Perspectives

Anecdotal, Historical and Critical Commentaries on Genetics

Edited by James F. Crow and William F. Dove

SEVENTY YEARS AGO IN *GENETICS*: H. S. JENNINGS AND INBREEDING THEORY

IN 1917 *GENETICS* was in its second year. The March issue contained a 58-page article by H. S. JENNINGS, analyzing mathematically the consequences of inbreeding and selection. He had a 37-page article on the same subject in the very first issue of the journal, January 1916, and the entire September issue that year (127 pages) was devoted to his article on the genetics of *Diffugia*, a shelled rhizopod. In those days *GENETICS* was not so crowded.

JENNINGS was the first to use microorganisms to study behavior and genetics. He foresaw the value of using simple species to attack basic biological problems, and in the process founded *Paramecium* genetics. In *Diffugia* he demonstrated templated replication of some shell structures. Only after the discovery of DNA replication was the significance of such a supramolecular copying process appreciated. His contributions to population genetics are less well known, but had a significant place in its history.

HERBERT SPENCER JENNINGS (1868–1947), named by a father who was caught up in the new wave of Darwinism (another son was named Darwin), spent most of his childhood in Tonica, Illinois. He taught himself to read at age 3, soon read biology texts and Shakespeare, and continued to devour books the rest of his life. Too poor to go to college, he spent 4 years in various jobs, including three rural teaching posts. His first class had half a dozen students, “one totally ineducable and the others little better.” The pay was \$25 per month, and he walked 7 miles each morning and evening. Characteristically, he used the noon recesses to study *The Decline and Fall*. Then a bizarre thing happened. His former high school teacher, by then a Professor at Texas A & M, remembered his brilliance and got him a position there as assistant professor of botany. JENNINGS, who had never been to college, was teaching college students! He started many lectures, he said, with knowledge an hour ahead of those in the class “and came out even.” In 1888 Texas A & M had 227 students, fewer than its 1987 Cotton Bowl marching band. The experience was not entirely happy. The serious, shy scholar found a stu-

dent body more interested in horseplay than learning and a faculty split into two warring factions. His last article (1946) was a wryly humorous account of life at Texas A & M 58 years earlier. At the end of the year he was fired.

He had, however, earned enough to enroll at the University of Michigan, and with the later help of an assistantship he graduated in 1893 at age 25. After one postgraduate year there he went to Harvard, getting his Ph.D. in 2 years. After a year in Germany, he taught successively at Montana, Dartmouth and Michigan. Among his writings during this period was a 486-page book on the anatomy of the cat (REIGHARD and JENNINGS 1901). (I write this with nostalgia: this book and formaldehyde fumes are among my vivid memories of an anatomy course in the hot Kansas summer of 1935.) Later, JENNINGS was appointed to the faculty of the University of Pennsylvania, and finally to Johns Hopkins. He was promised that he would eventually succeed W. K. BROOKS as director of the Johns Hopkins Zoological Laboratory. Conveniently, BROOKS died 2 years later. The search committee recommended T. H. MORGAN for the position, but JENNINGS documented the earlier commitment and got the job in 1910. He retired in 1938 and stayed on as professor emeritus. He continued to write until shortly before his death in 1947.

JENNINGS' academic career can be divided into three phases. The first decade was devoted to the study of behavior. He was convinced that behavior, including human, was determined by the physical structure and its responses to previous experience. He held the monistic view, then still controversial, that mind and matter were inseparable. He thought that the route to understanding behavior in higher forms was through lower ones. His book *Behavior of the Lower Organisms*, published in 1906, became a classic and was reprinted as recently as 1976.

In 1907 he shifted his interest to genetics, the initial object being to test the generality of Mendelism. Again he decided that the optimum strategy would be to concentrate on the simplest organisms and chose

his favorite, *Paramecium*. His judgment was good but his luck was bad, for *Paramecium* turned out to be more reluctant than *Drosophila* to reveal its genetic mechanisms. JENNINGS' breeding experiments were frustrated by his being unable to obtain conjugation except within a type. This greatly restricted the range of genetic experiments, yet he was able to obtain a remarkable amount of information by clever indirect methods. The complications of mating type were not fully understood until 30 years later when his student, T. M. SONNEBORN, made the key discoveries. JENNINGS was now retired, but the two of them wrote back-to-back papers on two species of *Paramecium* (JENNINGS 1939; SONNEBORN 1939). The analytical power of genetics was now at hand, but JENNINGS did not live to see its fruition at the hands of SONNEBORN and his students.

The third phase of JENNINGS' life, from World War I until his retirement in 1938, was spent mainly in teaching, administration, and public activities. He wrote a prize-winning book, *The Biological Basis of Human Nature* (1930), that was both authoritative and popular. His *The Universe and Life* (1933) represented his mature general and philosophical thought. SONNEBORN (1975), in a detailed and admiring biography, called it his "greatest and perhaps the most enduring" book. JENNINGS accepted the social aim of trying to improve, or at least not worsen, the quality of human genes in future generations. He was one of the first to express concern about the accumulation of deleterious mutations with relaxed selection. In those years there was a large group, including many influential geneticists, who had idealistic hopes for a better human society through eugenics. There were also those, mostly nongeneticists, who naively mistook the consequences of poor environment and unfamiliarity with English for innate stupidity. JENNINGS took the lead in emphasizing the complexities of the problem. He urged caution and pointed out the slowness of genetic changes compared to those brought about by environmental improvement. In the early 1920s he appeared before a Congressional committee to argue against geographically restrictive immigration laws. Although the great majority of geneticists probably shared his views, he was the most outspoken early critic of the simplicity and crudity of the old eugenics movement.

This essay was stimulated by JENNINGS' paper of 70 years ago. At that time the genetic consequences of inbreeding were of great interest, and not well understood. While the reduction of heterozygosity with repeated self-fertilization had been known since MENDEL, the well known RAYMOND PEARL (1913) tried to extend this to sib-mating. Starting with an $AA \times aa$ mating, he noted that the progeny were 100% heterozygous, and the two following sib-mated generations were both 50% homozygous. He saw no need to

calculate further and concluded that the 50% homozygosity remained indefinitely. HAROLD FISH, a modest, intelligent graduate student of WILLIAM CASTLE at Harvard, realized that this was wrong and laboriously worked out the correct results, showing that the homozygosity in the fourth generation was 62.5%, the fifth was 68.75%, and so on, reaching 99.5% after 25 generations. PEARL was so annoyed at the possibility of being publicly corrected by a graduate student that he asked that FISH be fired. Nevertheless, not only FISH and PEARL, but WHITING, DETLEFSEN and JENNINGS all published the correct results in the same year, 1914. It seems that almost everyone took "salutary pleasure" in correcting PEARL's error, in accordance with the Darwinian dictum quoted in this space last month. Yet none of the acrimony comes through in the published papers, which are exceedingly polite and generous.

How does JENNINGS fit in? He was the first to publish a general formula and to show that FISH's proportion of homozygotes in successive generations of sib-mating could be expressed in terms of the famous and well understood Fibonacci sequence. The relation is most transparent when written as the proportion of heterozygotes. In successive generations this is $1/1$, $1/2$, $2/4$, $3/8$, $5/16$, $8/32$, etc., in which each numerator is the sum of the two preceding. JENNINGS then studied more complicated systems, giving correct results for parent-offspring mating and for some kinds of selection and assortative mating.

The 1917 paper extends the analysis to two loci, where linkage enormously complicates the picture. This paper, 58 pages long, tries the patience of a contemporary geneticist, who knows how to obtain the results much more easily. Yet JENNINGS got there first. His work represents the high point of the method of the time, which was to calculate a few generations by strong-arm methods and hope to find a pattern. Soon afterward, HALDANE, FISHER and WRIGHT introduced more powerful and fruitful ways of looking at inbreeding and selection problems, and population genetics was under way.

SEWALL WRIGHT was FISH's office-mate at Harvard. FISH filled many pages with calculations, covering not only his desk but the floor. After helping FISH, WRIGHT decided that there had to be a better way and in 1922 published his simple algorithm for computing the inbreeding coefficient for any pedigree, however complex. What took FISH and JENNINGS pages of calculations can now be done on the back of an envelope by elementary genetics students.

Although PEARL, JENNINGS and WRIGHT became leading scientists, FISH all but disappeared. As a graduate student he was already married and had two children. Financial problems, and perhaps an unwillingness to stay with one problem, led him to drop out

of graduate school and take a position at Denison University, where he soon had a reputation as an excellent teacher. To complete the circle, one of his masters-degree students, LOUISE WILLIAMS, taught genetics at Smith College and later became MRS. SEWALL WRIGHT.

Although he had no training in mathematics, JENNINGS enjoyed doing calculations. Very late in his life he had his first encounter with the calculus, a joyous love affair. But JENNINGS recognized his mathematical limitations and soon realized that his elementary methods would no longer suffice. The concluding words of his 1917 paper are: "The present writer would find it a relief if someone else would deal thoroughly with the laborious problem of the effects of inbreeding on two pairs of linked factors." I ruefully empathize. The influx of skilled mathematicians into population genetics has greatly advanced the field, but it has made it tough for amateurs.

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