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The Evolutionary Biology of Sex

Biology of Sex Special

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In 1861, Charles Darwin wrote "We do not even in the least know the final cause of sexuality; why new beings should be produced by the union of the two sexual elements, instead of by a process of parthenogenesis". It was hardly possible to begin to answer this question at that time, in view of the contemporary lack of knowledge of genetics and cell biology. Since then, research into the cellular basis of reproduction has shown that sexual reproduction is the norm for the majority of eukaryotes, with huge consequences for their biology. The evolution of sex and some of its consequences are the subject of the series of reviews, and a Primer, in this special issue of *Current Biology*.

Sexual reproduction involves the fusion of haploid gametes to form a diploid zygote; during the subsequent first division of meiosis — the timing of which in relation to zygote formation is highly variable among different types of organism — maternal and paternal chromosomal homologues replicate, pair up, and exchange pieces of DNA. This either involves non-reciprocal exchanges of relatively short stretches of DNA (gene conversion), or reciprocal exchanges of long sequence tracts (crossing over). Gene conversion and crossing over cause individual chromosomes to become a patchwork of maternal and paternal material. The maternal and paternal centromeres disjoin at anaphase of meiosis 1, and genes on different chromosomes segregate independently of each other. These three processes together result in genetic recombination: the production of gametes that combine genetic contributions from both parents. Prokaryotes such as bacteria lack regular cycles of sexual reproduction, but often exchange DNA fragments between individuals at a sufficient rate to leave a footprint of genetic recombination on DNA sequence variation within populations (see review by Ochman). Many of the enzymes involved in recombination in prokaryotes are homologous to those of eukaryotes, indicating an ancient origin of the processes involved in exchange.

Regular sexual reproduction probably evolved very early in the history of the eukaryotes, and all contemporary asexual multicellular organisms are the result of the secondary loss of sexuality. All mammals and birds reproduce sexually, and there is only a handful of parthenogenetic species of reptiles, amphibia and fish; similarly, only about 0.1% of species of flowering plants reproduce asexually. Most of these asexual species seem to have evolved recently, as they have close sexual relatives and have not proliferated into diverse forms. There are a few apparent exceptions to this, notably the Bdelloid rotifers and the Darwinulid ostracods, which probably represent 'ancient asexual' lineages. Asexuality seems to be commoner among single-celled eukaryotes, although the cryptic occurrence of sex often cannot be excluded.

In organisms with a division into males and females (dioecy) the maintenance of sexual reproduction faces a severe problem. This is the so-called 'two-fold cost' of sex: a new mutation causing females to produce daughters asexually (without any other effect on fitness) will double in frequency each generation within the female section of the population, eventually replacing the sexual females and causing the extinction of males. A similar problem also faces hermaphrodite organisms, which have both male and female function in the same individual. Here, the initial advantage of a mutation that causes eggs to be produced asexually or by self-fertilisation is closer to one-and-a-half-fold than two-fold.

It is thus surprising that sexual species are so common, and have not rapidly become asexual, or (in the case of hermaphrodites) completely self-fertilising. And, given the occurrence of sexual reproduction, why should genetic recombination be maintained, given that the suppression of recombination among polymorphic genes that interact in their effects on fitness is favoured by natural selection (as first pointed out by R.A. Fisher in 1930)? In the case of mammals, we know that they cannot reproduce asexually: genetic imprinting specifically inactivates some genes in either the paternally or maternally derived genomes, which means that both a maternal and a paternal set of chromosomes are needed for successful development. This does not explain the general prevalence of sex, because most other groups of animals and plants do not have imprinting of this kind, and asexual reproduction has evolved repeatedly among them.

The problem of the genetic cost of sex does not apply to its origin in the first place. Regular sexual reproduction first evolved among single-celled eukaryotes, which lacked any differentiation of gametes into male and female (anisogamy). The distinction between male and female gametes (many small versus few large) is very old, but is not needed for gamete fusion, as organisms like *Chlamydomonas* and yeast demonstrate. There is only a small advantage to reproducing asexually in the absence of anisogamy. A small advantage to a genetic variant that conferred sexual reproduction would thus allow it to spread. Similarly, there is no reproductive penalty to genes that increase the frequency of genetic recombination (recombination modifiers).

The search for selective advantages to sex and recombination has gone on since the first truly scientific discussions of this question by Fisher and Muller in the 1930s (see review by Agrawal). It is often rather glibly

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assumed that there is an obvious advantage to sex from generating increased variability; however, population genetic models show that sex and recombination can actually reduce variability in fitness, given certain types of interactions in fitness effects among genes. The problem of the relative importance of the numerous scenarios in which sex and recombination are favoured by selection is still unsolved, but it now seems likely that we have a nearly complete list of the likely candidates.

Even if a species reproduces sexually, however, individuals have the choice of either mating with close relatives, or mating with unrelated individuals. There are many examples of adaptations that lead to the avoidance of inbreeding, especially in hermaphrodites, which can easily self-fertilise. In lower eukaryotes, there are often two or more mating types, such that gametes carrying the same mating type cannot fuse. These exist in the absence of anisogamy. The genetics and molecular biology of mating type genes is complex, and very variable among different species (see review by Heitman). The evolution of these systems poses some fascinating and largely unsolved problems.

The answer to the question of why hermaphrodite species of higher eukaryotes usually (but not always) avoid self-fertilisation was provided by Charles Darwin himself. He compared plants that had been produced by self-fertilisation or outcrossing, and found the fitness of selfed progeny to be much less than that of the outcrossed progeny (the phenomenon now known as inbreeding depression). He argued that natural selection will therefore disfavour self-fertilisation. Until the 1970s, Darwin's explanation was largely ignored by botanists working on the mating systems of plants, who tended to appeal to rather vague, species-level advantages of variability conferred by outcrossing. For example, in 1950 G. Ledyard Stebbins wrote "the evolution of genetic systems involves competition, not between individuals, but between evolutionary lines". More recently, the application of population genetic principles to the study of the evolution of plant mating systems has led to a return to more Darwinian principles. The great diversity of plant mating systems has been very favourable to the testing of ideas about the evolutionary advantages and disadvantages of outbreeding and inbreeding, and has generated a large theoretical and empirical literature (see review by Charlesworth).

Darwin also considered the problem of why some anisogamous sexual species are dioecious, whereas others are hermaphrodite. He discovered the existence of plant species which appear to represent intermediate stages in the evolutionary transition between hermaphroditism and dioecy: gynodioecy (hermaphrodites and females), and androdioecy (hermaphrodites and males). The conditions for the invasion of an hermaphrodite species by a mutant conferring maleness or femaleness (which simply requires loss of one or other sexual function) involve both protection from self-fertilisation and an increase in fertility via the remaining sexual function, due to the reallocation of resources between male and female reproduction (Charlesworth). A second, complementary, mutation would allow the evolution of full dioecy, although it is likely that more than one such mutation is usually involved.

The fact that at least two genetic changes are involved in this transition can be shown to imply that there is selection to reduce recombination between the loci concerned (otherwise neuters would be produced). A similar requirement for two closely linked mutations is also likely to apply to the evolution of genetic sex determination from environmental sex determination, which seems to occur frequently in vertebrates. This requirement is probably the starting point for the evolutionary divergence of X and Y chromosomes (Z and W in the case of female heterogamety), which were initially largely homologous genetically. But fully developed sex chromosomes fail to cross over with each other over all or most of their lengths in the heterogametic sex. This genetic isolation has been accompanied by the evolutionary degeneration of the Y or W chromosomes, which are effectively asexual and hence lose the benefits of recombination and sexual reproduction. Recent molecular analyses of sex chromosome systems have led to many new insights into their evolution (see review by Graves).

Once separate sexes have been established, the question of the frequency of production of males and females in the population becomes important. It is commonplace that males and females are often approximately equally frequent at birth, even if there is differential mortality with respect to sex. Classic theory, usually attributed to Fisher but in fact tracing back to Darwin and to Düsing in the 19th century, shows that a 1:1 sex ratio (or more strictly, equal parental allocation of resources to sons and daughters) is favoured, if sex ratio is under the control of nuclear genes. This is because, regardless of the relative numbers of males and females, equal numbers of genes are transmitted to the next generation by males and females. The rarer sex thus has a higher per capita fertility, conferring an advantage on a gene that causes its carriers to produce more offspring of this sex. A 1:1 ratio is therefore the evolutionary equilibrium. However, this can be subverted by cytoplasmic agents, such as mitochondria or maternally transmitted endosymbionts, which are not transmitted through sons, and therefore gain an advantage from biasing the sex ratio in favour of males (see the Primer by David Queller). Similarly, if brothers compete for access to females (local mate competition), there is selection for a female-biased sex ratio, explaining what is seen in many parasitoid Hymenopterans, where mothers can control sex ratio by determining whether an egg is fertilised (and develops into a diploid female) or is unfertilised (and develops into a haploid male). Somewhat similar principles underly the allocation of resources to male and female functions in hermaphrodites (Charlesworth review).

Whether sex is genetically or environmentally determined, there is huge potential for the divergence of the two sexes in structure, physiology and behaviour. Again, Darwin was the first to recognise this clearly, especially in regard to his theory of sexual selection. He was particularly concerned to understand why many species have males with conspicuous ornaments,

which are likely to render them vulnerable to predation and yet confer no obvious advantage in contests with other males. He proposed the idea of female choice of mates, with females preferring the more ornamented males. Even if the traits concerned reduce the survival ability of the males, they can spread because of their advantage in competition for mates. This idea was poorly received, and largely neglected until the late 1950s, when John Maynard Smith provided evidence for female choice in *Drosophila subobscura*. It is now one of the cornerstones of behavioural ecology, with a large body of supporting evidence (see review by Pomiankowski).

These ornaments are likely to be deleterious to females, either because of physiological costs or because of increased conspicuousness to predators; genes that express their effects in producing the ornaments only in males are the most likely to be selected in this context. This explains why males are usually the more conspicuous of the two sexes, if any differences exist. This is just one example of the principle of sexually antagonistic effects of genes on fitness: an allele may be advantageous in one sex and disadvantageous in the other (see review by Chapman). This may be important in the evolution of Y and W chromosomes: linkage to the sex determining region of an incipient sex chromosome of sexually antagonistic genes (if they are not limited in expression to one sex) is favoured by selection, as first pointed out by Fisher in 1931. This could eventually lead to suppression of crossing over throughout most of the sex chromosomes in the heterogametic sex, setting the stage for the degeneration of Y and W chromosomes. This principle can be taken further: males may be selected for traits that enhance their own fitness, even if they reduce that of the females with whom they mate, for example by causing physiological reactions that reduce the chance of their sperm being displaced by a rival's. Similarly, females may be selected to resist the effects of such male traits. Experimental studies of *Drosophila* and comparative studies of groups such as water striders have provided compelling examples of such situations.

Overall, the evolutionary biology of sexual reproduction is one of the most flourishing branches of the field, and presents a striking example of a field in which it has been essential to synthesise data and ideas from disparate disciplines, including classical genetics, molecular genetics, population genetics, behavioural ecology, evolutionary ecology and comparative biology. Many of its core concepts can be traced back to Charles Darwin and R.A. Fisher. The papers in this volume show how the work of these two great pioneers can be connected to modern empirical and theoretical research.