Brian Charlesworth

Why bother? The evolutionary genetics of sex

It is an astonishing finding – derived from more than a century of painstaking research into the cellular basis of reproduction in a huge variety of organisms – that sex is the most prevalent mode of reproduction among the great division of life (the *eukaryotes*), which includes animals, green plants, algae, fungi, and protozoa.[1]

To geneticists, sexual reproduction is the formation of a new individual from a cell (*zygote*) produced by the union of two different cells (*gametes*). In the case of animals, the gametes are an egg and a sperm. When the resulting individual reproduces, its gametes contain a patchwork of genetic information derived from each of the two gametes that generated it (a process called *recombination*). Recombination happens regardless of whether the zygote divides to form many separate single-celled individuals (as in simple organisms, like yeast), or whether the daughter cells remain associated to produce a complex multicellular organism, like an oak tree or a person. In contrast, with asexual reproduction, a single parent produces offspring that are usually exact genetic replicates of itself.

We have good grounds for believing that regular sexual reproduction evolved very early in the history of the eukaryotes, and that most instances of asexual reproduction among them are the result of subsequent evolution. All mammals and all birds reproduce sexually, but only

Brian Charlesworth, a Foreign Honorary Member of the American Academy since 1996, is Royal Society Research Professor at the University of Edinburgh. He is the author of "Evolution in Age-Structured Populations" (1980) and coauthor of "Evolution: A Very Short Introduction" (2003) in addition to numerous journal articles. His recent research focuses on molecular evolution and variation, the evolution of genetic and sexual systems, and the quantitative genetics of life-history traits.

1 I thank Deborah Charlesworth for her comments on the manuscript. J. Maynard Smith, *The Evolution of Sex* (Cambridge: Cambridge University Press, 1978); G. Bell, *The Masterpiece of Nature* (London: Croom-Helm, 1982). A regular cycle of sexual reproduction is absent from the other division of life (*prokaryotes*), which encompasses bacteria and viruses. There are, however, often detectable exchanges of pieces of genetic information between individuals within prokaryote populations, involving a variety of processes that act as a substitute for sex. See J. Maynard Smith, N. H. Smith, M. O'Rourke, and B. G. Spratt, "How Clonal are Bacteria?" *Proceedings of the National Academy of Sciences* 90 (1993): 4384 – 4388.

a few dozen species of reptiles, amphibia, and fish reproduce asexually.[2] Similarly, only about 0.1 percent of the over three hundred thousand species of flowering plants are thought to reproduce asexually.[3]

Most asexual species seem to be of recent evolutionary origin, since they have close sexual relatives and evidently have not had time to proliferate into diverse forms.[4] There are only one or two cases where an asexual group of multicellular organisms seems to have been around long enough to diversify, most notably the Bdelloid rotifers. These minute animals, which live in transient freshwater habitats (such as drops of water on mosses), have been classified into several hundred species on the basis of anatomical and molecular differences among them. No males have ever been found – and study of their genomic makeup supports the view that they represent an ancient asexual group, many millions of years old.[5] Nonetheless, the Bdelloid rotifers represent the exception, and not the rule.

Asexuality seems to be more common among single-celled eukaryotes, like protozoa, but the difficulty of studying their life cycles in nature makes it hard to exclude the cryptic occurrence of sex. And even so, regular sexual reproduction is widely distributed among single-celled eukaryotes. The common features of the cellular and molecular mechanisms involved in sexual reproduction in these and multicellular eukaryotes show that the cellular machinery involved in sexual reproduction probably had a single origin around the time of the evolution of the first eukaryotes, about two billion years or so ago.

The big question about sex is: why bother? It seems much simpler for organisms to produce offspring without going to the trouble of making gametes, which in the case of animals like ourselves can only meet each other as a result of elaborate behavioral and anatomical adaptations. Why should there be males? Why don't women simply produce babies in the same way as Bdelloid rotifers: an egg is generated by the same process of cell division that makes the cells of the rest of the body; it then develops into an offspring. Indeed, why not just split in half and regenerate the missing half, as some flatworms do?

These questions are not new: as Edward Gibbon maliciously pointed out, the early fathers of the Christian church were sorely troubled by the question of why God had not provided human beings with "some harmless mode of vegetation" with which to propagate themselves. Their objections to sex were, of course, purely moral. But even the amoral intellectual framework of neo-Darwinian evolutionary biology has raised a searching question concerning the prevalence of sex – or, more specifically, about its so-called twofold cost, which John Maynard Smith brought to the attention of biologists in 1971.[6] One can

2 Maynard Smith, *The Evolution of Sex*; Bell, *The Masterpiece of Nature*.

3 A. M. Koltunow, "Apomixis – Molecular Strategies for the Generation of Genetically Identical Seeds Without Fertilization," *Plant Physiology* 108 (1995): 1345 – 1352.

4 Maynard Smith, *The Evolution of Sex*; Bell, *The Masterpiece of Nature*.

5 I. Arkhipova and M. Meselson, "Deleterious Transposable Elements and the Extinction of Asexuals," *Bioessays* 27 (2005): 76 – 85.

6 J. Maynard Smith, "The Origin and Maintenance of Sex," in G. C. Williams, ed., *Group Selection* (Chicago: Aldine-Atherton, 1971), 163 – 175.

understand this cost by considering a sexual population with an equal number of males and females in each generation. Now imagine that within this population a mutation arises that causes females to reproduce asexually by means of all-female offspring. If the mutation has no other effect, the average number of offspring per mother will be unchanged. The mutant females will thus produce twice as many daughters as their sexual competitors. A simple calculation shows that the frequency of the mutants within the female population will double each generation while they are still rare, and that they will spread rapidly through the population, replacing the sexual females and causing the extinction of males.

We can make a similar but slightly more complicated argument for hermaphrodite organisms, which include most flowering plants and many marine invertebrates. Here the benefit of a mutation that produces asexual eggs is closer to one-and-a-half-fold than twofold – still a substantial advantage.[7] A mutation that causes fertilization of the egg cells by the male gametes of the same individual, without significantly reducing the individual's ability to fertilize others' eggs, also has a considerable advantage.[8] But though many hermaphrodites can fertilize themselves, the majority of hermaphrodite species reproduce primarily by matings between separate individuals (*outcrossing*).

The results of these exercises in population-genetic calculations show how surprising it is that sexual species are so common and have not rapidly evolved either asexual reproduction or (in the case of hermaphrodites) complete self-fertilization. The question of why hermaphrodites avoid self-fertilization has turned out to be the easier one to answer, as was shown by Charles Darwin himself. The answer lies in the phenomenon of *inbreeding depression*: the viability and fertility of the progeny of matings between close relatives are usually much lower than those of the progeny of matings between unrelated individuals. Darwin compared experimentally produced individuals, which had been created either by self-fertilization or outcrossing in many different species of plants. He found an almost universal tendency for the performance (survival, size, seed production) of the self-fertilized progeny to be much worse than that of the outcrossed progeny.[9] He concluded, rightly, that natural selection disfavors self-fertilization. Subsequent calculations have shown that a reduction of about 50 percent in fitness to self-fertilized progeny will prevent the spread of a mutation that causes self-fertilization.[10] Much larger reductions are often observed in outcrossing species.[11] Oddly, until the 1970s, botanists working on

7 D. G. Lloyd, "Benefits and Handicaps of Sexual Reproduction," *Evolutionary Biology* 13 (1980): 69 – 111; B. Charlesworth, "The Cost of Sex in Relation to Mating System," *Journal of Theoretical Biology* 84 (1980): 655 – 671.

8 R. A. Fisher, "Average Excess and Average Effect of a Gene Substitution," *Annals of Eugenics* 11 (1941): 31 – 38.

9 C. R. Darwin, *The Effects of Cross and Self Fertilisation in the Vegetable Kingdom* (London: John Murray, 1876).

10 Lloyd, "Benefits and Handicaps of Sexual Reproduction"; Charlesworth, "The Cost of Sex in Relation to Mating System."

11 C. Goodwillie, S. Kalisz, and C. G. Eckert, "The Evolutionary Enigma of Mixed Mating Systems in Plants: Occurrence, Theoretical Explanations and Empirical Evidence," *Annual Reviews of Ecology, Evolution and Systematics* 36 (2005): 47 – 79; S. C. H. Barrett, "The Evolution of Plant Sexual Diversity," *Nature Reviews Genetics* 3 (2002): 274 – 284.

the mating systems of plants largely ignored Darwin's explanation, perhaps because they failed to grasp the implications of population genetics for understanding evolution.

This explanation of the prevalence of outcrossing raises two further questions. First: why are all hermaphrodite species not highly outcrossing? Second: what causes inbreeding depression? There are, indeed, many examples of hermaphrodite species that reproduce nearly exclusively by self-fertilization, including the nematode worm *Caenorhabditis elegans* and the plant *Arabidopsis thaliana*, two of the most important 'model organisms' used in the study of cellular and developmental processes. Just as with asexuality, highly inbred species seem often to have originated fairly recently in evolutionary time from outcrossing relatives.[12] This is true of the two I just mentioned.

As was also clear to Darwin, the probable cause of a transition from outcrossing to inbreeding is difficulty in obtaining mates: if you cannot find someone else to fertilize your eggs, it is better to fertilize them yourself, even if the offspring are of inferior quality. This situation can arise when a species invades a new habitat where population density is low. As expected on this idea, oceanic island populations are rich in inbreeders compared with animals and plant populations on the mainland from which the colonizing species came. Many other geographical patterns associated with breeding systems support this interpretation.[13] Thus, it seems likely that inbreeding depression will generally maintain outcrossing, unless fertilization success in outcrossing falls below a threshold value, underneath which there is a net reproductive advantage to inbreeding.

Darwin, however, did not have a convincing explanation for inbreeding depression. But modern genetics has led to the realization that inbreeding makes individuals *homozygous*. In other words, the copy of a given gene received through the egg is identical to that received through the sperm. If this gene carries a harmful mutation, which happens at a low but not entirely negligible frequency, the offspring will receive only the mutant type. In an outcrossing population, on the other hand, a rare harmful mutation will nearly always be carried in a single dose, since the copy of the gene in the other gamete that forms an individual will usually be normal.

The exposure of harmful mutations in a gene in double dose, with no normal copy present, is thought to be a major source of inbreeding depression.[14] Although such mutations are individually very rare within a population, there are so many genes in the genome (about twenty-five thousand in the case of humans) that, collectively, we all carry several hundred harmful mutations (different ones are present in different people).[15] Most of these have very small effects on fitness, but one or two among the mutations an individual carries can be lethal when made homozygous, as experiments on the effects of inbreeding in fruit flies and fish have demonstrated.[16]

12 Ibid.

13 Ibid.

14 B. Charlesworth and D. Charlesworth, "The Genetic Basis of Inbreeding Depression," *Genetical Research* 74 (1999): 329–340.

15 S. Sunyaev et al., "Prediction of Deleterious Human Alleles," *Human Molecular Genetics* 10 (2001): 591–597.

16 M. J. Simmons and J. F. Crow, "Mutations Affecting Fitness in *Drosophila* Populations,"

We therefore have a well-supported theory of what controls evolutionary transitions from outbreeding to inbreeding in hermaphrodites. Similar considerations probably apply to the less intense forms of inbreeding found in some species with separate sexes. We now need to ask if there are factors that can overcome the twofold cost of sex, and maintain sexual reproduction against mutations causing asexual reproduction, analogous to the effect of inbreeding depression in preventing the spread of mutations causing inbreeding. There has been a long and hard search for these, and it is fair to say that there is still no consensus about which of them is the most important.

It is worth making a couple of points before discussing this question in detail. First, we know that mammals cannot reproduce asexually, because a mammal needs both a paternal and a maternal complement of genes in order to develop successfully from an egg. This is because of a phenomenon known as *imprinting*: some genes are temporarily altered chemically during gamete formation in such a way that they only produce functional products if they enter the zygote through the sperm, others only if they enter through the egg.[17] While only a small minority of the total set of genes is imprinted, failure to express both copies of some of the imprinted genes results in death. It is therefore impossible for a mammalian female to reproduce like a Bdelloid rotifer. We need look no further for an explanation of mammalian sexuality than this developmental requirement. But while the reasons for imprinting are of great interest, and a matter of ongoing debate, they do not concern us here. Imprinting does not provide a universal explanation of the maintenance of sex, since other groups of animals and plants do not have imprinting and contain many examples of asexual reproduction among them.

A second point is that the problem of a large cost of sex does not apply to the origin of sex. The comparative evidence already discussed suggests that sexual reproduction first evolved among single-celled eukaryotes, which lacked any differentiation of gametes into male and female, i.e., all gametes were of approximately equal size, as is the case today in many single-celled organisms.[18] With no asymmetry of gamete size, there is only a slight automatic advantage to asexual reproduction.[19] This means that a small advantage to a genetic variant conferring the ability to reproduce sexually would allow it to spread. In principle, therefore, we can explain the origin of sex by identifying the sources of such an advantage.

Annual Review of Genetics 11 (1977): 49 – 78; A. McCune et al., "A Low Genomic Number of Recessive Lethals in Natural Populations of Bluefin Killifish and Zebrafish," *Science* 296 (2002): 2398 – 2401.

17 I. M. Morison, J. P. Ramsay, and H. G. Spencer, "A Census of Mammalian Imprinting," *Trends in Genetics* 21 (2005): 457 – 465.

18 The distinction between male and female gametes is an ancient one, but it is not a requirement for the sexual fusion of gametes. Once sex evolved, there was probably selection pressure in many (but not all) groups for some individuals to produce numerous, small, mobile gametes (the male gametes), and others to produce a few, large, immobile ones (female gametes). See Maynard Smith, *The Evolution of Sex*; M. G. Bulmer and G. A. Parker, "The Evolution of Anisogamy: A Game-Theoretic Approach," *Proceedings of the Royal Society B* 269 (2002): 2381 – 2388.

19 Maynard Smith, *The Evolution of Sex*; Charlesworth, "The Cost of Sex in Relation to Mating System."

We still have to solve the problem of how sex is maintained in the face of its cost in species with male and female gametes. One solution is to appeal to the differential extinction of asexual populations.[20] Imagine the following situation: we have a set of sexually reproducing species, among which from time to time a member is successfully invaded by an asexual mutant. However, the asexual species do not do as well as their sexual rivals, in terms of their long-term ability to survive extinction, and so they eventually disappear. With the right balance between this species-level disadvantage and the rate of conversion from sex to asex, the majority of species will remain sexual.

This explanation fits many of the broad patterns of the distribution of asexuality. Similar patterns apply to highly inbreeding species; once a species has become highly inbreeding, it behaves in many ways as though it is asexual. This is because individuals that are homozygous for most of their genes produce offspring that are genetically nearly identical to themselves. It seems that the long-term evolutionary fate of both inbreeders and asexuals may be such that extinction is much more likely for them than for their outcrossing, sexual relatives.[21]

Evolutionary biologists are, for good reason, rather hostile to the idea that selection among species plays a major role in evolution, compared with selection among individuals. As R. A. Fisher once wrote, "Unless individual advantage can be shown, natural selection affords no explanation of structures or instincts which appear to be beneficial to the species."[22] However, even Fisher was prepared to make an exception for "sexuality itself" and proposed an explanation for the maintenance of sex based on the inability of asexual species to evolve as rapidly as sexual rivals.[23]

It may, therefore, be sufficient to look for factors that confer a quite modest advantage to sexual reproduction, not necessarily large enough to prevent invasion by an asexual mutant, but which cumulatively increase chances of survival in the long run. There is no shortage of candidates; indeed, as the Grand Inquisitor said in *The Gondoliers*, "[T]here is no probable, possible shadow of doubt – no possible doubt whatever . . . " that we have identified the major candidates. As in his case, however, we do not know which is the right one, and of course the different possibilities are not mutually exclusive. I will only briefly survey some of the major theories under discussion, as well as some of the relevant empirical evidence.[24]

The major advantage of sexual reproduction is the fact that genetic recombination can only occur with sex. Briefly mentioned at the beginning of this essay, this process now needs to be defined more precisely. Gametes are hap-

20 Maynard Smith, *The Evolution of Sex*.

21 Ibid.; Barrett, "The Evolution of Plant Sexual Diversity."

22 Fisher, "Average Excess."

23 R. A. Fisher, *The Genetical Theory of Natural Selection. A Complete Variorum Edition* (Oxford: Oxford University Press, 1999).

24 Maynard Smith, *The Evolution of Sex*; Bell, *The Masterpiece of Nature*; R. E. Michod and B. R. Levin, eds., *The Evolution of Sex* (Sunderland, Mass.: Sinauer, 1988); N. H. Barton and B. Charlesworth, "Why Sex and Recombination?" *Science* 281 (1998): 1986 – 1990; S. P. Otto and T. Lenormand, "Resolving the Paradox of Sex and Recombination," *Nature Reviews Genetics* 3 (2002): 256 – 261.

loid cells – they contain only one copy of each gene in the genome. The genes are parts of DNA molecules called *chromosomes*, and each chromosome carries a set of hundreds or thousands of genes concerned with different cellular functions. (In the human genome, there are twenty-three different chromosomes in an egg or a sperm cell.) In a primitive unicellular organism, such as the green alga *Chlamydomonas*, the two gametes fuse to form a zygote. The zygote is thus *diploid*, i.e., it contains two sets of chromosomes, one from each parental gamete. After a resting phase, the zygote then undergoes two cell divisions called *meiosis*, but each chromosome only undergoes one round of division. The number of chromosomes is thereby reduced to the haploid number. If this did not happen, chromosome numbers would double at each cycle of sexual reproduction.

An extraordinary thing happens at the first division of meiosis: each pair of maternal and paternal chromosomes comes together, and the partners line up beside each other. A number of breaks occur at the same place on each partner, and these are repaired in such a way that the material on each partner is now partly maternal and partly paternal, in a reciprocal pattern. The resulting products then part from each other at the first division of the cell. This is followed by the second division, resulting in four haploid cells, in which each chromosome is made up of segments of paternal and maternal material. These cells go on dividing by the normal cell division process, in which chromosomes split into two daughter chromosomes. Eventually, these differentiate into gametes, which fuse with other gametes to restart the cycle.

This basic pattern is found throughout the single-celled eukaryotes, forming a major part of the evidence for the ancient origin of sex. Much the same holds true for animals like ourselves, except that with us the diploid zygote divides by normal cell divisions to produce the diploid cells that make up most of our body. Meiosis is postponed until the production of eggs or sperm in the reproductive organs.

Why bother?

Accompanying the process of sexual fusion of cells is, therefore, a process of mingling of material from maternal and paternal chromosomes. This is why no two people in the world are exactly alike genetically, except for identical twins. To see this, consider the case of a mating between two *Chlamydomonas* gametes, which differ at two different locations on a chromosome. One gamete is *AB* and the other is *ab*, where the alternatives at each site are *A* versus *a* and *B* versus *b*, respectively. The zygote will contain both *AB* and *ab*. In the absence of recombination, the gametes derived from this zygote will be either *AB* or *ab*, with equal probability. But with recombination, we will also see the combinations *Ab* and *aB*. The frequency with which these are found is the *recombination frequency* for the two locations – and it is higher, the larger the distance between them on the chromosome.

Geneticists discovered recombination by carrying out crosses in which they could detect the presence of the variants at the two locations because they affected visible properties of the individuals carrying them. We can measure recombination frequencies by counting the numbers of offspring of the four different types. Exactly the same holds for humans as for *Chlamydomonas*, except that our diploidy and small family sizes make it much harder to measure recombination. Genes at distant locations on the same chromosome, and genes on differ-

ent chromosomes (which behave independently of each other during meiosis), have recombination frequencies of 50 percent. Locations very close to each other on a human chromosome typically have a recombination frequency of around one in one hundred million.

Recombination through sexual reproduction allows the production of all possible combinations of variants at different locations in the genome. This has some staggering implications. Suppose we have one thousand locations in the genome, each with two different variants in the population. The number of possible types of gametes that can exist is then 2 raised to the power of 1000, i.e., approximately 10 followed by 300 noughts. It is currently estimated that there are about six million variants at chromosomal sites in human populations, so the true number of combinations is something like 10 followed by 1.8 million noughts.

But if there were no sex and no recombination, new mutations would remain associated with whatever genetic variant they happened to be combined with originally. If in our example the population were initially *ab*, a mutation to *A* would create *ab* and *Ab*. The population is likely to be mostly *ab* for a long time, so that a mutation from *b* to *B* would probably arise in an *ab* gamete, giving just three types in the population (*ab*, *Ab*, and *aB*). The combination *AB* can be generated only by a (very unlikely) further mutation event, or by recombination in zygotes that carry both *aB* and *Ab*. This is not possible if there is no sexual reproduction, or if the population is highly inbred (in the latter case, nearly all zygotes carry identical pairs of gametes, so that recombination has no effect). Indeed, populations that reproduce asexually, or by very close inbreeding, characteristically show far fewer combinations of variants at different locations than do sexual populations, just as this argument predicts.

Now, if *A* and *B* represent variants that confer higher fitness on their carriers, the combination *AB* is likely to be the fittest of the four, yet it is unlikely to be produced in the absence of sex and recombination. This suggests that these facilitate the action of natural selection, by speeding up the production of selectively favorable combinations of genetic variants. This idea was first clearly stated around 1930 by R. A. Fisher[25] and H. J. Muller,[26] and still forms the core of much thinking about the evolutionary advantage of sex.

This effect can be realized in numerous different situations. One is when a population faces selection pressure to adapt to a new environment. Under a wide range of circumstances, sex and recombination then help to accelerate adaptation. Moreover, mathematical models demonstrate that genetic factors that influence the frequency of recombination also increase in frequency in the population under these conditions, because they become associated with the favorable gene combinations they create.[27] Environments that continually change – such as those created by interactions between hosts and their parasites, which are constantly adapting to each other – are especially likely to create selection pressures of this kind. Some have suggested that selection pres-

25 Fisher, *The Genetical Theory of Natural Selection*.

26 H. J. Muller, "Some Genetic Aspects of Sex," *American Naturalist* 66 (1932): 118 – 138.

27 Barton and Charlesworth, "Why Sex and Recombination?"; Otto and Lenormand, "Resolving the Paradox of Sex and Recombination."

sures from parasites may be the major factor favoring sex.[28]

The possibility that adaptation to a new environment promotes increased recombination has been demonstrated by experiments involving selection for traits such as DDT resistance in flies: these have shown increases in recombination frequencies in addition to the trait under selection.[29] A recent experiment on flour beetles revealed a similar effect of selection for resistance to a parasite.[30] Furthermore, experiments where a novel environment challenges *Chlamydomonas* populations show that populations that are allowed to reproduce sexually evolve faster than populations that can only reproduce asexually.[31] Therefore, a body of experimental data supports the plausibility of this type of mechanism, although it falls short of proving that it is indeed the main cause of the origin and maintenance of sex.

Recombination also allows more efficient removal of harmful mutations from the genome. While natural selection usually keeps these mutations at very low frequencies, again the sheer number of genes in the genome ensures that the total number of such mutations in the population is very large. Mathematical models demonstrate that it is harder for the population to remove deleterious mutations from the genome in the absence of recombination, creating a selection pressure to maintain recombination frequencies at a nonzero level.[32] These models predict that if recombination stops, harmful mutations would eventually become more prevalent, even spreading throughout the species.[33]

The Y chromosomes of many species with separate sexes, including humans, provide a test case. Here, males have a Y chromosome and an X chromosome, which pair up at meiosis but only recombine over a very small portion of their length. Females have two X chromosomes, which recombine normally with each other at meiosis. In mammals, the Y carries a gene that causes individuals to develop as males; in the absence of an intact Y chromosome, an embryo will develop as a female. Thus, the Y chromosome determines gender. But, paradoxically, its lack of recombination means that most of the Y behaves like an asexual genome. This makes it very vulnerable to the accumulation of harmful mutations. Despite clear evidence from some remaining genetic similarities that the human X and Y chromosomes were once almost identical in genetic makeup (about two hundred million years ago), only a handful of genes out of the thousand or so that were originally present on the Y now remains – thus, it is *degenerate*.[34]

28 Barton and Charlesworth, "Why Sex and Recombination?"; Otto and Lenormand, "Resolving the Paradox of Sex and Recombination"; W. D. Hamilton, "Sex Versus Non-sex Versus Parasite," *Oikos* 35 (1980): 282 – 290.

29 S. P. Otto and N. H. Barton, "Selection for Recombination in Small Populations," *Evolution* 55 (2001): 1921 – 1931.

30 O. Fischer and P. Schmid-Hempel, "Selection by Parasites May Increase Host Recombination Frequency," *Biology Letters* 1 (2005): 193 – 195.

31 N. Colegrave, "Sex Releases the Speed Limit on Evolution," *Nature* 420 (2002): 664 – 666.

32 Barton and Charlesworth, "Why Sex and Recombination?"; Otto and Lenormand, "Resolving the Paradox of Sex and Recombination."

33 W. R. Rice, "Experimental Tests of the Adaptive Significance of Sexual Reproduction," *Nature Reviews Genetics* 3 (2002): 241 – 251.

34 B. T. Lahn and D. C. Page, "Four Evolutionary Strata on the Human X Chromosome," *Sci-*

This pattern has been observed repeatedly in other groups where Y chromosomes have evolved, quite independently of each other.[35] In a species of fruit fly called *Drosophila miranda*, a whole chromosome has become attached to the Y chromosome, and is inherited in exactly the same way as the original Y. It is, however, only about one million years old, giving us an opportunity to study the early stages of its degeneration.[36] Harmful genetic changes on the new Y chromosome have clearly accumulated:[37] about one-third of the genes that have been examined contain mutations that destroy their function, and all of the genes seem to have some minor but harmful mutations.[38] The evolution of Y chromosomes thus provides particularly striking evidence that the removal of recombination from a large part of the genome leads to its gradual evolutionary decline.

In this case, the survival of the population is not endangered, since selection has acted to compensate for the degeneration of the Y by raising the rate at which gene products arise from the unimpaired X chromosome in males.[39] However, in an asexually reproducing species, it seems likely that the accumulation of harmful mutations would continue until the species suffers a serious loss of fitness. Coupled with the reduced ability to adapt to changes in the environment, the apparent inability of most asexual or highly inbreeding species to maintain themselves does not seem surprising. Indeed, it is actually the persistence of apparently ancient asexual groups, like the Bdelloid rotifers, that raises the most challenging questions about the evolutionary significance of sex.[40]

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ence 286 (1999): 964 – 967; D. Charlesworth, B. Charlesworth, and G. Marais, "Steps in the Evolution of Heteromorphic Sex Chromosomes," *Heredity* 95 (2005): 118 – 128.

35 Ibid.

36 Ibid.; M. Steinemann and S. Steinemann, "Enigma of Y Chromosome Degeneration: Neo-Y and Neo-X Chromosomes of *Drosophila miranda* a Model for Sex Chromosome Evolution," *Genetica* 102/103 (1998): 409 – 420; D. Bachtrog, "Sex Chromosome Evolution: Molecular Aspects of Y Chromosome Degeneration in *Drosophila*," *Genome Research* 15 (2005): 1393 – 1401.

37 Steinemann and Steinemann, "Enigma of Y Chromosome Degeneration."

38 Bachtrog, "Sex Chromosome Evolution."

39 I. Marín, M. L. Siegal, and B. S. Baker, "The Evolution of Dosage Compensation Mechanisms," *Bioessays* 22 (2000): 1106 – 1114.

40 Maynard Smith, *The Evolution of Sex*; Arkhipova and Meselson, "Deleterious Transposable Elements."