and physics have resolved Zeno's deep paradoxes.

Drawing on these parallels, Churchland can surely issue a counter-challenge. After two millennia of wrestling with conundrums about knowledge and mind, during which advances have been made by relying on and contributing to the nascent sciences, philosophy should continue to look to what sources it can for possible lines of solution. Neuroscience is plainly a possible guide. Claiming that it cannot help us to solve the really big problems is a hollow rejoinder unless we are offered some alternative place in which to seek insight.

Scientism owes its readers a vision of how the great philosophical questions could be fruitfully approached without making use of the deliverances of science. Perhaps we need a thoughtful exploration of just how much Stendhal and Molière have to teach us about ourselves, and just how their approaches lie beyond the reaches of science. Until then, it is premature to chide those whose philosophical explorations are illuminated by their knowledge of science. Darkness is no substitute. □

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Balanced views?

Brian Charlesworth

Fifty Years of Genetic Load: An Odyssey. By Bruce Wallace. *Cornell University Press: 1991. Pp.174. $31.50.*

BRUCE Wallace has had a long and distinguished career as an experimental population geneticist. Together with Theodosius Dobzhansky, he was one of the founders of the 'balance' theory of variation in natural populations. This theory was elaborated in the early 1950s as an alternative to the 'classical' view, whose chief exponent was the geneticist H. J. Muller, famous for his work on the fruitfly *Drosophila*. The classical view holds that nearly all loci in the genome are predominantly represented in a population by a wild-type allele, and that the rare variant alleles at a locus are deleterious and maintained solely as a result of mutation pressure. Because there are many loci in the genome of a higher organism such as *Drosophila* or humans, the presence of these rare, deleterious alleles contributes to a substantial reduction in the average darwinian fitness of a population below that of a hypothetical, mutation-free individual with maximum fitness. This reduction in fitness, measured relative to the maximum fitness, is the genetic load of the population. In addition to mutation, genetic load may be created by genetic variation actively maintained by natural selection, for example by a fitness advantage to the heterozygote for a pair of alleles over the two homozygotes for the alleles.

According to the balance view, a substantial proportion of the loci in the genome exhibit allelic variation that is actively maintained by such 'balancing' selection. The first crucial test of the predictions of the two rival theories was provided in the 1960s by the detailed examination of the level of natural variability at samples of loci, by means of the gel electrophoresis of many different proteins. The classical theory apparently failed this test, because a pattern of widespread variability at many loci was usually detected in population surveys. But at about the same time, the neutral theory of molecular evolution and variation was being elaborated. According to this theory, random sampling of alleles in finite populations can interact with mutation to produce a pattern of genetic variability similar to that found in natural populations, provided that the fitness effects of the mutant alleles are sufficiently small. Thus, the mere observation of extensive genetic variation does not confirm the balance view: it has to be shown that the variation is related to fitness.

Although there are a few cases where the action of selection on protein variability has been unequivocally established, the difficulties of experimentally detecting changes in fitness are so great that the issue is so far undecided. The rapidly growing body of evidence from DNA population studies has already made it clear that there is usually much more evolution and variation for nucleotide changes that do not affect the amino-acid sequence of proteins than for changes altering protein sequences. This indicates that most amino-acid changes are deleterious, and that most variability at the DNA level probably fits the neutral model. The increasing sophistication of statistical techniques for detecting the footprints left by selection on DNA and protein sequences offers some hope that the role of selection in maintaining variability will soon become clearer.

Wallace's book provides a personal account of the course of his work and thought on the nature and significance of genetic load. He describes how he experimented to determine the effects of irradiation on *Drosophila* populations; to his surprise, and contrary to the predictions of mutational-load theory, he found no relation between radiation treatment and measures of the fitness of flies in his populations, despite evidence for a high frequency of genes with deleterious homozygous effects on fitness. This led him to conclude that heterozygote advantage is commonly responsible for the maintenance of genes with deleterious homozygous fitness effects, a keystone of the balance theory. To test whether random gene changes often induce mutations with favourable heterozygous fitness effects, he did a series of ingenious and laborious experiments with irradiated *Drosophila* chromosomes. The experiments confirmed his suspicions. This extraordinary finding stimulated much research, resulting in a welter of conflicting results.

Wallace emphasizes the results that confirmed his ideas, and does not review all the relevant literature. The consensus view today is probably that nobody yet knows how to reconcile the conflicting results of the radiation experiments, and that they do not provide unequivocal support for the balance hypothesis. Nonetheless, Wallace holds firm to his belief in pervasive balancing selection, and devotes several chapters to expounding his views on how such selection, acting at many loci, is consistent with the survival of the population, despite the large genetic load that would be imposed if all loci acted independently. He plumps for a combination of density-dependent regulation of population size, and selection based on only the fittest proportion of the population contributing to the next generation. Again, the treatment is one-sided, and objections to his views are not adequately discussed.

It should be clear from these criticisms that Wallace's book cannot be recommended as an introduction to the current state of play on the topic of maintenance of genetic variation; nor is it a reliable history of this important aspect of evolutionary genetics. Rather, it is of interest to those who wish to understand how he came to arrive at his views, which are by no means widely accepted today but which have certainly been important in stimulating experiments on natural variation at the level of the gene. □

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