*J. Genet.*, Vol. 64, No. 1, July 1985, pp. 3–5. © Printed in India.

# J B S Haldane – an appreciation

JAMES F CROW
Department of Genetics, University of Wisconsin, Madison, WI 53706, USA

If all men are unique—and genetics makes this abundantly clear—what is the adjective for Haldane? Perhaps, as M J D White has reminded us, he is best captured in the words "infinite variety"; in my book, he is far more deserving of Shakespeare's description than Cleopatra. Of course, I did not know Cleopatra, but I *did* know Haldane. I can only regret that I did not have the chance to know him better.

Who else can match this record? Haldane wrote articles about the association of oxygen and carbon monoxide with hemoglobin, acidosis, exercise physiology, effects of insulin on blood volume, growth regulation in termites, enzyme kinetics, potential difference across a cell membrane, renal physiology, carbon monoxide poisoning, origin of life, respiratory physiology, anthropology, space-time, the origin of the universe, quantum mechanics and philosophy, theory of price fluctuations, anthropology, philosophy of science, chemical warfare, chess, science fiction, theoretical statistics, protection from air raids, effects of oxygen at high pressures (even how it tastes), scientific fraud, civil defense, origin of language, dance of the bees, history of religions, probability theory, and Hindu philosophy. And I have omitted genetics, the subject in which he made his greatest contributions.

His bibliography lists articles in German, French, Italian, English (of course), and one in a language I don't recognize. Doubtless he was familiar with others, for he often quoted from Hindu writings, and he certainly knew Latin and Greek. He had a poem published at age 71. He wrote science fiction. He wrote a popular science book for children. He authored 23 books, more than 400 scientific papers, and one can only guess how many popular articles, essays, newspaper stories, and reviews. He turned them out at the slightest provocation, and seemingly effortlessly.

Haldane was a great writer of popular science. Arthur Clarke, who ought to recognize good writing when he sees it, called him the most brilliant scientific popularizer of his generation. He could come closer to putting complicated scientific ideas into basic English than anyone I can think of. He could explain science simply, and get across the basic idea, skipping irrelevant details, yet not producing a caricature. At the same time he had the capacity to come up with a colorful, unexpected, pithy, often irreverent expression that sticks in mind. (One that sticks in my mind right now is his observation that, since in a capitalistic society the rich get richer and the poor have more children, there should at least be some moral improvement.)

How could he do so much? One clue is his remarkable memory. He could—and would—quote verbatim large passages from Shakespeare, Dante, Rabelais, *The Koran*, and various Hindu writers. He often wrote papers, and included the bibliographic references from memory. It is said that after working out a mathematical problem he threw the pages away, not needing them any more. Actually, there are mistakes in both his math and his bibliographies, but they only serve to call attention to the

overwhelming proportion that is correct. I personally recall an occasion when, during a discussion of some astronomical problem, he not only did a large computation in his head, but remembered the appropriate numerical constants.

A second reason that Haldane accomplished so much is that he worked hard, despite occasional appearances to the contrary. A third is that he was not bothered by perfectionism. When he wrote something, he usually published it right away and didn't agonize over revisions and rewordings. A fourth reason is that he didn't do any significant amount of experimental work, if we except his experiments on himself and other human volunteers. This gave him more time to think, write, and talk—all of which he indulged in freely.

At this time of revival of the *Journal of Genetics*, which surely would be pleasing to Haldane were he to know about it, I should emphasize his role in genetics. In Sewall Wright's words "Haldane's contribution to genetics was of a unique sort. He conducted no systematic breeding experiments, yet few geneticists have had more influence on the steady course of development of the subject than he during his long career." His best known work was his quantitative theory of natural and artificial selection and his work on genetic loads and the cost of natural selection. But he did much more.

He first learned of Mendelism in 1901 when his father took him to hear a lecture on the newly rediscovered laws of Mendel. He was eight at the time and said later that he found the lecture "interesting but difficult". He wrote a paper on linkage in mice about 1912, published in 1915. If he had published it sooner, he might have been even more famous. He worked out formulae for standard errors of recombination measures and for mapping functions. He demonstrated balanced lethals in data from *Antirrhinum*. He was an early contributor to the theory of segregation and linkage in polyploids. He was one of the first to demonstrate interference by studying the distribution of chiasmata. He demonstrated partial sex-linkage in mosquitos. These are only the early beginnings of a lifetime characterized by an interest in *all* aspects of genetics.

Haldane is best known among geneticists as one of the three founders, along with R A Fisher and Sewall Wright, of population genetics and the mathematical theory of evolution. Haldane's earliest contribution was a systematic working out of a large number of oligogenic models of selection and inbreeding. His paper on metastable equilibria was ahead of its time, as were several others. He introduced the matrix method of studying regular inbreeding systems, later developed further by Fisher. He also considered truncation selection for polygenic traits. He was one of the first to offer a theory of clines.

One of Haldane's early results attracted very little attention during his lifetime, but has become very useful in recent years. As long ago as 1927, he showed that the probability of ultimate fixation of a mutant allele with a heterozygous selective advantage, $s$, is approximately $2s$. This formula, and successive improvements by Fisher, Malécot, and Kimura, plays an essential role in Kimura's theory of evolution of neutral and near-neutral alleles by random drift.

Among Haldane's papers, the two that have most influenced my own research, were written 20 years apart. The first, "The effect of variation on fitness", was published in 1937. Here he shows that, for independent, strongly selected mutants, the effect of mutation on population fitness is equal to the genomic mutation rate, multiplied by a factor between one and two depending on dominance. This is the basis for the "genetic load" argument later used by H J Muller. The second paper, "The cost of natural selection", published 20 years later, asked for the total amount of selection required for

a gene substitution. It turned out to have a surprisingly simple answer, determined mainly by the initial frequency. These two papers are uniquely Haldane. In each, he discovered a new, surprising, original idea. Both have been controversial and have had to be modified to fit more realistic situations; but the basic ideas were Haldane's. They had the Haldane touch.

I am pleased that this Journal, to which Haldane contributed so much, is being revived. I only regret that it will no longer have him as an editor, reviewer, contributor, and sometimes curmudgeon.