. C. C. Li was the third in a family of four sons and went to a British school, Tientsin Anglo-Chinese College, and got his B.S. degree in 1936 from the University of Nanking, an American missionary school. From 1937–1940, he went to the Cornell University College of Agriculture, where he obtained his Ph.D. in Plant Breeding and Genetics. He met Clara in the International House of the University of Chicago, where he studied Mathematics for two summers, and married her in 1941. In 1940–1941, he did a postdoc in Mathematical Statistics at Columbia University.

"When you are starving, you really can't do anything. You can't think. You just lie there like a Zombie"

C.C. and Clara Li set off for their honeymoon in Shanghai soon after their wedding, which was the beginning of a long story. They boarded a ship from San Diego and were trapped in the storm of World War II. Instead of reaching Shanghai, the ship made a circuitous route and they had to disembark in Kowloon. Because the Japanese had attacked Pearl Harbor and Hong Kong almost simultaneously, the Lis were stranded in Kowloon for nearly 2 months. With several hundred American dollars in their possession, they faced starvation. American dollars were useless and could not be exchanged for local currency. Finally, after 38 days of walking, they reached Free China.

"The communists did not believe in the autonomy of science. In their world, ideology overruled science"

C. C. Li got a job at the Agricultural College of National Kwangsi University and later worked at the University of Nanking. At age 34, he became a professor and the chair of the Agronomy Department at National Peking University. The Communist government took over mainland China in 1949, and among other things, officially sup-ported the new "dialectical" genetics propounded by Lysenko. Dr Li was teaching Mendelian genetics and statistics. The Communist regime disbanded these courses and replaced them by Lysenkoist "new" genetics. Dr Li was asked to resign from the Chairmanship of the department, which he did promptly. The resignation, however, didn't solve any of Dr Li's problems. The Communists wanted him to denounce Mendel in support of Lysenko. "How could I denounce this man? This man is my god. He discovered the laws of inheritance." The Communists tried various ways to purge C. C. Li, including trying to make him out to be an American spy. Sensing what was in store, C.C., Clara, and their 4-year-old daughter, Carol, fled away to Hong Kong, a British territory then. Immediately thereafter, Dr Li wrote a letter to the *Journal of Heredity* titled "Genetics Dies in

China." It was through the personal efforts of Hermann J. Muller, who earlier had to flee for his life from Moscow because he ran afoul of Lysenko, that C. C. Li was able to find a job at the University of Pittsburgh and emigrate to the USA.

Introduction to Population Genetics [Li 1948] . . . and after

C. C. Li's textbook [Li 1948] dominated the field of population genetics for over two decades. He wrote this while teaching at the University of Nanking. "The purpose was to introduce population genetics not only to China, but also to a larger audience everywhere." There is no doubt that at least an entire generation of geneticists learned population genetics from this book. The 1948 edition was published by the National Peking University Press, but "since the Communist troops entered the city of Peking, the book was never on sale publicly. Fortunately, the American Embassy shipped the book to the US My brother, Jerome Li, who was in the US, reprinted 500 copies of the book." A revised version of the book was later published in 1955 by the University of Chicago Press [Li 1955], and has been translated into many Asian and European languages.

Sewall Wright was particularly thankful to C.C. for including a clear description and illustrations of Wright's method of path coefficients in this book. In later years, Li himself made many contributions to path analysis and wrote a text-book, *Path Analysis, A Primer* [Li 1975].

C. C. Li's contributions to population genetics have been wide-ranging, profound, and expository. With Bentley Glass, he provided the basic framework for estimating admixture proportions from allele frequency data [Glass and Li 1953]. He wrote about 10 papers on segregation analysis, of which two stand out. In one [Li 1964], he suggested the "first appearance time method," and in another [Li and Mantel 1968], he suggested the "singles method." Both methods were derived from his keen insight into the properties of the binomial distribution. Davie [1979] pointed out that the "singles method" works for any level of ascertainment, if we change only one word in the definition of "singles:" from "singleton recessives" to "singleton probands." Nicholas [1982] concluded that "the singles method is the only C. C. Li (1912–2003) 83 method that needs to be used in simple segregation analysis."

Li and Horvitz [1953] proposed some methods of estimating the inbreeding coefficient (F), starting with various possible interpretations of the definition of F. "Horvitz and I always thought that ours was an unfinished paper because we did not calculate the variances of those estimates." This paper is somewhat unique in that its number of citations peaked about 40 years after its publication [Chen and Tai 1998]. Having learnt this, Dr Li was very pleased, remarking, "I thought it was a dead paper."

Eighty years later . . .

Dr Li was the first to discover that, in 1903, W. E. Castle had anticipated the Hardy–Weinberg law by 5 years [Li 1967]. The Hardy–Weinberg law provides a sufficient condition (that of random mating) for genotype proportions to reach equilibrium values. No one, since 1908, had investigated whether random mating was a necessary condition. Dr Li showed, in 1988, that it was not a necessary condition, and actually proved the existence of an infinite number of nonrandom mating populations in which genotypes can be in Hardy–Weinberg proportions [Li 1988].

"This is absurd"

The period 1983–1996 witnessed a burst of publications by C. C. Li. The major thrust of his work during this period was on paternity probabilities and DNA matches. Dr Li studied the properties of the "paternity index," a measure to assess the chance from genetic data that an accused individual is the father of a child, and discovered that the value of this measure can decrease after a nonexclusion. "This is absurd," he reasoned, and went on study many related problems. He derived the probability that the DNA profiles of two random individuals will match. He noted that preexisting methods used improper conditioning events and priors. He studied the effect of population subdivision on match probabilities, and then went on to study "when can subdivision be ignored?" In 1996, he wrote an expository paper entitled "Population Genetics of Coincidental DNA Matches" for which he received the Gabriel Lasker Award as the best paper of the year in *Human Biology* [Li 1996]. Interestingly, one reviewer of the manuscript of this paper remarked that it was the "hand of a master," while another recommended outright rejection! It may be noted that the publication of this article coincided with the infamous murder trial of O. J. Simpson in Los Angeles, where the defense emphasized the lack of "appropriate" ethnic matching in the control DNA samples.

"Avoidance of research is certainly no road to progress"

Dr Li was a keen follower of the controversies that arose with Arthur Jensen's work on IQ. There are thick files in his office containing his correspondence with Arthur Jensen on these matters. As a matter of fact, immediately after its publication, he purchased a copy of *The Bell Curve* and read it with great interest. The two questions that interested C. C. Li were: 1) is intelligence (as defined by IQ tests) determined by heredity? and 2) is there a racial difference in such a test score? When many scientists were arguing that for social and other reasons, it is best not to study such problems, Dr Li said that "both are matters in basic

science, and they must be treated and studied as such. . . . Avoidance of research is certainly no road to progress. . . . There should be no more room for emotion than in studying the mobility of amoeba." Dr Li's major contribution during this controversial period was to show [Li 1970] that it was unnecessary to use two different sets of reasons to explain why some children from a certain class perform worse than their fathers and why other children perform better than their fathers. Under Mendelian segregation (one single explanation), this is exactly what is expected. He stated that only very rigid social forces can make "like beget like."

Hilarious and Powerful

After C. C. Li delivered his talk in the conference on "Intelligence: Genetic and Environmental Issues," held in 1970, he was asked, "Since all tests are arbitrary devices, should we attach any meaning to the test scores? Particularly, I mean the IQ tests." Dr Li replied, "Despite the arbitrary nature of all types of tests, the results or scores do mean something. If they mean nothing else, they at least measure the scoring ability with respect to that particular test. Whether the scoring ability should play a role in society is entirely another problem. The champions in track do have better running ability than the rest of us. Whether we should make them senators or governors is a different question. A popular pitcher of the Pirates got elected to public office in the Pitts-burgh area. If the IQ scores really differ between two groups (any two groups, not necessarily blacks and whites), I shall accept it as a fact without any implications. I accept a good pitcher as a good pitcher, but I do not necessarily vote for him in November, in spite of the fact that an administrator also needs a strong arm."

Another person commented, "You are talking about science all the time. What I want to know is if you were told that the Chinese intelligence is 15 points below the whites, what would you do?" Dr Li replied, "Absolutely nothing! Incidentally, there is no 'if' about it. I have been told something like that many times since my boyhood, long before the test scores became popular. I seem to hear less and less about that as time goes by. This could be because of my age; I hear less and less about everything else too."

"Progressing from eugenics to human genetics"

Dr Li was always critical about eugenic programs: "Almost every one of the programs of the eugenic movement is questionable on close examination." The resurgence of the eugenics movement in certain places prompted him to revisit some of the major underlying issues [Li 2000]. In this paper, he studied the following problem: When a eugenic law prescribes the elimination of diseased individuals (aa) for the elimination of the disease-causing gene, how quickly can such a law actually attain its goal? He obtained the following general result: The number of generations required to reduce any gene frequency (q) to half its value is 1/q. Thus, to reduce q from 1/200 to 1/400, it will take 200 generations. "Two hundred generations is approximately three times as long as the period from Jesus Christ to our generation . . . the smaller the change, the longer it takes. . . . They [the eugenecists] will not accomplish their aims, for example, to eliminate recessive genetic diseases from the population. Similar to our usual saying that half-truth is whole lie, we may say that half-understanding is whole misunderstanding." He concluded this paper with the following remarks: "There are indeed many things we could do to alleviate our suffering from genetic diseases. But these must be done in a noncoercive way. . . . We prefer the counseling method with full respect for individual rights, and deplore government regulations to constrain freedom of choice of mates and the right to have children. We hope with all our might and knowledge, we shall make our human society human and not return to the ways of the wild animal kingdom."

Dr Li consistently advocated genetic counseling. In 1977, as a member of the Congressional Commission for the Control of Huntington's Disease and Its Consequences, Dr Li wrote a minority report, when the other members of the Commission ridiculed his suggestion for developing an early test for detection of heterozygotes followed by genetic counseling. "Genetic counseling and eugenic law . . . are as different as day and nighty . . . [Genetic counselors] respect, not deny, your civil liberties and your basic human rights. . . ."

"Because I teach a course on experimental design, I do not believe in personal opinion. We do things according to experimental results"

In 1955–1956, the University of Pittsburgh decided to construct a new building for the Graduate School of Public Health. The building contractor provided the Building Committee of the University a choice of four different types of bricks. The Building Committee was at a loss! One member asked C. C. Li whether he could make a suggestion. Dr Li suggested that some temporary walls, with different orientations, be constructed near the site of the building with all four types of bricks. By the time the framework of the building was completed and the bricks were ready to be laid, the choice was obvious. "If you look at them today, the bricks are still clean; they don't catch dirt," Dr Li said about 35 years later.

". . . And after three, people will forget that any other kind of calendar ever existed"

C. C. Li was a strong advocate of a calendar that was originally suggested by an Italian priest, Abbe Marco Mas-

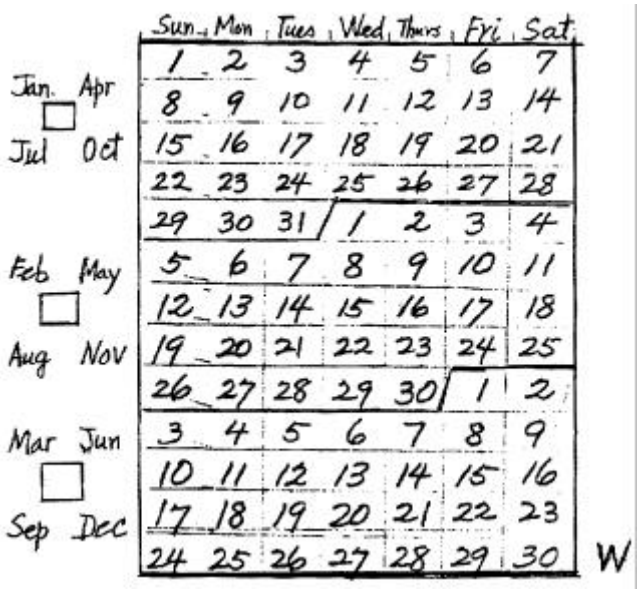

Figure 1. Mastrofini calendar in C. C. Li's own handwriting.

trofini, in 1834. The basis for this calendar was simple. Take one day off the ordinary 365 days of a year. Then the remaining 364 days can be divided into four equal quarters of 13 weeks each. This way, we will have four equal quarters, and the date of a month will always correspond to a certain day of a week (figure 1). The day that was taken off will not be part of the regular calendar; it is to be designated as a World Holiday (W). Dr Li was confident that once adopted "after one year, people will hate to go back to the old calendar; after two years, people will wonder how they ever got along in the old days; and after three, people will forget that any other kind of calendar ever existed." The United Nations proposed this calendar in 1956, and most countries thought it acceptable. However, the USA and the UK vetoed it!

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