Perspectives

Anecdotal, Historical and Critical Commentaries on Genetics

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John Maynard Smith: January 6, 1920–April 19, 2004

Brian Charlesworth[1]

School of Biological Sciences, University of Edinburgh, Edinburgh EH9 3JT, United Kingdom

JOHN Maynard Smith was one of the most influential evolutionary biologists of the generation that succeeded the "founding fathers" of population genetics, as he was fond of calling Fisher, Wright, and Haldane. Maynard Smith's father was a London surgeon, but died when John was 8 years old. His mother came from a well-to-do Edinburgh family. His childhood holidays were spent with his grandparents in rural Somerset, where, without any encouragement from adults, he developed a strong interest in natural history (Maynard Smith 1985). Stag hunting was a major occupation of the local inhabitants, and John alleged that the start of each hunting season was celebrated by the local church with the anthem "As pants the hart for cooling stream/ while heated in the chase/so longs my heart for Thee, O Lord/and Thy redeeming Grace." At 13, he entered Eton College, the best-known public (*i.e.*, private) school in England. He detested this bastion of the English ruling classes, although he admitted that the mathematics teaching was very good (Maynard Smith 1985). He then studied engineering at the University of Cambridge, where he was one of the first undergraduates to get married. His wife, Sheila, is a mathematician, who later worked on human genetics and then on bacterial genetics until her retirement from the University of Sussex.

In 1938, John visited Berlin, where his uncle was the British military attaché. He used to claim that his uncle hatched a plot to assassinate Hitler during a parade, using a sniper posted on the roof of the French embassy. This would have had the desirable effect (from the British point of view) of both eliminating Hitler and provoking a conflict between France and Germany. Unfortunately, the plan was vetoed by the British government. In response to what he saw happening in Berlin, and to his experiences at Eton, John joined the British Communist party, in which he was very active until 1947. After that, his allegiance gradually faded, and he left the party in 1956 following the brutal Soviet suppression of the Hungarian revolution (Maynard Smith 1985). In later years, he became a critic of Marxism, while retaining left-of-center political views.

During the war, John worked on aircraft design in factories in Coventry and Reading, but decided to change to biology after the end of the war, having decided that aircraft were "noisy and old-fashioned." He studied zoology at University College, London (UCL), where Haldane held the Weldon Chair of Biometry. He stayed on as a graduate student of Haldane's but never took his Ph.D., as he was given an appointment in the zoology department at UCL. (If you are as good as Haldane or Maynard Smith, a Ph.D. is an unnecessary adornment.) Haldane, always called "Prof" by John, was his life-long hero and his colleague until 1957, when Haldane moved to India (Maynard Smith 1985). John once wrote:

> I first read a book of essays by Haldane, it was *The Inequality of Man*, when I was at Eton. I was led to read them because he was regarded by at least some of the masters as a figure of immense wickedness. Although I did not know it, this chance encounter with Haldane's writings had a big influence on my future career. . . . . When, ten years later, I decided to chuck in engineering to study biology, I went to University College, London, because I wanted to study under Haldane . . . (Maynard Smith 1968a, p. vii).

In common with Haldane, John was an outstandingly clear lecturer and writer, with an immense breadth of knowledge and interests. While both were adept at spotting biologically significant theoretical problems, neither used particularly elegant mathematics: they were more interested in getting useful solutions, even if their methods caused professional mathematicians to grind their teeth (John was once annoyed by an eminent theoretician's reference to the "rough and ready methods of Maynard Smith").

They were also both outstanding communicators of science to the general public, in John's case through

[1]*Author e-mail:* brian.charlesworth@ed.ac.uk

television as well as his writings. John's Penguin paperback book *The Theory of Evolution* (Maynard Smith 1958c) must have stimulated the interest of many young readers in evolutionary ideas; I certainly remember reading it avidly as a teenager around 1960. But, in contrast to Haldane, who was renowned for his irascibility (and for being one of the few participants to actively enjoy World War I), John was a kindly and gentle person. In 10 years of association with him as a close colleague, I cannot recall any angry words between us, even when I made a fool of myself. John often told how he had to beg Haldane not to have daily rows, since they ruined his ability to work afterward. Haldane seemed genuinely surprised that John did not enjoy fighting. Nevertheless, John had a keen eye for stupidity and pomposity and could occasionally let fly. He attended the funeral of George Price, who sadly committed suicide while suffering from religious obsessions. The officiating clergyman told John that Price's problem was that he thought that he had a hotline to God, to which John responded "Just like St. Paul."

John received many scientific honors during his career, including election as Fellow of the Royal Society and Foreign Associate of the National Academy of Sciences. He was awarded the Darwin, Royal, and Copley Medals of the Royal Society, as well as the Balzan, Crafoord, and Kyoto Prizes. He did not receive any of the honorific titles dispensed to the great and the good by the British Government, claiming that Sheila would divorce him if he accepted one. His FRS came at the absurdly late age of 57. It is rumored that this reflected the antagonism that persisted for a long time between the schools of Haldane and Fisher, with much regrettably petty behavior on the part of both great men. John recalled giving a lecture to the United Kingdom Genetical Society as a struggling young scientist. Shortly after he started, Fisher got up, ostentatiously put on his coat and scarf, and then stumbled over the feet of people sitting in his row in order to leave the room. Haldane used to unnerve speakers he disliked by sitting in the front row, placing his large, domed head in his hands, and exclaiming "Oh God, Oh God!" in a penetrating voice.

Despite his great fame, John remained a humorous and unpretentious person during the whole of his life, although he certainly did not display any false modesty. He was unusually accessible to young scientists and was often to be seen in the bar at meetings, exchanging ideas with a crowd of colleagues, young and old, until late in the evening. He was very open to new ideas, even if there was a strong chance that they were wrong, and even if he did not much like the person who was proposing them. He created an exceptionally exciting atmosphere at Sussex, with numerous sabbatical visitors from overseas (in my time there, these included Rolf Hoekstra, David Penny, Sue Riechert, and Monty Slatkin), as well as postdocs of various nationalities (such as Jim Bull, Peter Hammerstein, David Queller, Jon Seger, Curt Strobeck, and Wolfgang Stephan). All this was achieved with very little grant funding: John did most of his work with pencil and paper or a primitive desktop computer. He was the kind of thinker who needed to talk through his ideas before they crystallized. His curiosity and intellectual strengths forged many collaborations that flowed out of his love of discussion and argument (much of it over morning coffee or evening beer). He was not very successful as a trainer of graduate students, at least in his later years. This was partly, no doubt, due to the scarcity of biology graduates interested in, or able to do, theoretical work, and partly to the fact that his policy was to "let them be around" rather than direct a research project. He could be quite overpowering in discussion and usually dominated any conversation in which he took part (occasionally he met his match with some of the larger egos in the business). Nonetheless, he would listen carefully to objections to his viewpoint if you were persistent enough and was far more interested in getting at the truth than in winning an argument. He was always generous in his evaluations of the achievements of others and quick to assist the careers of young people whose talents he had noticed.

John's early work in the 1950s was mostly on the genetics of *Drosophila subobscura*, which Haldane's laboratory was developing as a European rival to *D. pseudoobscura*. The study of the population genetics of this species has been revived in recent years, mainly by Greek and Spanish scientists (Krimbas 1993; Navarro-Sabaté *et al.* 2003). This owes much to John's early studies. John once said that his biggest scientific failure was to have overlooked the significance of intragenic recombination that Thea Koske and he detected in a mapping experiment on *D. subobscura* (Koske and Maynard Smith 1954). If he had interpreted this correctly, he might have shared in the epoch-making discoveries of that time on the structure of the gene. It is interesting that this work was briefly cited by Pontecorvo in his classic monograph synthesizing work on intragenic recombination:

> . . . the highest recombination (0.5 per cent) so far measured between two non-complementary (*i.e.*, functionally allelic) recessives in organisms higher than phage is that found by Koske and Maynard-Smith [sic] (1954) between two *ar* alleles of *Drosophila subobscura* (Pontecorvo 1958, p. 34).

John was very interested in animal behavior over the whole of his career, and his last book, with his colleague David Harper, is *Animal Signals* (Maynard Smith and Harper 2003). His studies of the effects of inbreeding on male mating behavior and reproductive success in *D. subobscura* (Maynard Smith 1956) caused him to become an advocate of the evolutionary significance of sexual selection by female choice of mates. As John noted over 40 years later (Maynard Smith 2000), sexual selection involving female mate choice was largely disregarded by most of the leading early 20th century evolutionary biologists, with the notable exception of Fisher (1930). There is, for example, only a single reference to it in Ernst Mayr's *Animal Species and Evolution* (Mayr 1963). In 1958, John wrote a perceptive article in a Darwin centennial volume (Maynard Smith 1958b), in which he anticipated the "good genes" theory of the evolution of female mate choice, currently the subject of much research in behavioral ecology. He summarized his studies of mate choice in *D. subobscura* as follows:

> There was an association between those characteristics of males making for mating success (probably athletic ability) and those making for fitness as a parent (the production of a large quantity of sperm). It has not been shown that a similar association exists in natural populations, but it seems very likely that it would do so (Maynard Smith 1958b, p. 242).

I am not sure that this last point has yet been convincingly established.

Using his engineering training, John also did theoretical work on the mechanics of bird flight, suffering difficulties with mathematically ignorant reviewers, which resulted in rejection of several of his papers (Maynard Smith 1985). He claimed that one of them once queried a derivation that involved a differential coefficient, wondering why the d's were not cancelled in the numerator and denominator. He became used to assuming mathematical illiteracy when explaining his work to biologists and was deeply embarrassed when an anonymous visitor brought into the lab by Haldane turned out to be Alan Turing. John became a great admirer of Turing and used his ideas on reaction-diffusion processes (Turing 1953) in some influential work on the genetics of pattern formation (Maynard Smith 1960; Maynard Smith and Sondhi 1960).

During the late 1950s and early 1960s, John pioneered the use of Drosophila as a model organism for studying the biology of aging, providing one of the earliest demonstrations of the survival cost of reproduction (Maynard Smith 1958a) and also evidence against the somatic mutation theory of aging (Lamb and Maynard Smith 1964). The evolution of life-history traits in general, and aging in particular, has become a flourishing branch of evolutionary biology, and Drosophila is now a major tool for analyzing the functional biology of aging (Partridge and Gems 2002).

In 1965, John left UCL to become the founding Dean of the School of Biological Sciences at the then new University of Sussex, situated in an attractive park on the outskirts of Brighton, which was formerly the property of the Earl of Chichester. John very effectively built up a thriving group of biologists, biochemists, and experimental psychologists. This achievement was later undermined by the assault on British universities launched by the Thatcher government during the 1980s, when several of his closest colleagues left the university around the time of his retirement in 1985. John, however, remained at Sussex for the rest of his life and was pleased to see a renaissance take place over the last decade or so, with a very active group in evolutionary biology emerging. He avoided becoming an administrator at a higher university or national level, although he became Dean again for a couple of years before retirement, in response to the strain the school was under at the time.

After moving to Sussex, John concentrated increasingly on theoretical work and eventually abandoned experimental work. This was partly due to the time needed for his administrative work and partly because he no longer felt overshadowed as a theoretician by Haldane, who had died in 1964. (John often said "Anything I could do, Haldane could do faster.") He contributed significantly to the early development of theoretical models of molecular variation and evolution, in response to the empirical studies of protein sequence evolution and electrophoretic variation initiated in the 1960s. Unlike many British and American evolutionists at that time, John was not at all hostile to the neutral theory of molecular evolution and variation, introduced by Motoo Kimura (Kimura 1968) and by Jack Lester King and Thomas Jukes (King and Jukes 1969). He used the neutral theory as the basis for several of his finest articles.

In particular, he and his statistician colleague John Haigh developed and analyzed the concept of "hitchhiking" (Maynard Smith and Haigh 1974), in which the spread of an advantageous mutation reduces variation at linked neutral loci. This idea has become very important for interpreting data on natural variation in DNA sequences, following the discovery that DNA sequence variation is often greatly reduced in regions of the genome with low frequencies of genetic recombination (Andolfatto 2001). There is also increasing evidence for signatures of hitchhiking events in regions of the genome with normal levels of recombination in a variety of species, including humans (Sabeti *et al.* 2002). The two Johns also made a very perceptive early contribution to human molecular variation, using population data on human hemoglobin variants in Europe collected by Hermann Lehmann's group (Lehmann and Carrell 1969) to show that the amount of variation in northern European populations is inconsistent with neutral equilibrium and that there must have been a severe population bottleneck (Haigh and Maynard Smith 1972). Millions of dollars that have been spent on human SNP data sets confirm this conclusion (Marth *et al.* 2004).

John contributed extensively to the wave of theoretical work on the evolution of sex and genetic systems that was initiated in the late 1960s, which freed this field from its long domination by the species-level advantage theories of Darlington (1939) and Stebbins (1950) and replaced these by arguments based on selection among individuals within populations. In particular, he drew attention to the paradox of the "cost of sex": the fact that a mutant that arises in a sexual species with two

John Maynard Smith (right) with Sewall Wright in 1980. Wright was visiting the University of Sussex after receiving the Darwin Medal from the Royal Society. The photograph was taken by Jim Bull.

sexes and causes females to produce daughters asexually will double in frequency each generation (Maynard Smith 1971). Although the idea had been suggested by others previously (*e.g.*, White 1945), John was the first to perceive the profound difficulty it posed for explaining the prevalence of sexual reproduction among eukaryotes. He summed up the state of the field in his 1978 book *The Evolution of Sex* (Maynard Smith 1978), which is still the best overview available.

John's most influential single contribution was his development, initially in collaboration with George Price, of the concept of the evolutionarily stable strategy (ESS). This invokes the principle that, for a trait value to represent an equilibrium with respect to natural selection, a necessary condition is that all possible deviant trait values are at a selective disadvantage when introduced at a low frequency into a population whose members initially all have the trait value in question. Unless fitnesses depend on the frequencies of competing phenotypes or genotypes, the ESS corresponds to the selective optimum. But in many cases, such as sex ratios or behavioral traits governing social interactions, frequency-dependent fitnesses are inherent in the biological context.

Determination of the outcome of selection by calculating trajectories of gene frequencies or of mean trait values using quantitative genetic models would be tedious and usually intractable as far as simple mathematical solutions are concerned. By simply testing whether rare variants are kept out of the population, the ESS approach allows informative results to be obtained in complex situations, *e.g.*, the well-known result that a 1:1 allocation of resources between male and female offspring is favored by selection on nuclear genes in a randomly mating population. While this approach had been used earlier, notably by Fisher (1930) and Hamilton (1967), John's work developed the underlying logic explicitly and showed how it could be applied to many evolutionary problems, which had previously been regarded as impossibly difficult to solve with simple theoretical models. While there are clearly limitations to the ESS method, especially in cases where the genetics of a trait constrain the outcome of selection, it has proved to be an immensely useful tool. Over the past 30 years, a large theoretical and empirical literature has appeared, applying ESS methods to a very wide range of biological phenomena. For instance, the prediction by ESS methods of sex ratios in haplodiploid species, where they are readily controlled by maternal decisions about fertilizing eggs, is one of the real success stories of evolutionary biology, in terms of relating theory to data (West *et al.* 2002). John's main contributions to ESS theory are summarized in his 1982 book (Maynard Smith 1982).

John was very interested in general ideas in biology and contributed to debates on such topics as group selection *vs.* kin selection (he coined the latter term: Maynard Smith 1964), sympatric speciation (Maynard Smith 1966), punctuated equilibrium (Maynard Smith 1983), and the evolutionary role of developmental constraints (Maynard Smith *et al.* 1985). With Eörs Szmathmáry, he developed a set of frankly speculative ideas about the major events in biological evolution (from the evolution of life itself and the evolution of cells to the evolution of language), described in their 1995 book *The Major Transitions in Evolution* (Maynard Smith and Szmathmáry 1995). He also published three excellent textbooks: *Mathematical Ideas in Biology* (Maynard Smith 1968b), *Models in Ecology* (Maynard Smith 1974), and *Evolutionary Genetics* (Maynard Smith 1989).

After his formal retirement in 1985, John turned his attention to the analysis of data on molecular variation and evolution in bacteria, collaborating with Brian Spratt's microbial genetics group, then at Sussex. This work, along with that of several other bacterial population geneticists, has led to the realization that there is much more exchange of genetic information among bacterial cells in nature than was formerly believed (Maynard Smith *et al.* 1993). John's recent work involved the development of methods for interpreting patterns of DNA sequence variation in populations with sporadic and patchy recombinational exchange (Maynard Smith and Smith 1998; Smith *et al.* 2003). This has important implications for understanding bacterial pathogenicity (Maynard Smith *et al.* 2000), as well as being of great intrinsic interest. It is obviously very unusual for someone to remain at the frontline of research for nearly 20 years after retirement.

In the past two years of his life, John suffered increasingly but uncomplainingly from the effects of mesothelioma, but continued working until the very end. Despite his physical frailty, he spoke briefly at the December 2003 meeting of the United Kingdom Population Genetics Meeting and gave a characteristically lucid and entertaining talk on bacterial population genetics. Many of those present felt that this was their last chance to hear him give a public lecture, which unfortunately proved to be the case. John's breadth of interests and achievements, combined with his engaging personality, were unique and will be sadly missed.

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