analysis of records for British aristocrats extending across twelve centuries suggests that a similar tradeoff exists in humans. Positive correlations have been found between species longevity and cellular DNA repair capacity and resistance to oxidative stress. For example, the activity of the enzyme poly(ADP-ribose) polymerase-1, which mediates the immediate response to DNA damage (e.g., caused by irradiation), has been shown to correlate strongly with species lifespan, as has the cellular capacity to withstand a broad range of chemical stressors (e.g., hydrogen peroxide). Long-lived fruitfly populations produced by artifical selection generally show increased resistance to stress, as do mutant nematode worms carrying mutations that increase the lifespan. In many instances, it appears that genes affecting rate of aging map onto pathways involved in energy regulation (e.g., insulin-receptor signaling).

The findings from a wide range of model systems confirm the predicted links between somatic maintenance and longevity and point to the central importance of energy allocation within the organism's life history. Similar conclusions have also been derived from evolutionary analyses of cases of life-history plasticity, such as the life-extending effects of rodent calorie-restriction and the availability of switching into a long-lived, stress-resistant larval form (the dauer) in the nematode *Caenorhabditis elegans*. The evolutionary theories of senescence are not mutually exclusive, and it is likely that a combination of genetic factors may be involved, some broadly shared across individuals, populations, and species, and others more particular.

[*See also* Life History Theory, *article on* Human Life Histories.]

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— THOMAS B. L. KIRKWOOD

SEX, EVOLUTION OF

A very broad definition of sex is that it is the process that forms individual organisms containing genes from more than a single source (or parent). This covers a number of processes occurring in organisms ranging from bacteria to humans. In bacteria, individuals actively take up DNA from the environment and recombine it into their genomes (transformation). Gene transfer can also be caused by parasitic plasmids and phages that move between individual bacteria, carrying genes with them. In most of this article, however, we will be concerned with the more commonly known form of *sexual reproduction* that occurs in eukaryotes. This involves (1) the alternation between a haploid stage (single set of chromosomes) and a diploid (double set of chromosomes) stage; and (2) the exchange of genes between the chromosomes of a diploid pair (*recombination*), which can lead to the production of individuals with novel genotypes.

More specifically, sexual reproduction in eukaryotes involves the alternation of (1) the creation of haploid germ cells or gametes from a diploid cell by meiosis (a special kind of cell division), and (2) fertilization, the fusion of haploid cells (gametes) to form a diploid cell (the zygote). During meiosis, the chromosomes of a diploid pair can exchange genetic material by a process that is termed *crossing-over*. This recombination can break links between genes that were previously linked on the same chromosome, or create links between previously unlinked genes.

The process by which sexual reproduction occurs is remarkably diverse across the eukaryote species. In some species, sex is an obligate part of the life cycle (e.g., humans and other mammals, many insects), while in others it is an optional component of reproduction, induced under special circumstances (e.g., water-fleas, some insects, some parasitic nematodes, most protists and fungi). In some species, fertilization is followed immediately by (zygotic) meiosis, and so most of the life cycle is spent as haploid (e.g., algae or protozoa such as malaria parasites); in others, gametic meiosis is followed by fertilization, and so most of the life cycle is spent as diploid (e.g., humans). Some organisms have clearly differentiated (*anisogamous*) "male" and "female" gametes (e.g., humans), and others are *isogamous* (e.g., some protozoa).

The Problem of Sex. The relatively widespread occurrence of sex is often described as one of the greatest problems for evolutionary biology. Why is this so? Sex is puzzling because it can involve a large cost. First, sex or recombination breaks up favorable gene combinations that have increased in frequency under the action of natural selection. Put simply, it destroys the genotypes that were good enough to win the natural selection

lottery to survive and reproduce (this is sometimes termed the *recombination load*, because it results from recombination breaking up genotypes).

Second, in species with anisogamy (separate male and female gametes), sexual reproduction involves a "cost of producing males." Asexual females can potentially produce twice as many daughters as sexual females, because sexual females must "waste" half of their resources on producing males (assuming, as is commonly expected and observed, 50 percent males). Consequently, the ratio of asexual to sexual females should double each generation, resulting in a "twofold cost of sex" (Figure 1). For example, suppose that each female produces two offspring that survive to reproduce. In an asexual species, both these offspring would be females, and so the asexual population size would double each generation. In contrast, with sexuals, one of the offspring would be male and one female, and so the sexual population size would remain constant. In this simple numerical example, it is clear that asexuals could rapidly outcompete sexuals.

Given these costs of sex, we would therefore expect natural selection to favor asexual reproduction in wild populations. However, it often does not: sexual reproduction is widespread throughout the animal and plant kingdoms. The rest of this article will focus on why sex occurs. This actually involves a number of subtle questions: on the evolution of sex, the maintenance of sex, the timing of sex, and the amount of sex. We discuss sex in bacteria and eukaryotes separately, because they have independent origins and are likely to have different explanations.

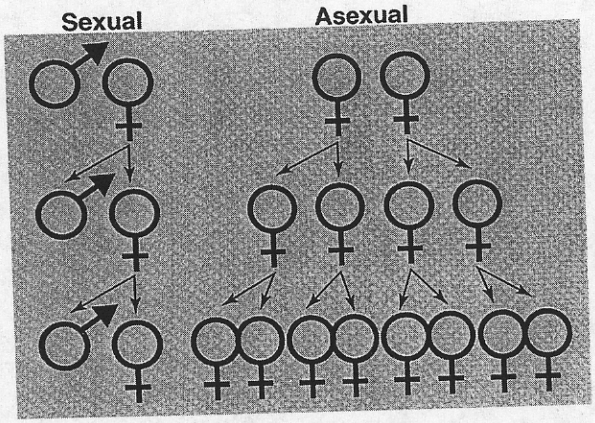


FIGURE 1. The Twofold Cost of Sex. Asexual females can potentially produce twice as many daughters as sexual females, because sexual females must "waste" half of their resources on producing males (sons). This means that the ratio of asexual to sexual females should double each generation (the twofold cost of sex). Here is an example in which each female produces two offspring that survive to reproduce. In an asexual species, both these offspring would be females, and so the asexual population size would double each generation. In contrast, with sexuals, one of the offspring would be male and one female; and given that it takes two parents to make an offspring, the sexual population size would remain constant. Courtesy of Andrew D. Peters.

Sex in Bacteria. Why do bacteria actively take up DNA from the environment and recombine it into their genomes (transformation)? When considering sex in bacteria, it is important to realize that this process is split into two components—*competence*, the active uptake of DNA fragments from the environment, and recombination of the host genome with those fragments. Did competence evolve to facilitate recombination, or did it evolve for another reason?

Three hypotheses have been suggested to explain competence: (1) competence evolved to allow recombination, which provides some fitness advantage (much as we believe sex is an adaptation in eukaryotes, providing a fitness advantage, as described in later sections); (2) competence evolved to provide a template to repair damaged DNA; or (3) competence evolved for the acquisition of nucleotides as a source of food. In recent years, experimental work by Rosemary Redfield has tested these hypotheses. Redfield (2001) found that DNA uptake was not induced by DNA damage, as would be predicted by the DNA repair hypothesis, but it was induced by starving, supporting the acquisition of food hypothesis. Furthermore, the amount of competence induced under starvation can be reduced by supplying specific nucleotides (i.e., an alternate food source).

If DNA uptake by bacteria is to acquire food, why does recombination occur? One strong possibility is that it occurs by accident. DNA uptake is targeted toward fragments similar to those in the bacteria's own genome. Although this might suggest the importance of DNA repair or some advantage of recombination, most of the DNA is degraded for food before anything else can happen. An alternative (untested) explanation is that similar DNA might be easier to get across the cell membrane. All the genes involved in recombination have other functions in the cell that can explain why they cause recombination (e.g., DNA repair). Selection for these functions dwarfs any benefits that would be obtained from recombination, which generally leads to a decrease in fitness. Consequently, a strong possibility is that DNA uptake occurs to acquire food, and that occasionally an accident then leads to some DNA being recombined into the genome.

This suggests that selection for the ability to recombine has been weak or nonexistent in bacteria, and that transformation did not evolve for genetic exchange. Although recombination is relatively rare in bacteria (not a part of its normal life cycle) and involves only small fragments, this does not downplay its importance; there

is abundant evidence for horizontal gene transfer, and this can often have considerable consequences, such as when it confers antibiotic resistance. Nonetheless, this makes sex in bacteria very different from that in eukaryotes, where meiotic sexual reproduction evolved for recombination.

Sex in Eukaryotes. How is sexual reproduction distributed among the eukaryotes? Sex occurs in almost all eukaryote groups. In particular, it is typical among the crown taxa (animals, plants, fungi). However, even among these groups (e.g., lower vertebrates, invertebrates, flowering plants), asexual (parthenogenetic) species occur, showing that asexuality is mechanistically possible and has evolved many times, and that there must be some factor maintaining it. Although the eukaryote phylogeny is not sufficiently resolved to know how many times meiotic sex has evolved, current opinion suggests that sexual reproduction probably arose in a protist, a unicellular eukaryote, as an optional component of a reproductive cycle that was usually asexual (mitotic).

The taxonomic distribution of asexuality in the eukaryotes is not random. Asexual reproduction tends to be found in odd populations, species, or even whole genera, within a larger taxonomic group that reproduces sexually. Consequently, asexuality is a derived state and apparently not long-lived on an evolutionary time scale. There are a couple of exceptions to this, notably a suborder of rotifers (Bdelloidea) and the Darwinulid ostracods.

Before we move on to discuss possible advantages to sex, we note that there is an important difference between explaining the initial evolution and the maintenance of sex. In species that lack a specialization of germ cells into male and female forms (called *isogamous* organisms), the twofold cost of sex (i.e., production of males) does not need to be paid, and so only a slight advantage would be required for the initial evolution of sex to be favored. In anisogamous organisms, females pay all the costs of provisioning the large egg with cytoplasm and nutrients. Males do not provision their tiny sperm. In isogamous organisms, males and females do not exist, although mating types do, often denoted "+" and "−." Here both mating types provision the gametes. So females of anisogamous species pay double the cost of producing gametes. It is only in anisogamous species with more advanced sexual reproduction that explaining the maintenance of sex becomes more problematic. Consequently, the major problem is explaining why so many plants and animals always reproduce sexually.

Theoretical Advantages of Sex. In the nineteenth century, August Weismann suggested that the advantage of sexual recombination was that it provides new genetic variation for selection to act upon. Sex leads to the mixing of genes from different individuals and the production of novel genotypes. The crux of Weismann's idea was that some of these novel genotypes would have a relatively high fitness and some of them would have low fitness. Consequently, by creating new genotypes, sex increases the distribution (variance) of fitness values. Natural selection would then favor the individuals with relatively high fitness. The power of natural selection to increase the mean fitness of a population depends upon the variation in fitness (in the extreme, if there was no variation, and all individuals in a population had equal fitness, then natural selection could not increase mean fitness). Consequently, by increasing the variation in fitness, sex allows the efficiency of natural selection to be increased and hence accelerates the increase in mean fitness (i.e., increases the fitness of grandchildren, etc.). Put simply, sex allows the better genes to be concentrated in a few "extra-fit" individuals, and the worst genes to be lost via particularly low-fitness individuals.

In the latter half of the twentieth century, this idea was dismissed by George Williams as being based upon group (or clade) selection, a force generally accepted not to be important, and a number of models were developed that could provide an advantage to sex at the level of the individual or gene. However, Weismann's idea has recently regained support. In particular, it has been realized that Weismann's mechanism underlies most of the formal genetic models that provide an advantage to sex; that the Weismannian mechanism provides an advantage at both the group and gene level; and that competition between asexuals and sexuals is at the group level in that genes do not flow between the groups by reproduction. Burt (2000) provides a recent and excellent review of this modern Weismannian perspective.

Of course, this does not answer the question of why sexual reproduction should lead to an increase in the variance of offspring fitness. Mechanisms that do this can be broadly classified into two groups: environmental (or ecological) models, and deleterious mutation models. Furthermore, these models can be distinguished depending upon whether they are deterministic and work in large (infinite) panmictic populations, or stochastic and require finite (and usually small) populations or certain population structures. In the rest of this section, we briefly summarize the most popular hypotheses for sex; a thorough review is provided by Kondrashov (1993). Although more then 20 hypotheses have been suggested and new ones are published with regularity, we will not (and could not hope to) cover all of these. In addition, many require extremely restrictive assumptions and so are not likely to be generally important, and it is not unusual for new models to be merely reformulations of or tweaks on old ideas.

Fisher-Muller hypothesis. One of the earliest hypotheses for sex states that sexual reproduction and re-

combination allow beneficial mutations that initially appear in separate individuals to be combined. In an asexual species, multiple beneficial mutations will only fix if the second (and later) beneficial mutations occur in an individual that already carries the first beneficial mutation. Consequently, sex increases the rate at which adaptive mutations are fixed in a population and hence accelerates evolution. However, the usefulness of this explanation for providing a short-term benefit to sex sufficient to balance the twofold cost has been questioned, because it requires relatively small populations and the frequent occurrence of beneficial mutations with sufficiently large fitness consequences.

Deterministic environmental models. There is a wide range of environmental models that can provide an advantage to sex. These models rely upon epistasis (nonadditive gene interactions, which are not required for the Fisher-Muller hypothesis) and suggest that sex accelerates adaptation to a changing environment by creating new gene combinations. The biological basis of such selection pressures may involve a variety of biotic or abiotic mechanisms.

Early models suggested that sex provides an advantage because different genotypes may do better in different environments, and that spatial or temporal variation in the environment would favor new gene combinations that can utilize the currently abundant habitat. The version of this idea that is reliant upon spatial variation in the environment is termed the "Tangled Bank." It assumes that different genotypes do better in different environments (niches). This provides an advantage to sex, because an asexual clone is restrained by the narrowness of the environments that it can exploit (i.e., the narrowness of its ecological range). Sexual reproduction leads to a diversity of genotypes that are able to exploit different environments. Bell termed this kind of model the Tangled Bank from a phrase in the concluding paragraph of Darwin's *Origin of Species*, which expresses the complexity of natural habitats that must strike anyone who contemplates a clump of moss or a bed of weeds. Another analogy sometimes used to describe this kind of idea, introduced by George Williams, is that of buying lottery tickets. Asexual reproduction is like buying several lottery tickets with the same number, whereas sexual reproduction is like buying fewer tickets, but each with a different number—consequently, the sexual strategy is more likely to provide a winning ticket. Finally, this advantage to sex can also be increased by competition between siblings. The reasoning here is that asexual reproduction will lead to offspring with the same genotype, who will therefore compete for the same habitat, reducing their mean fitness. In contrast, sexual reproduction leads to genetically diverse offspring, who will utilize different environments, decreasing competition among them.

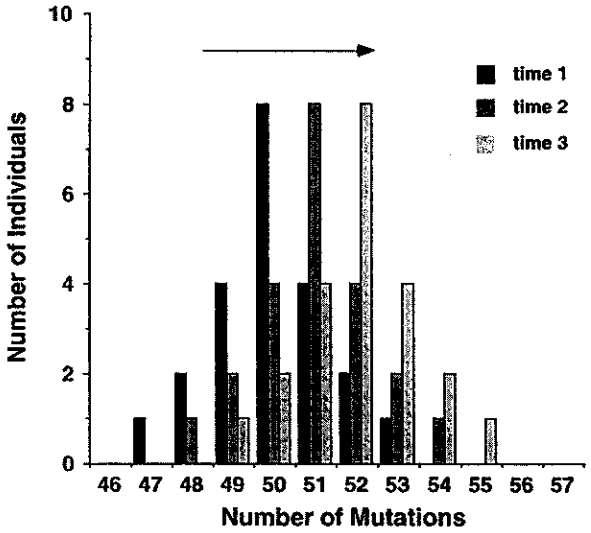


FIGURE 2. Muller's Ratchet.
Shown is the distribution of the number of deleterious mutations per individual in a population, at three time periods. Between each time period, the class of individuals that have the least number of deleterious mutations is lost as a result of chance events (failure to reproduce or mutation). In asexual populations, this class of individuals cannot be recreated, and so the accumulation of deleterious mutations is irreversible and inevitable. Courtesy of Curt M. Lively.

Currently the most popular environmental hypothesis is the "Red Queen." This states that sex provides an advantage in competitive interactions between competing organisms (antagonistic coevolution). Several people, especially Hamilton, have championed the idea that parasites could provide the driving force, favoring sexual reproduction in their hosts. The idea here is that parasites evolve to be able to infect the currently common host genotypes. Sex is then favored in the hosts, because it allows the production of novel genotypes that may be more resistant to the parasites. Over time, this will lead to continuous oscillations in host and parasite gene frequencies (host-parasite coevolution)—a "coevolutionary dance." The title of the Red Queen hypothesis was assigned by Graham Bell from the episode in which Lewis Carroll's Alice learns from the Red Queen that "it takes all the running you can do, to keep in the same place"—that is, you keep having to have sex just to stay ahead of the parasites, but you can never escape them. We have focused here on a scenario in which parasites drive the Red Queen and favor sex in their hosts, but there are other possibilities, such as host immune responses driving sex in their parasites.

Muller's ratchet. Muller's ratchet is the inevitable accumulation of deleterious mutations in asexuals that occurs through chance events (Figure 2). In any popu-

lation, there will be a distribution of the number of deleterious mutations per individual. Now consider the class of individuals that has the least number of deleterious mutations. Given a finite population size, there is a probability, in each generation, that this class of individuals will be lost. This might occur through the random chance that none of them reproduce or that they all mutate at the same time. Ignoring the possibility of back or compensatory mutations, this accumulation of deleterious mutations is irreversible. In sexual populations, recombination allows this class of individuals with the least number of mutations to be recreated. Consequently, the mean number of deleterious mutations in an asexual lineage can only increase, and the ratchet clicks forward one notch. Although Muller's ratchet clearly provides an advantage to sex, it is a stochastic process and is thought to operate too slowly to compensate for the twofold cost (i.e., asexuals would replace sexuals before the fitness of the asexuals declined below that of sexuals). In addition, it has been shown that only a small amount of sex is required markedly to reduce the accumulation of deleterious mutations by Muller's ratchet.

Mutational deterministic hypothesis. Alexey Kondrashov pointed out that deleterious mutations can provide a short-term advantage to sex that can compensate for its twofold cost if each additional deleterious mutation leads to a greater decrease in fitness than the previous mutation (termed *synergistic epistasis* between deleterious mutations) (Figure 3). When this is the case, sexual reproduction increases the variance in the number of deleterious mutations that will be carried by offspring. The low fitness of individuals carrying above-average numbers of deleterious mutations will then lead to a larger number of deleterious mutations being eliminated. If the deleterious mutation rate is sufficiently high, then this process can compensate fully for the twofold cost of sex. Early theoretical work suggested that the deleterious mutation rate needed to be greater than 1.0 per genome per generation to balance the twofold cost of sex, but more realistic models suggest that several other factors (e.g., finite populations, variation in the extent of epistasis) mean that a mutation rate greater then approximately 2.0 is required.

Some recent models have examined the consequences for the mutational deterministic hypothesis of greater selection against mutations in males. This could occur via mate choice or competition for mates (sexual selection). In these models, a lower deleterious mutation rate can be required to explain sex. Furthermore, the requirement for synergistic epistasis can be removed. Although these models can make it easier to explain sex, they are restrictive in that they do so only for sexual species in which sexual selection is important.

A common feature of most models discussed above (but possibly not some environmental models such as the Red Queen) is that sex provides an advantage because it increases the variation in offspring fitness. Hence, sex increases the response to selection, as suggested by Weissman—despite leading to the production of less fit offspring in the short term, termed the recombination load. This increase in the variance of fitness occurs because sex breaks up nonrandom gene associations (linkage disequilibrium). Consequently, these models work because they provide a mechanism for generating nonrandom gene associations (linkage disequilibrium); the mechanism is either genetic drift in stochastic models with additive interactions, or epistasis in deterministic models. These mechanisms relate to whether a hypothesis can explain the maintenance of sex in the short term by preventing the successful invasion of an asexual clone (e.g., deterministic mechanisms such as the Red Queen or the mutational deterministic hypothesis), or whether it can lead only to the long-term extinction of asexuals (e.g., stochastic processes such as Muller's ratchet).

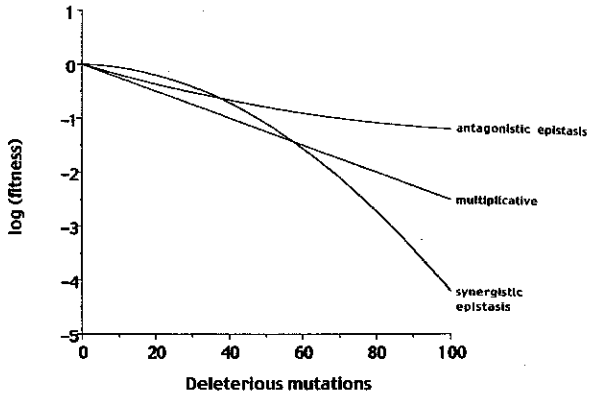


FIGURE 3. Interactions Between Deleterious Mutations. The relationship between (log) fitness and the number of deleterious mutations may be linear (multiplicative); each extra mutation lead to a greater decrease in fitness (synergistic epistasis); or each extra mutation lead to a smaller decrease in fitness (antagonistic epistasis). The mutational deterministic hypothesis requires synergistic evidence. To date, most experimental data suggest, on average, multiplicative interactions. Courtesy of Stuart A. West.

What Hypothesis Do the Data Support?

Comparative data. The earliest empirical work that attempted to explain sex was correlational and focused on the ecological hypotheses. In these studies, the occurrence of sex or rate of recombination is examined, either across or within species, with respect to key ecological variables. These studies emphasize finding predictions that discriminate among different hypotheses. For example, Curt Lively (1987) examined the snail *Potamopyrgus antipodarum*, in which both sexual and asexual forms can be found living in the same area.

Lively found that, across different populations in New Zealand, the proportion of sexual individuals was positively correlated with the frequency of their parasites, supporting the Red Queen hypothesis (Figure 4). In contrast, the proportion of sexual individuals was not correlated with the temporal or spatial variation in habitat, as predicted by the Tangled Bank hypothesis. Similarly, Austin Burt (2000) and Graham Bell (1982) found that the recombination rate was greater in mammals with longer generation times, which are likely to suffer greater parasite pressure, supporting the Red Queen hypothesis. In contrast, the recombination rate did not correlate with brood size, a likely correlate of the amount of competition between siblings, as predicted by the Tangled Bank hypothesis.

These comparative studies have provided support for the Red Queen hypothesis, and they have played an important role in the rejection of some of the environmental models (such as the Tangled Bank). Furthermore, it is fundamental that any theory of sex must be able to explain the distribution of sex both across and within species. However, because these studies are correlational, they are open to multiple explanations, and *post hoc* scenarios can be developed that allow the results to be explained by environmental or mutation-based models. In particular, with some ingenuity, the mutational deterministic hypothesis can explain most patterns that are predicted by the Red Queen. For example, patterns such as those observed by Lively could be explained by arguing that parasites are the factor that selects against individuals with high mutation loads (although in this case with the snails, this is unlikely because the parasites are sterilizing, and there is no evidence that asexuals, who should have higher mutation loads, are more susceptible to infection per se). Similarly, the pattern observed by Burt and Bell could be explained if species with longer generation times have higher deleterious mutation rates (for which there is much evidence—see Figure 5). Thus, while there is no doubt that the comparative data support the Red Queen hypothesis, they seem incapable of rejecting the mutational deterministic hypothesis. This fact, along with their theoretical plausibility, has made Red Queen and the mutational deterministic hypotheses the major contending explanations for sex.

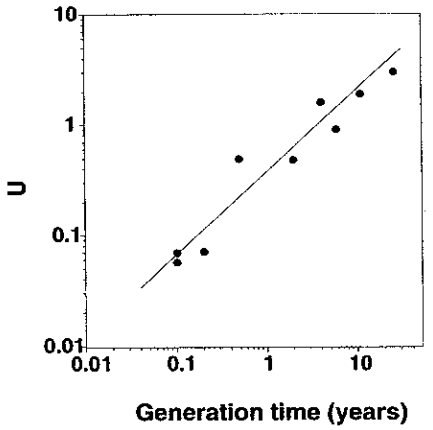
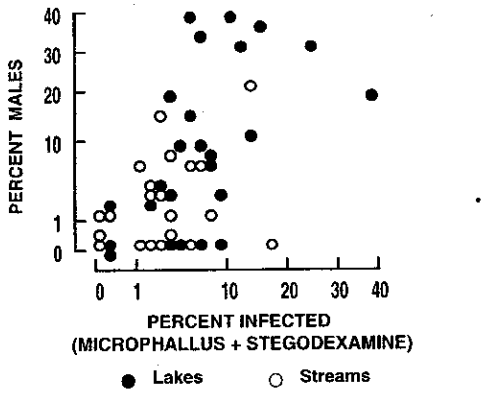


FIGURE 5. Estimates of Deleterious Mutation Rate (U) Obtained by Comparing Genomic Data from Different Species, Plotted Against Generation Time.
These data suggest that the deleterious mutation rate increases strongly with generation time but is below 1.0 for a large number of sexual species (e.g., many insects and nematodes). Data from Keightley and Eyre-Walker (2000).

FIGURE 4. The Relative Frequency of Sexual and Asexual Forms of the Snail *Potamopyrgus antipodarum* Across Different Populations in New Zealand.
The proportion of sexual individuals is positively correlated with the frequency of their parasites, supporting the Red Queen hypothesis, and not correlated with the temporal or spatial variation in habitat (lakes versus streams), as predicted by the Tangled Bank hypothesis. Data from Lively (1987).



Experiments and parameter estimation. Given that comparative work cannot decisively distinguish between the different hypotheses, it is necessary to test the assumptions of different models and measure crucial parameters. In recent years there has been a surge in such work.

The mutational deterministic hypothesis was thought to offer excellent opportunities for empirical testing. It clearly requires a deleterious mutation rate greater then 1.0–2.0 and synergistic epistasis between deleterious mutations. However, in practice it is not so easy to test these assumptions. The first attempts to estimate the deleterious mutation rate were by mutation accumulation experiments pioneered by Terumi Mukai in the 1960s on fruit flies (*Drosophila*). In these, selection was relaxed, deleterious mutations were allowed to accumulate for a large number of generations in replicate lines, and then the deleterious mutation rate was esti-

mated by the rate and form of fitness decline over time. Similar experiments have since been carried out on other organisms, including bacteria (*Escherichia coli*) and nematodes (*Caenorhabditis elegans*). Unfortunately, estimates of the deleterious mutation rate have varied widely among studies, and even between analyses of the same datasets. While some argue that the data are consistent with the mutational deterministic hypothesis, others argue that they are not. More studies are required from a range of sexual organisms.

More recently, indirect estimates of the deleterious mutation rate have been obtained by comparing genomic data from different species. Using this approach, Peter Keightley and Adam Eyre-Walker (2000) have estimated the deleterious mutation rate in a range of organisms, including humans, sheep, dogs, mice, and fruit flies (Figure 5). They found that the deleterious mutation rate increased strongly with generation time, providing a possible explanation for variation in the deleterious mutation rate across species. Importantly, their estimate suggests that the deleterious mutation rate would be below 1.0 for a large number of sexual species (e.g., many insects and nematodes). These data suggest strongly that the mutational deterministic hypothesis cannot explain sex. However, it should be noted that their estimates of the deleterious mutation rate are underestimates, and it has been argued that they may even be sufficiently underestimated to save the mutational deterministic hypothesis, and so the debate is certainly not closed.

The mutational deterministic hypothesis also requires another assumption that is in principle easily tested: each deleterious mutation must lead to a greater decrease in fitness then the last (synergistic epistasis) (Figure 3). Early experiments on fruit flies and algae supported the occurrence of synergistic epistasis, but these were either carried out without proper experimental controls or lacked a proper theoretical basis. More recently, experiments testing for epistasis have been carried out by examining how fitness varies with the insertion of a known number of deleterious mutations. Such experiments on bacteria (*E. coli*) and nematodes (*C. elegans*) showed no tendency toward synergistic epistasis, whereas work on fruit flies did (although this result relied on a single data point, consisting of the least fit individuals). Overall, this suggests that a general tendency toward synergistic epistasis is either absent or weak. Although this may suggest doom for the mutational explanation of sex, recent theoretical work suggests that the need for synergistic epistasis can be reduced by sexual selection (as discussed earlier) or by patterns of dispersal leading to populations being structured into subpopulations. In addition, methodological constraints mean that estimates of the importance of epistasis are usually expected to be underestimates.

In contrast, it has been less clear how to carry out such critical tests of the environmental models. To some extent, this is because theory has not been able to make such clear predictions; however, recent work has started to address this problem. For example, Curt Lively and Mark Dybdahl (2000) have shown that parasites are better at infecting locally common genotypes of the snail *P. antipodarum*, as predicted by the Red Queen hypothesis. This suggests that parasites track locally common host genotypes, a necessary condition of the Red Queen hypothesis. Furthermore, they have shown not only that locally common genotypes are disproportionably infected, but also that they subsequently show a drop in frequency, presumably because of their high infection rate. Future work is required to determine if genotypes then increase in frequency again after having been rare for some time, showing the kind of cycle in frequency predicted by the Red Queen. Experimental work has also supported the comparative data in its rejection of the Tangled Bank hypothesis. Experiments on plants and algae have shown that populations consisting of mixed genotypes show carrying capacities not much greater than that of the average of their components, and rarely greater than that of the best component.

A Pluralist Approach. Given the lack of a clear winning hypothesis, what can be said firmly about the explanation for sex? First, the Red Queen and the mutational deterministic hypothesis (including its more complex variants) appear to be the leading contending explanations for sex. Second, the empirical data, both comparative across species, and more detailed work within species are consistent with the Red Queen hypothesis but are not sufficient to prove decisively that it explains sex. Third, although this work is the subject of controversy, the best data that we currently have suggest that the mutational deterministic hypothesis cannot explain sex. In particular, deleterious mutation rates may be appreciable (e.g., >0.1) but not above the necessary 1–2 in a wide range of sexual species, and synergistic epistasis between deleterious mutations appears to be either absent or extremely weak.

This search for one hypothesis to explain sexual reproduction may be misleading, however. Considerable advantages may be gained from a pluralist approach that considers that different mechanisms may work simultaneously. First, acting alone, each of the various theories requires extreme, and possibly unreasonable, assumptions to be able fully to explain the maintenance of sex. However, even if a model is not able fully to explain the twofold cost of sex, it may play an important role. For example, the genomic estimates of the deleterious mutation rate suggest that, across a wide range of sexual species, it is large enough to play an important role but cannot explain sex alone. Perhaps deleterious mutations pay half the cost and coevolving parasites pay the other half.

Second, different mechanisms may interact synergistically. In particular, environmental and mutational mechanisms may complement each other, covering each other's weaknesses. For example, host-parasite coevolution, as envisaged in the Red Queen hypothesis, provides an extremely short-term advantage to sex that slows down the spread of asexual clones. This allows more time for deleterious mutations to accumulate before the clone could potentially replace the sexual population; in addition, it keeps the asexuals at smaller population sizes and hence speeds up the rate at which they accumulate deleterious mutations. As another example, in regard to the fixation of beneficial mutations as described above in the context of the Fisher-Muller hypothesis, deleterious mutations can make it even harder for fixation to occur. The reason for this is that beneficial mutations must arise not only in the same individuals, but also in individuals with a relatively low number of deleterious mutations, or else they will be dragged down by their low-quality genetic background (termed the "ruby in the rubbish" problem by Joel Peck). These and other possible interactions between mechanisms are discussed in detail by Stuart West, Curt Lively, and Andrew Read (1999). Although it is a messy answer, a pluralist approach (especially one involving deleterious mutations and coevolving parasites) seems currently the most plausible explanation for sex to a wide range of evolutionary biologists.

Why So Much Sex? Before concluding, we briefly consider a more subtle and possibly more perplexing problem. Why do animals and plants have so much sex? Specifically, why is obligate sex (in every round of reproduction) so common in animals and plants? Models of most mechanisms that provide an advantage to sex suggest that occasional sex provides approximately the same benefit as obligate sex. In most unicellular eukaryotes and some animals (e.g., water-fleas, aphids, and some wasps), sexual reproduction is an occasional component of the life cycle. Why is this not the case for most plants and animals?

One possible explanation for this, covered in detail by Burt (2000), is that facultative or occasional sex is unstable. Specifically, selection could always favor a little less sex, leading eventually to asexual reproduction, even in a situation where obligate sexuals outcompete asexuals. The crucial point is that asexuals competing against sexuals involves competition at a different level (between groups) than does competition between facultatively sexual individuals that have different amounts of sex. Cases in which facultative sex occurs seem to represent historical serendipity, as suggested by the fact that sex is usually associated with some other life history difference, such as dispersal (aphids) or the production of overwintering eggs (water-fleas). Interestingly, the taxa in which facultative sex is common, such as protists and fungi, are generally isogamous, and so the twofold cost of sex is not paid; thus, it becomes much easier to explain the stability of occasional sex—it has a low cost and a high advantage. It is easy to imagine a situation in which occasional sex initially evolved under conditions in which obligate sex would not be stable; then a little sex opened the door for an increased rate of evolution that led to bigger more complex organisms with longer generation times; and finally, this led to an increase in deleterious mutation rates and parasite loads, until the point at which obligate sex could be favored in anisogamous species. Furthermore, recent theory suggests that sexual selection (mate choice and mate competition) increases the advantage of sex by purging less fit individuals.

This discussion of occasional sex also makes an important point for the highly influential balance argument of George Williams. Williams argued that the existence of facultative or occasional sex provided strong evidence against Weismann's hypothesis, because sex must be providing an immediate short-term fitness advantage, and this could not be done merely by increasing the variance in fitness. The discussion above suggests an alternative explanation for why facultative sex could be maintained.

Conclusions. Explaining sex has been termed "the queen of problems in evolutionary biology" (Bell, 1982). Although there is still no entirely conclusive answer, the increasing attention paid to this problem in the past three decades by theoretical and empirical biologists has at least led us to a better idea of the plausible explanations, and to a strong suspicion that the answer is complex, involving deleterious mutations and antagonistic coevolution, particularly with parasites.

[*See also* Red Queen Hypothesis.]

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— STUART A. WEST

SEX CHROMOSOMES

Many species of animals and some species of flowering plants have separate sexes. The differences between the sexes are often controlled by a pair of sex chromosomes, which are genetically and often structurally distinct. Most commonly, there is an X/Y chromosome system, with XX females and XY males, where sex is determined either by a gene or genes on the Y chromosome, as in mammals, or by the ratio of the number of X chromosomes to the number of the other chromosomes (autosomes), as in *Drosophila*. Less often, there is female heterogamety, with ZW females and ZZ males, as in birds, Lepidoptera, and some species of plants and lower vertebrates (Bull, 1983; Westergaard, 1958). The term *heterogametic sex* is used to refer to the sex that is heterozygous for the sex chromosomes, the term *Y chromosome* for systems with both male and female heterogamety.

In some, but not all, species with chromosomal sex determination, the X and Y chromosomes can be recognized as different in appearance by light microscopy. This difference is associated with the accumulation of various types of repetitive DNA sequences in disproportionate abundance on the Y chromosome (Bull, 1983; Charlesworth, 1996), and the Y chromosome is commonly described as being largely composed of heterochromatin (Bull, 1983; Graves, 1995). In common with other heterochromatic regions of the genome, it is often late-replicating in cell division.

Another difference from the autosomes is that the pair of sex chromosomes fail to cross over with each other in the heterogametic sex along all or part of their length. Crossing over occurs only in a segment of the sex chromosomes, called the pairing region or pseudoautosomal region (Bull, 1983; Graves, 1995; Westergaard, 1958).

A striking common feature of sex chromosome systems is the almost complete erosion of genes from the Y chromosome. The best-studied sex chromosome system is that of humans. Only nineteen homologous X–Y pairs of loci have been found after exhaustive searches (Lahn and Page, 1999). This is a much smaller number than would be predicted from the total amount of DNA in the human Y chromosome, whereas the X chromosomes have thousands of active genes. The Y chromosomes of groups such as mammals or *Drosophila* have thus lost most of their genetic activity, leading to the familiar phenomenon of sex-linked inheritance. In some groups, such as many Orthoptera, the Y chromosome has been completely lost, so that males are described as X0 in constitution (Bull, 1983; Charlesworth, 1996).

It is not yet clear whether plant Y chromosomes are as genetically degenerate as those of animals. There is evidence that the Y chromosome of the white campion *Silene latifolia* has lost essential genes, as plants having a Y but no X chromosome are usually inviable (Vagera et al., 1994; Westergaard, 1958), but it does carry functional copies of some genes that are present on the X (Delichère et al., 1999).

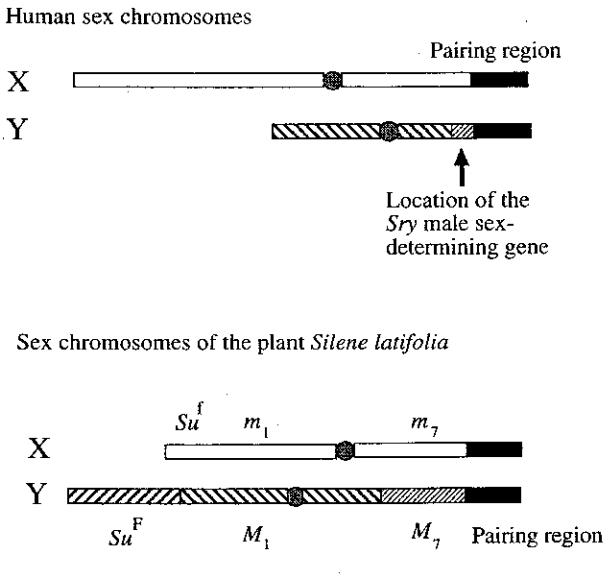

FIGURE 1. Diagram of the Sex Chromosomes of Mammals and a Plant. Drawing by Deborah and Brian Charlesworth.