Book Reviews

Accounting for Sexual Reproduction

The Evolution of Sex. JOHN MAYNARD SMITH. Cambridge University Press, New York, 1978. x, 222 pp. Cloth, $21.95; paper, $6.50.

Nearly 50 years ago, Fisher provided the most coherent justification yet given of the "genetical theory of natural selection," the theory of evolution by natural selection discriminating between "random" variants. As always, doubt had centered on whether random mutation could supply sufficient favorable variation to fuel the evolutionary process and whether the seeming perfection of adaptation was consistent with so "chancy" a cause. For Fisher, sex countered both objections. In the absence of change, environmental or genetic, selection tends to eliminate recombination: no use for sex here. Indeed, the only use of sex is to enable the simultaneous fixation of different favorable mutations. Sex, and recombination, thus seemed to testify both to an abundant stream of favorable mutations and to a genetic system organized to facilitate natural selection. Because in any other view of evolution sex was simply a mystery, Fisher's explanation seemed a triumphant justification of a mechanistic, testable, evolutionary theory.

However, Fisher's explanation soon lost favor. A full mathematical treatment was too difficult for him, as it has been for anyone since. The difficulty of quantifying the advantage of sex and of deciding how much it benefited the individual as well as the species (a point on which Fisher was undecided) discredited the theory, especially after people began to understand the cost of sex. Moreover, Fisher implicitly assumed that gene action was more or less additive, that one could predict the fitness of a genotype by adding the contributions of its component genes, an assumption probably crucial to his theory. Sewall Wright argued that nonadditive interactions between genes were responsible for all that was interesting about evolution, its multiplicity of adaptive peaks and blind alleys. Moreover, the biochemistry of gene action seems to guarantee that each gene affects the expression of all others in a manner that leaves no room for the additive assumptions of "beanbag genetics."

Maynard Smith has now presented his assessment of the controversy over the evolution of sex. It is a most interesting book. He is not quite sure what maintains sex, and his uncertainty of mind is reflected in the poor organization of the book: it seems to have lacked an editor. On the other hand, he has thought long and dispassionately on the subject, and the book reflects his care and objectivity.

The root of the problem is the "50 percent cost of sex." Maynard Smith explains this cost very clearly in his introduction, in the midst of outlining the rest of the book. His chapters on hermaphroditism, anisogamy, and sex ratio help explain the provenance of this cost. He shows how selection leads most populations to spend as much effort on male as on female functions, whether this means raising as many male as female offspring, as in gonochores, or spending as much effort seeking to fertilize the eggs of others as making eggs, as in hermaphrodites. The theory of anisogamy explains why sperm are so much smaller than eggs, why one gamete should sit and wait with the baggage while the other travels fast and light to seek her out: the evolution of anisogamy suggests some costs of sex that usually go unmentioned. A sperm is so small that a fertilization is genetically a "free good," and thus the object of a competition that rarely increases the number or the quality of the offspring. The cost of sex is the offspring that are sacrificed by wasting effort on this competition.

How might the cost of sex be overcome? Sex is useless unless either the genotype or the environment is changing. Moreover, in the absence of new mutations, environmental change rarely favors recombination. George Williams has proposed that for organisms like trees, where many seedlings from rather few parents compete for a gap sufficient for one adult, a sexual parent, whose offspring all differ, has as many chances as it has offspring in that gap of producing the best genotype there, whereas an asexual parent, whose offspring are all alike, has only one chance at the gap, however many seedlings it leaves there. This explanation of sex, however, cannot be general.

Maynard Smith thus ends by agreeing with Fisher: nearly the only possible use of sex is to enable the simultaneous fixation of different new mutations. In an asexual population, a favorable new mutant will succeed only if it occurs in the one individual whose descendants will spread through the population. If the population is genetically uniform save for this one mutant, the mutant would have the same chance of success as if the population were sexual. The greater the genetic variation in the asexual population, the less likely this mutant is to be part of its best genotype. Sex allows a mutant to be tested in many genotypes and to be selected more nearly according to its average contribution to fitness rather than according to the fitness of the genotype where it originates. Maynard Smith remarks that if a mutant occurs frequently it samples many genotypes: sex is useful only for those mutants that are so new that they occur only sporadically, rather than at a definite rate. One may also remark that sex makes sense only if the fitness of a genotype can be predicted from the contributions of its genes: if good genes do not make good genotypes, sex is useless. Sex presumes additivity.

Given that sex facilitates evolution, what maintains it? Maynard Smith shows that selection favors sexual species of animals, as Van Valen inferred earlier for plants. Asexual forms are rarer in the tropics, where plants and animals are more likely to be running coevolutionary races with predators and competitors. Sexual and asexual forms occasionally exist in the same population, suggesting that in these populations, at least, sex confers sufficient advantage on individuals to overcome its cost. Maynard Smith also shows that, since recombination rate is controlled by selection within populations, some individual advantage accruing to recombination must balance the pressures to congeal the genotype.

What is this advantage? Maynard Smith shows mathematically that, as Fisher once hinted, a gene enhancing recombination would benefit substantially from the spread of a new favorable recombinant, if it were closely enough linked to that recombinant to "hitch a ride on its coattails." He considers the analogy with alleles increasing mutability, which "hitch rides" from the spread of new favorable mutants to which they are closely linked. Mutator alleles create many mistakes, but each mistake kills only one mutator, whereas a good mutant can spread its mutator right through a population. If Maynard Smith is right, alleles increasing recombination rate affect recombination only in loci very near their own, rather than in the genome as a whole. If correct (and even Maynard Smith is not sure), this view has startling implications for the efficacy of small selective differentials. It does not seem to explain why genes come in many chromosomes.

In sum, this small book about sex bears on fundamental issues in evolutionary theory. If Maynard Smith is right, the availability of suitable mutations must limit evolutionary rate, at least at times: paleontologists dispute this, citing the rapid evolution of elephants, with their long generations. If he is right, genetic variation must be largely additive, and very small selective differentials must be effective: both are topics of heated and emotional debate. For all its weighty implications, this book is pleasant, even charming, rich with interesting asides, admirable for its balanced perspective.

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Nuclear Transplantation

Cloning. Nuclear Transplantation in Amphibia. A Critique of Results Obtained with the Technique, to Which Is Added a Discourse on the Methods of the Craft. ROBERT GILMORE MCKINNELL. University of Minnesota Press, Minneapolis, 1978. xii, 320 pp., illus. $22.50.

The title of this book may capture the public fancy, but the subtitle more accurately describes its contents. Cloning is one use of nuclear transplantation, but there are many others. Nuclear transplants have proved valuable in the analysis of histocompatibility reactions, in distinguishing genetic from epigenetic determinants of sex differentiation, in studies of pigmentation patterns and serum proteins, and in the examination of nucleocytoplasmic interactions within and between species. In addition, polyploid animals have been produced by nuclear transplantation. These uses, however, are not the central subject of this book. Rather, the book is primarily concerned with whether the genomes of differentiated cells are equivalent to one another and whether a nucleus from a differentiated cell can replace the zygote nucleus and lead to normal development. This is one of the major questions of developmental biology, and has been for many decades. Although the answer is not in yet, in recent years the notion that the nuclei of differentiated cells are genetically equivalent has been promulgated both within the scientific community and to the lay public. Moreover, it is commonly believed that the implantation of differentiated nuclei into enucleated eggs leads frequently to perfectly normal development. This is not the case. The cloning of adults is not practical at the present time.

McKinnell carefully examines all of the evidence relevant to cloning in Amphibia and provides the reader with a well-balanced account. His critical, scholarly review of the evidence raises questions that everyone, particularly developmental biologists, should consider seriously. With two or three possible exceptions, the results he describes of nuclear implantation into enucleated eggs demonstrate that adult nuclei become irreversibly differentiated. All investigators agree that, in general, the older the cell from which a nucleus is taken the smaller the probability that normal development will ensue after the nucleus is transplanted into an enucleated egg. This is true for *Rana pipiens* and for *Xenopus*, the two principal amphibians used in these experiments. Moreover, as McKinnell properly brings to attention, the particular spectrum of abnormalities produced in embryos developing after nuclear transplantation is related to the source of the nucleus, whether from endodermal, mesodermal, or ectodermal cells. Recycling the nuclei of such abnormal embryos through new generations of replication, by transplantation into eggs, generally results in a reappearance of a similar syndrome of abnormalities. Such results clearly suggest that during development the nuclei become restricted in the variety of gene programs that can be expressed. Nevertheless, the number of cell types that can be produced after transplantation of such nuclei is impressive and much greater than the original cell was destined to produce.

McKinnell examines in detail the specific examples or exceptions that seem to indicate that the nuclei from differentiated cells retain their totipotency. He points out that in no case has a truly adult nucleus taken from an adult animal and transplanted into an enucleated egg ever resulted in the development of a normal adult individual. However, nuclei from truly adult cells after a period of growth in tissue culture or after several cycles of replication in eggs have been successfully transplanted and have given rise to a few adults. More often, though, even these nuclei give rise to abnormal development.

McKinnell properly points out that generalizations in biology are usually based on the mass of evidence rather than on the few exceptions, but in the case of the equivalence of the nuclei of adult cells the exceptions seem to predominate in the thinking of both the public and most developmental biologists. The overwhelming mass of evidence suggests to this reviewer, as it does to McKinnell, that nuclei do become irreversibly differentiated during the development of an organism and that they are not able to replace the zygote nucleus when transplanted into an egg. The few exceptions seem to be just that—exceptions. It is quite possible that a few cell types or a few cells in an adult may retain their totipotency, or that under unusual conditions the differentiated state of the genome can be reversed, but such reversal is rare. Its rarity, even after many cycles of chromosomal replication, implies that the DNA itself is changed during cell differentiation.

Although it is not discussed by McKinnell, an increasing amount of evidence suggests that chromosomes are not so fixed in structure as we once believed. Consider the evidence concerning the differential replication of parts of the DNA during polytenization of *Drosophila* chromosomes and the changes in the heterochromatin of *Cyclops* chromosomes, the existence of "jumping genes," the well-studied insertion of viral DNA into chromosomes, the production of antibody protein molecules involving the sequential reading of DNA occupying different sites in the genome, and the existence of nontranslated DNA inserts into structural genes. This evidence all points to a modifiability of chromosome structure. Perhaps programmed changes in structure also occur as the basic change leading to stable cell differentiation, with parts of the genome permanently on and other parts permanently off. Nothing but the DNA seems to be left to account for the failure of replicating transplanted nuclei to bring about normal development. All molecules associated with the DNA in the chromosomes would have been diluted out during replication after transplantation of differentiated nuclei. Only