Recombination and loss of complementation: a more than two-fold cost for parthenogenesis

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Introduction

In a sexual species with an equal ratio of males and females, a mutation on a gene that causes a female to produce only parthenogenetic female offspring is certain to be transmitted to all the eggs produced by that female, whereas a gene that permits meiosis is transmitted only to half the eggs. Put another way, asexual females can produce twice as many daughters as sexual females, so that the ratio of asexual to sexual females should, at least initially, double at each generation. This argument (Maynard-Smith, 1971, 1978) is known as the ‘two-fold cost of meiosis’, although the cost is not always actually two-fold and not necessarily associated with meiosis (Lewis, 1987). In fact, in species with isogamous gametes there is no such cost, and the argument therefore does not hold for the origin of sexual reproduction, when gametes were almost certainly isogamous. In species with anisogamous gametes, however, asexual reproduction (parthenogenesis) should replace sexual reproduction given the two-fold cost. The maintenance of sexual reproduction remains a major question in evolutionary biology.

Abstract

Certain types of asexual reproduction lead to loss of complementation, that is unmasking of recessive deleterious alleles. A theoretical measure of this loss is calculated for apomixis, automixis and endomitosis in the cases of diploidy and polyploidy. The effect of the consequent unmasking of deleterious recessive mutations on fitness is also calculated. Results show that, depending on the number of lethal equivalents and on the frequency of recombination, the cost produced by loss of complementation after few generations of asexual reproduction may be greater than the two-fold cost of meiosis. Maintaining complementation may, therefore, provide a general short-term advantage for sexual reproduction. Apomixis can replace sexual reproduction under a wide range of parameters only if it is associated with triploidy or tetraploidy, which is consistent with our knowledge of the distribution of apomixis.

Long-term explanations and the balance argument

There are many possible explanations for why sexual reproduction is maintained (reviewed by Kondrashov, 1993; Barton & Charlesworth, 1998; Otto & Lenormand, 2002) that derive, in different ways, from Weismann’s idea that sexual reproduction increases the variability on which natural selection can act (Burt, 2000). Ecological models suggest that sexual reproduction counterbalances its two-fold cost by creating new gene combinations, which allow sexual species to adapt to changing biotic interactions, with parasites being especially likely to provide the driving coevolutionary force (Jaenike, 1978; Bremermann, 1980; Hamilton, 1982, 1993; Seger & Hamilton, 1988; Hamilton et al., 1990; Burger, 1999). Mutation-based models suggest that sexual reproduction gets rid of deleterious mutations more efficiently (Kondrashov, 1982, 1988, 1994; Lynch et al., 1993). These advantages may explain the prevalence of sex in nature, although it is still debated whether or not they should be considered together in a pluralist approach (West et al., 1999).

These explanations suggest that, because of the two-fold cost, sexual reproduction should be displaced by parthenogenesis in the short term, but that, in the long term, asexual lineages will go extinct because they cannot evolve quickly enough to adapt to changing environments or because they accumulate deleterious mutations, while sexual species speciate. The end result is
that, at any one time, most species are sexual (Maynard-Smith, 1978).

Another important argument, however, suggests that this cannot be the complete explanation (Maynard-Smith, 1978). In a population of both sexual and asexual forms, asexuals should, at least initially, have a strong advantage and should replace the sexuals. If sexual reproduction persists, it must have some short-term advantage that counterbalances its two-fold cost. This is the ‘balance’ argument, put forward by Williams (1975). In other words, as the two-fold advantage of parthenogenesis occurs immediately at the first appearance of an asexual mutant, there should be an immediate, counterbalancing advantage for the sexually-reproducing species. Although some immediate advantages have been proposed, these hypotheses are far from being satisfactory (Maynard-Smith, 1978). Kondrashov’s synergistic epistasis theory (Kondrashov, 1982, 1988, 1994) is usually considered a short-term explanation, but even in this case fitness for asexual reproduction requires a period of time of the order of hundred generations to reach its equilibrium value that outweigh the two-fold cost of meiosis (Charlesworth, 1990).

Asexual reproduction

Asexual reproduction can be of three main forms (Fig. 1). In apomixis a meiotic division is suppressed, and a single division produces diploid offspring. In automixis meiosis is normal, producing four haploid pronuclei that then merge to restore diploidy. In endomitosis a normal meiosis is preceded by a round of chromosome replication.

It is well known that automixis quickly produces homozygosity at all or most loci, which is detrimental in most typical diploid outbreeding species. Therefore, not surprisingly, this kind of reproduction is very rare (Maynard-Smith, 1978). Endomitosis is also rare in nature (Vrijenhoek et al., 1989), probably because DNA damages cannot be repaired with endomitosis (Bernstein et al., 1988). Apomixis, on the contrary, is widely distributed in animals and plants, although it is usually facultative, i.e. alternating with episodes of sexual reproduction or only partial (a part of the offspring is produced sexually). Obligate apomixis is usually considered a secondary phenomenon, and exists, for example, in Oomycota, Phaeophita, Rhodophyta, flowering plants and Arthropoda. Sporadic apomixis may occur in most taxa (Kondrashov, 1997). The major problem, given the two-fold cost of meiosis, is to explain why apomixis does not prevail in nature (Maynard-Smith, 1978).

Apomixis

The term ‘apomixis’ is used, at least in plants, to refer to different kinds of asexual reproduction. In plants it is

Fig. 1 Asexual reproduction with no recombination. Homologs are in different colours (white and grey), sister chromatids are in the same colour. Centromeres are at the top of each chromosome. Automixis can be of four kinds: (a) fusion of cleavage nuclei; (b) fusion of sister nuclei; (c) fusion of nonsister nuclei; (d) fusion of random nuclei. Endomitosis can be of three kinds: (a) pairing of sister chromosomes; (b) pairing of nonsister chromosomes; (c) random pairing (not shown). Apomixis is the meiotic diplospory type.
possible to divide apomixis into the following groups (a good account of apomixis in plants is Asker & Jerling, 1992):

*Meiotic diplospory* (described in Figs 1 and 2): a restitutional meiosis; the reductional division is skipped; recombination does occur. The so-called *Taraxacum*-type and *Ixeris*-type belong to this group.

*Mitotic diplospory*: meiosis is replaced by mitosis; recombination does not occur. The so-called *Antennaria*-type belongs to this group.

*Apospory*: a somatic cell acts as a spore; recombination does not occur. The *Hieracium*-type belongs to this group.

These three groups are usually referred to together as 'gametophytic apomixis' while 'sporophytic apomixis' is the development of an embryo directly from a somatic cell (sometimes known also as adventitious embryony – different from *apospory* in that it does not proceed through the formation of a spore but directly of an embryo).

Apomictic reproduction with recombination was named 'subsexual reproduction' by Darlington (Darlington, 1937; Darlington & Mather, 1952) to describe some aberrant offspring in cultivation experiments of apomictic lineages. These aberrations were caused by the homoyzosity of genes distal to the site of crossing over (that is, loss of complementation for deleterious recessive mutations). Therefore 'subsexual reproduction' *sensu* Darlington is the kind of apomixis associated with recombination (meiotic diplospory), as in *Taraxacum officinale* (van Baarlen et al., 2000).

The genus *Taraxacum* contains some 2000 apomictic species, which are all triploid (mainly) or tetraploid, and 50 sexual species, which are all diploid. The common dandelion (*Taraxacum officinale*) exists in two forms: sexual diploids and polyploid apomicts. The diploids reproduce sexually and predominate in central and southern Europe, whereas the polyploids reproduce parthenogenetically by apomixis and are distributed in southern and eastern Europe, where they overlap with the sexual forms, and in the north. Note that apomictic dandelions are obligate apomicts, which never produce sexual seeds, although many apomictic species are only facultative apomicts. *Taraxacum* apomicts are triploid and avoid formation of unbalanced gametes and sterility by circumventing the first meiotic (reductional) division. As shown by van Baarlen et al. (2000), chromosome pairing and chiasma formation occur, although at lower levels than in sexual diploids. Therefore, the first meiotic prophase is initiated so that recombination can occur, although the first reductional division does not take place.

Loss of complementation may provide such an answer. With asexual reproduction, complementation is partially lost. This means that recessive deleterious mutations that were masked in the heterozygous state become homozygous. If this cost (which is absent in sexual reproduction with outcrossing) were larger than the two-fold cost of meiosis, parthenogenesis would not have an immediate advantage in a sexual population.

This argument is well-known (Maynard-Smith, 1978) for *automixis*. In automixis, loss of complementation depends mainly on the kind of nuclear fusion, which can be of four different types: between cleavage nuclei (generated by the same pronuclei), between sister nuclei, between nonsister nuclei and random (Fig. 1). Recombination is not the primary cause of loss of complementation; indeed it may even reduce it (see Fig. 2).

For *endomixis*, loss of complementation depends mainly on the kind of chromosome pairing, which can be between sister chromosomes (generated by the same chromosome at the first duplication), between nonsister chromosomes, or random (Fig. 1). If pairing is between sister chromosomes, loss of complementation does not occur. Again, recombination influences loss of complementation (Fig. 2), but is not the primary cause.

For *apomixis* (meiotic diplospory) on the contrary, loss of complementation occurs only with recombination (Figs 1 and 2). According to the terminology introduced by Stern (1936) for mitotic segregation, with one crossing over, recombinants can segregate in three possible ways (Fig. 3): *x* segregation occurs when recombinant chromatids segregate to opposite poles; *z* segregation occurs when both recombinants segregate in one daughter cell and both nonrecombinants segregate in another daughter cell (in this case the linkage relationships of genes is changed but there is no phenotypic difference from cells that did not experience a recombination event); *y* segregation occurs when sister chromatids fail to disjoin and segregate to the same daughter cell. Although *y* segregation is not normally observed, *x* and *z* segregation usually occur with equal frequencies. Loss of complementation occurs in the part of the progeny originated by *x* segregation. This means that in the part of the chromosome opposite to the centromere, all the recessive deleterious mutations, which were masked by diplody in heterozygous state, become homozygous.

I have shown (Archetti, 2003) that loss of complementation may provide an explanation for the origin of sexual reproduction; however in the discussion about the origin, because of the absence of anisogamy, one does not take into account the two-fold cost of meiosis. The focus of this paper is to provide a general, quantitative measure of loss of complementation, to test whether its cost may outweigh the two-fold cost of meiosis and provide a short-term explanation for the maintenance of sexual reproduction.
Methods

A quantitative measure of loss of complementation and fitness

Diploid apomixis, one crossing over

With only one crossing over per replication, each recombination event will produce loss of complementation in all parts of the chromosome, from the site of crossing over, distal to the centromere (that is opposite to the centromere). Imagine that the centromere is at one end of the chromosome and there are \( n \) sites where crossing over can occur. If we assume that these \( n \) sites have the same distance between each other, then they divide the chromosome into \( n \) parts with the same length. Let \( m \) be the number of the \( n \) parts where complementation is lost (and \( \phi = m/n \) the fraction of chromosome). If there is only one crossing over event per replication, then it is possible to derive analytically the fraction of chromosome where complementation is lost after successive generations. The progeny generated by \( z \) segregation will have exactly the same loss of complementation as the parent. In the progeny generated by \( x \) segregation, instead, recombination will increase loss of complementation only if crossing over occurs at a site that is between the centromere and the part of the chromosome where complementation is already lost. Therefore, for example, if \( \phi = 0 \), the progeny generated by \( x \) segregation will be made of individuals in which all the possible values of \( \phi \) from \( 1/n \) to 1 will have the same frequencies; if \( \phi = 1/4 \), for example, 1/4 of the progeny generated by \( x \) segregation will not have further loss of complementation, and will maintain \( \phi = 1/4 \), whereas for the other 3/4 of the progeny, \( \phi \) will be between \((1/4 + 1/n)\) and 1.

In general, with \( x \) segregation, \( m \) times recombination will not increase loss of complementation, and \((n - m)\) times it will; with \( z \) segregation it will never increase. In other words, if \( m' \) is the number of parts with loss of complementation in the offspring, each individual

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**Fig. 2** Asexual reproduction with one recombination event. Compare with Fig. 1.
we must consider that selection against deleterious recessive mutations eliminates more easily individuals with higher loss of complementation. The effects of unmasking recessive deleterious mutations (loss of complementation) can be quantified by the number of lethal equivalents ($\lambda$). One lethal equivalent is one gene whose effects, when no longer masked by diploidy, are lethal for its bearer (or, assuming no epistasis and exactly additive effects, more genes whose effects summed together are lethal when unmasked). The fitness of an asexual individual, is $w = (1-\phi \lambda)$; if $\phi \lambda > 1$, then $w = 0$, because an individual can have more than one lethal equivalent but cannot be killed more than once.

Therefore, if $x_i$ is the frequency of individuals with $m = i$, and $w_j = 1 - (i/n)\lambda$ (with the constraint that $w_i$ is not <0) is the fitness of an individual with $i$ parts [$i \in (0,n]$ of the chromosome with loss of complementation, then after one generation $x_m$ is given by (see Table 1):

$$T \cdot x_m = \sum_{i=0}^{m} \frac{1}{2n} x_i w_i + \frac{m-1}{2n} x_m w_m + \frac{1}{2} x_m w_m$$

where $T$ is a normalizing factor obtained by summing the right-hand side over all $m$.

**Diploid apomixis, multiple crossing over events**

In general, there may be more than one crossing over per chromosome. Indeed there are often multiple crossing over events per chromosome per replication, usually at least one, and on average about one to three per chromosome (Bell, 1982), although in triploid apomictic species this number is probably lower (for example see van Baarlen et al., 2000).

With multiple crossing over events, if they occur between the same two chromatids, recombination will abolish complementation only in chromosomes produced by $x$ segregation (see Fig. 4), as for the case of one crossing over; however, the fraction of chromosome where complementation is lost will change. It can be verified to be $n/[2(n+1)]$, after one generation, where $n$ is the number of recombination events, among all chromosomes (not only the ones undergoing recombination). Note that $n$ recombination events, here and in the rest of the paper, means $n$ crossing over events that lead to recombination of flanking genes (and not only gene conversion at the site of initiation).

The calculation becomes more difficult after successive generations. Moreover, there is no compelling reason to assume that, given multiple crossing over events, they always occurs between the same two chromatids; indeed, they are well known to occur between all (nonsister) chromatids. In this case, loss of complementation not only increases; it also occurs in progeny other than those generated by $x$ segregation. The fraction of chromosome with loss of complementation depends on the number of crossing over events, on which chromatids participate in the exchange and on the order of crossing over events.

**Table 1** Offspring produced by apomixis with one crossing over event per replication.

<table>
<thead>
<tr>
<th>Progeny</th>
<th>Parent Fitness</th>
<th>$x_0$</th>
<th>$x_1$</th>
<th>$x_2$</th>
<th>$x_3$</th>
<th>$x_n$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$x_0$</td>
<td>$w_0$</td>
<td>1/2</td>
<td>1/2n</td>
<td>1/2n</td>
<td>1/2n</td>
<td>1/2n</td>
</tr>
<tr>
<td>$x_1$</td>
<td>$w_1$</td>
<td>-</td>
<td>1/2 + 1/2n</td>
<td>1/2n</td>
<td>1/2n</td>
<td>1/2n</td>
</tr>
<tr>
<td>$x_2$</td>
<td>$w_2$</td>
<td>-</td>
<td>-</td>
<td>1/2n</td>
<td>1/2n</td>
<td>1/2n</td>
</tr>
<tr>
<td>$x_3$</td>
<td>$w_3$</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1/2 + 3/2n</td>
<td>1/2n</td>
</tr>
<tr>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>$x_n$</td>
<td>$w_n$</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1/2 + n/2n</td>
</tr>
</tbody>
</table>

$x_i$ and $w_i$ are, respectively, the frequency and the fitness of individuals with $m = i$ (see text).
Unfortunately, in this case, an analytical description of loss of complementation is much more difficult than for the case of one crossing over. Moreover one should iterate the frequency of all possible patterns (each pattern is characterized by the number of crossing over events, by which chromatids participate in recombination and in which order) over successive generations. I did not manage to find a general formula to quantify loss of complementation for the case of multiple crossing over events, but the procedure to calculate it can be reproduced by a simple algorithm.

In principle, it is possible to calculate the fraction of chromosome where complementation is lost for every possible pattern of recombination. However the number of possible patterns becomes so great as the number of crossing over events increase, that it becomes difficult to calculate loss of complementation for all patterns for more than four or five recombination events in a reasonable amount of time. Therefore, I have calculated the mean fraction of chromosome where complementation is lost by choosing 1 million random patterns. This is an approximate procedure, but it yields a measure reasonably close to the deterministic one (when checked, for up to four crossing over events, it was virtually exact). I randomly chose a pair of nonsister chromatids and a random site where crossing over occurs. Then, when another crossing over event occurs, I again chose at random two chromatids and a site of crossing over, and so on for a given number of crossing over events. This procedure is consistent with the fact that chromatid interference does not occur, that is, that crossing over occurs on one chromatid independently of whether that chromatid has been involved in the previous crossing over. Chromosome interference, the biased probability of crossing over in the neighbourhood of a previous crossing over, is not taken into account (results not shown here suggest that it is not very important). Fitness of asexual individuals is calculated exactly as for the case of one crossing over.

**Polyploidy, automixis and endomitosis**

This procedure can be used to measure loss of complementation not only for apomixis, but for all kinds of automixis and endomitosis, with the difference that segregation occurs in different ways (see Fig. 2). Moreover it can be used to calculate loss of complementation for triploidy and tetraploidy, which I will discuss below. I assume that, at each replication, if there are multiple crossing over events, they occur always between the same two chromosomes (but, as discussed above, not necessarily between the same two chromatids), that is, only bivalents are formed. In triploid *Saccharomices cerevisiae* it seems possible that three homologs pair at the same time (Loidl, 1995), but in Taraxacum only bivalents occur (van Baarlen *et al.*, 2000).

**Frequency of asexual reproduction**

If \( s \) is the number of asexual females and \( S \) the number of sexual individuals, in one generation the proportion of asexual females will increase from \( s/(S + s) \) to \( 2s/(S + 2s) \); when \( s \) is small this is a doubling in each generation. This is the reason why meiosis is usually said to have a two-fold cost (Maynard-Smith, 1978). The cost is actually two-fold only when compared with an asexual with no loss of complementation. However, when the effects of loss of complementation are considered, the proportion of asexual females will increase, in one generation, from \( s/(S + s) \) to \( 2sW/(S + 2sW) \), where \( W \) is the mean fitness of asexual individuals calculated with the method...
described above. Therefore the frequency of asexual individuals \((f)\) after one generation will be:

\[
f' = \frac{2fW}{(1-f)+2fW}
\]

(2)

Fitness of sexual individuals is assumed \(= 1\), with respect to the effect of deleterious recessive mutations. That is I assume a large outcrossing population in which, because of random mating, the frequency of individuals with deleterious recessive mutations in homozygous state is negligible. The production of gametes followed by syngamy may produce homozygous recessive mutations at some loci only if syngamy is with a gamete with recessive mutations exactly at the same loci, which is unlikely with outcrossing and a large number of loci. With asexual reproduction, on the contrary, loss of complementation occurs for all loci on the whole chromosome or on whole parts of the chromosome, irrespective of the number of loci and of the population size (see Fig. 3).

With one crossing over per meiosis, the fitness of asexual individuals can be calculated exactly using (1) and their frequency iterated using (2). On the contrary, with multiple crossing over events, it is not feasible to calculate exactly loss of complementation (and therefore fitness) as with (1) because, as explained above, one should iterate the frequency of all possible patterns, which vary not only according to the number and order of crossing over events, but also according to their combinations over successive generations. Therefore I use a partially stochastic approach. I introduce a certain number (1000) of asexual individuals that undergo selection, reproduce and transmit their patterns to the next generation. To ensure that there are enough patterns to calculate the mean loss of complementation and approximate an infinite population, I keep the number of asexual individuals constant. The measure of loss of complementation is always calculated on 1000 patterns (using more than 1000 patterns increases the time required for simulation drastically without significantly increasing the precision). In fact, this is not a stochastic simulation, but rather a method to approximate a deterministic simulation (on the other hand, this method avoids stochastic fluctuations caused by small numbers of individuals, both in the calculation of loss of complementation and in the population dynamics). Of course, this method is correct in this case only because selection on loss of complementation is neither density- nor frequency-dependent.

Therefore, the procedure used in the simulations is the following: (i) each asexual individual (in a population of 1000 individuals) produces two new individuals (according to the schemes in Fig. 2); (ii) loss of complementation \((\phi)\) and fitness \((W = 1 - \phi \lambda)\) is calculated for each of these (2000) new individuals (with the procedure described in the previous paragraph); (iii) the new (1000) individuals for the next generation are chosen from among the progeny of the current individuals with a probability proportional to their fitness. Individuals already chosen are not excluded from being chosen again.

### Results

#### Apomixis

**One crossing over**

In the hypothetical case of no selection \((\lambda = 0)\), loss of complementation in the asexual lineage increases constantly after further generations (Fig. 5), because, at each replication, recombination produces homozygosity on more and more parts of the chromosome (the increase of loss of complementation is slower after successive generations because when a part of the chromosome is already homozygous, it is less likely that further recombination events will occur on parts of the chromosome that still have complementation). In a real population, however, there will be some variation among individuals. The ones that preserve complementation in a greater part of the genome will produce more offspring, so that the population’s mean loss of complementation after further generations will be ‘slower’ than the hypothetical loss of complementation without selection.

When selection is taken into account (see Methods) loss of complementation decreases. With one crossing over at each reproductive event, there is always half the progeny (produced by \(z\) segregation) in which loss of complementation does not increase, and this is the reason why fitness never gets below 0.5 (Fig. 6). With one crossing over, asexual reproduction replaces quickly sexual reproduction (see Table 2) if the number of lethal

![Fig. 5 Loss of complementation for diploid apomixis with one crossing over. No selection. Loss of complementation is the fraction of chromosome where complementation is lost.](image)
equivalents is ≤1, whereas if it is >1, fitness for the asexual gets so quickly close to 0.5 that the two-fold cost of meiosis is almost immediately balanced (Fig. 6) and the frequency of asexual individuals will not increase much (Fig. 7). Indeed, if the cost of sex is was even slightly less than two-fold, asexuals could even disappear because their fitness is very close to 0.5 (this depends on the fact that x segregation and z segregation occur with the same frequency). Results obtained using the recurrence (1) correspond almost exactly to those obtained when the approximate procedure for the calculation of loss of complementation (see Methods) is used.

Therefore, with one crossing over event, fitness for asexual reproduction never gets below 0.5 and asexual reproduction can always invade sexual reproduction, although with more than one lethal equivalent the fitness for the asexuals is so close to 0.5 that it immediately almost compensates the two-fold cost of meiosis, and asexual reproduction does not increase in frequency. However this is no longer the case when more than one crossing over occurs (see following section).

**Multiple crossing over events – one generation**

With one recombination event, half the progeny (those originated by z segregation) have no loss of complementation, and the other half (those originated by x segregation) have, on average, loss of complementation in 50% of the chromosome. The loss of complementation values vary with more recombination events (Fig. 8), although the mean value increases only slightly. The mean fitness for apomixis depends on the number of lethal equivalents and recombination events (Fig. 9). Note, again, that whatever the number of lethal equivalents, fitness can never be below 0.5 with one recombination event because crossing over may occur only between two of the four chromatids and loss of complementation occurs only in one half of the progeny (with x segregation). However, when the number of crossing over events increases this is no longer the case, and the cost because of loss of complementation may outweigh the two-fold cost of meiosis already at the first generation, for example with two recombination events if $\lambda = 4$ or with five recombination events if $\lambda = 2$ (Fig. 9).

**Multiple crossing over events – further generations**

Even if the frequency of recombination and the number of lethal equivalents are such that apomixis manages to invade a sexual population, after further generations complementation will be lost on more and more parts of the chromosome. Therefore, the frequency of apomicts may increase at the beginning, because of the two-fold cost of meiosis, but it is possible that it will then decrease because of the cost induced by loss of complementation. The higher is the number of recombination events, the quicker loss of complementation will be (Fig. 10). In this case, with multiple crossing over events, loss of complementation may quickly induce a cost for asexual reproduction that is greater than the two-fold cost of meiosis (Fig. 11). Asexual reproduction still replaces sexual reproduction if the number of lethal equivalents is <0.5 (Table 2). With 0.5 lethal equivalents, after complementation is completely lost in the asexuals, there is an equilibrium where asexual and sexual forms coexist. Sexual reproduction suffers the two-fold cost of producing male gametes; asexual reproduction suffers the cost of having unmasked semi-lethal (0.5 lethal equivalents) mutations. However, this situation is, of course, unstable and holds only for exactly 0.5 lethal equivalents and exactly two-fold cost. With more than 0.5 lethal equivalents, however, loss of complementation outweighs the two-fold cost of meiosis after few generations (Fig. 11) and asexual reproduction does not manage to replace sexual reproduction, indeed it disappears within few generations (Table 2).
Consider now the case of triploid apomicts. With three copies of the same gene, loss of complementation is expected to be slower. Indeed loss of complementation for a triploid apomictic lineage with recombination is much slower than for the case of diploidy (Fig. 12). Tetraploidy leads to similar results; the difference with the triploid case is rather small, much smaller than the difference between the diploid and the triploid case (Fig. 12). The reason is that with tetraploidy both bivalents undergo crossing over. In the triploid case when complementation is lost at an allelic position between two chromosomes, there is still another allele on the third chromosome, therefore two different alleles may remain; in the tetraploid case complementation is lost in both pairs of chromosomes (although not necessarily at the same position at the same generation, because crossing over may occur at different positions), therefore two different alleles may remain as well. Loss of complementation will be slower in the tetraploid case because there are two copies of each allele, but apparently it is not drastically different from the triploid case. Both in the triploid and in the tetraploid case, asexual reproduction replaces sexual reproduction even if the number of lethal equivalents is very high (Table 2). Note that with a high frequency of recombination and with a high number of lethal equivalents, apomixis may be even slightly slower in replacing sexual reproduction with tetraploidy than with triploidy.

### Automixis

For apomixis, fusion of *cleavage nuclei* immediately abolishes complementation on the whole chromosome, although the effects of fusion of *nonsister nuclei* are equivalent to apomixis, therefore I will not discuss these two cases further.

### Table 2: Evolution of asexual reproduction. Each entry is the number of generations (mean value for 10 runs) for the disappearance (frequency <0.001, in italics) or the fixation (frequency >0.999, in bold) of asexual reproduction after an asexual mutant is introduced with a frequency of 0.001 in a sexual population.

<table>
<thead>
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<th>Lethal equivalents (λ)</th>
<th>Rec*</th>
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<th>2</th>
<th>4</th>
<th>6</th>
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<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
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</tr>
<tr>
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<td>20</td>
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</tr>
<tr>
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<td>42</td>
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</tr>
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<td>192</td>
<td>25</td>
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*Number of crossing over events (for 1.25 and 1.5, one crossing over always occurs and a second crossing over occurs with a probability, respectively, of 25 and 50%).

†Type of gamete fusion (for automixis) or chromosome pairing (for endomitosis).

The ploidy level is indicated (3X = triploid, 4X = tetraploid) if not diploid.

nd: asexual reproduction persists at very low frequency for many generations.
Figure 13 shows loss of complementation and fitness for automixis with fusion of random nuclei and with fusion of sister nuclei. In the latter case (which is equivalent to the suppression of the second meiotic division) loss of complementation does not depend on the number of recombination events (this is not intuitive perhaps, but can be checked by drawing all the possible recombinant products, easily at least for two recombination events). In both cases the deleterious effects of recombination are significant, and an automictic lineage can replace a sexual population only if the number of lethal equivalents is very low (Table 2).

**Endomitosis**

With endomitosis, recombination does not seem to affect much loss of complementation, which depends mainly on the kind of chromosome pairing. With sister (originated after the first duplication) chromosome pairing there is no loss of complementation at all. With nonsister pairing, homozygosity increases but it does not depend much on recombination (Fig. 14). Although pairing may feasibly occur between sister chromosomes, it seems that there is no reason why pairing should occur preferentially between homologous nonsister chromosomes. Pairing may, however, be random between sister or nonsister chromosomes. Although triploidy slows down...
the rate of loss of complementation (Fig. 14), its effect is not so important for endomitosis as for apomixis. However, with selection, triploidy may favour endomitosis, but only if the frequency of recombination is low. In this case endomitosis may replace sexual reproduction even if the number of lethal equivalents is rather high. With higher frequencies of recombination, instead, endomitosis is favoured by diploidy (Table 2).

Comparison of the results

Comparing the results for the three kinds of asexual reproduction (see Fig. 15 and Table 2) leads to the following conclusions.

Fitness for apomixis depends strongly on recombination. With diploidy, asexual reproduction does not manage to replace sexual reproduction because loss of complementation induces a cost on apomictic reproduction that is greater than the two-fold cost of meiosis. Therefore an asexual lineage disappears after few generations. The number of generations required for the extinction of the asexual lineage is between 10 and 100 with one lethal equivalent, and <10 with more than one lethal equivalent. Triploidy, however, slows down loss of complementation, and in this case apomixis can replace sexual reproduction. The effects of tetraploidy are similar to triploidy.

Fitness for automixis does not depend very much (or not at all) on recombination. Because of loss of complementation, automixis does not replace sexual reproduction unless the number of lethal equivalents is very low.

Fitness for endomitosis depends mainly on the kind of chromosome pairing (and recombination has some effect only with nonsister chromosome pairing). With sister chromosome pairing it can easily replace sexual reproduction, because in this case there is no loss of complementation. With a low frequency of recombination triploidy favours endomitosis, and with random pairing of chromosomes endomitosis can replace sexual reproduction if the number of lethal equivalents is rather low.

Discussion

The results obtained for automixis are not surprising. It was already well known (Maynard-Smith, 1978) that automixis quickly leads to loss of complementation, and for this reason it is rare in nature. Fusion of cleavage nuclei produces 100% homozygosity instantly. According to Nur (1971), the very few cases described are derived from haplo-diploid arrhenotokous ancestors (with the possible exception of the stick insect Bacillus rossius) because in haploids all genes are exposed to
selection, which makes the load of recessive deleterious mutations much lower than in typical diploid sexual outbreeding species. In *D. mangabeirai*, the only known species of *Drosophila* with natural parthenogenesis, automixis occurs with fusion of nonsister nuclei, nonetheless egg mortality is high because of loss of complementation (Maynard-Smith, 1978). The other types of fusion are more common, but automixis is absent in plants.

Endomitosis is very rare in nature: it is known, for example, in five genera of lizards, including *Lacerta, Hemidactylus* and *Cnemidophorus* (Vrijenhoek et al., 1989), and some insects e.g. the grasshopper *Moraba virgo* (Maynard-Smith, 1978). For endomitosis, loss of complementation depends mainly on the kind of chromosome pairing. Sister chromosome pairing is certainly possible, but in this case double strand breaks cannot be repaired (Bernstein et al., 1988) because there is no template to carry out the repair (the paired sister chromosome, which is supposed to provide the template, also has a break in the same position, as it is a copy). Thus, sister pairing cannot probably be the rule in endomitosis. Our knowledge of the details of pairing is still quite poor. In *Cnemidophorus tesselatus*, at least, evidence shows that recombination and nonsister pairing may occur (Parker & Selander, 1976).

In the rest of this discussion I will deal with apomixis. For apomixis, with recombination, results depend on the
Obligate apomixis in plants may only be an artefact due to poor screening or large population sizes [according to Asker & Jerling (1992), truly obligate apomicts are unlikely to exist at all], but some apomicts like Taraxacum may be actually 99% apomictic (it probably falls short of 100% because of incomplete penetrance of the dominant apomixis genes, which probably suppress sexual reproduction – P. van Dijk, personal communication). A tentative list of other ‘obligate’ apomicts (P. van Dijk, personal communication) includes Chondrilla, Ixeris, Erigeron, Eupatorium, Townsendia, Boechera (= Arabis) holboellii, and perhaps Rudbeckia and Hieracium subgenus Euhieracium. These are all triploid.

Why is polyploidy so commonly associated with apomixis? Diploid and apomixis are not incompatible (Nogler, 1982; Bicknell, 1997; Kojima & Nagato, 1997); therefore, triploidy possibly confers some advantage to apomixis, or the other way round. Indeed, Bicknell et al. (2000) have shown that the low frequency of diploidy compared with triploidy in Hieracium is due to some form of natural selection against diploids.

My suggestion is that, as I have shown, triploidy ‘protects’ apomixis against loss of complementation. Tetraploidy does not lead to drastically slower loss of complementation, therefore it is possible that this slight advantage compared with triploidy is not enough to counterbalance the disadvantages conferred by the increased ploidy level. In other words triploidy is enough to preserve complementation. However other types of apomixis have higher ploidy levels. Another possible explanation is that (P. van Dijk, personal communication) recombination rates in tetraploid apomicts are greater than in triploids, therefore, for this reason, loss of complementation could be slower in triploids than in tetraploids.

As triploidy leads to sterility (because of aneuploidy) with sexual reproduction, one might think that apomixis evolved after triploidy and allowed the triploid mutant to survive. However as triploidy produces instant sterility (with sexual reproduction), this would require that a mutation for apomixis evolve simultaneously with triploidy. Although possible, this seems implausible for so many species. The alternative possibility is that apomixis evolved first and triploidy followed. This situation seems more realistic for the following reasons. First, apomixis may persist, even in absence of triploidy, for some generations before it is displaced by sexual reproduction. Secondly, triploidy does not require a mutation as apomixis does; the fertilization of a diploid egg by haploid pollen suffices and seems to be the usual way that triploid parthenogenesis arises (Cuellar, 1974; Maynard-Smith, 1978): genetic modifiers first accumulate to cause parthenogenesis; accidental hybridization between such a race and males from a different sexual race then give rise to a triploid race, already capable of parthenogenetic reproduction.

Throughout this paper I have discussed the Taraxacum kind of apomixis. Loss of complementation will not occur in species with no recombination. Therefore, how

number of lethal equivalents and, drastically, on the ploidy level. Available data suggest that the number of lethal equivalents is between 1 and 6 for vertebrates and for Drosophila, whereas it is larger (between 2 and 10) for conifers and much smaller for short-lived angiosperms (much <1 in embryos of many herbaceous plants, possibly more after development) and ferns (<1.3) (Lynch & Walsh, 1998). Therefore it is probably a general rule that diploid apomixis cannot replace sexual reproduction: this will be possible only if the number of lethal equivalents is rather low.

Note that the number of generations required for the extinction of the asexual lineage in the model described here is much smaller (and in some cases apomixis does not even invade) than the number of generations estimated for Kondrashov’s (1982) model of synergistic epistasis, which requires a period of time of the order of a hundred generations (Charlesworth, 1990). It will be important, to understand the generality of this result, to know the number of lethal equivalents in many more species. If the number of lethal equivalents is enough to balance the two-fold cost of meiosis, the effect described here may provide a strong short term explanation for the maintenance of sexual reproduction (which does not even require specific assumptions of epistasis). On the contrary, loss of complementation can enhance the long-term effects of mutation accumulation in asexual lineages, thus fastening their extinction considerably.

The model presented here makes another prediction: apomixis can replace sexual reproduction, even if the number of lethal equivalents is very high, if it is associated with polyploidy.

Polyploidy seems to be the rule among obligate apomicts (triploidy in the Taraxacum type of apomixis). Obligate apomixis in plants may only be an artefact due to poor screening or large population sizes [according to Asker & Jerling (1992), truly obligate apomicts are unlikely to exist at all], but some apomicts like Taraxacum may be actually 99% apomictic (it probably falls short of 100% because of incomplete penetrance of the dominant apomixis genes, which probably suppress sexual reproduction – P. van Dijk, personal communication). A tentative list of other ‘obligate’ apomicts (P. van Dijk, personal communication) includes Chondrilla, Ixeris, Eri-

Fig. 15 Loss complementation for different kinds of asexual reproduction with one recombination event per replication. No selection. Apomixis (□): diploid (white), triploid (black) or tetraploid (grey). Automixis (○): sister pairing (white) or random pairing (black). Endomitosis, random pairing (●): diploid (white) or triploid (black).
general is the argument developed here and how relevant for the evolutionary theory of the maintenance of sexual reproduction, will depend on the frequency of recombination in apomixis and on the frequency of truly obligate apomicts in nature.

Acknowledgments
I am grateful to Peter van Dijk for many useful comments on apomixis in plants, and to Dieter Ebert and Alan Grafen for useful suggestions on the manuscript.

References
Hamilton, W.D. 1993. Haploid dynamic polymorphism in a host with matching parasites: effects of mutation/subdivi-
Erratum

In Archetti (2004), the following error was published in the Methods section, paragraph entitled Frequency of asexual reproduction on page 6.

However, when the effects of loss of complementation are considered, the proportion of asexual females will increase, in one generation, from \( s/(S + s) \) to \( 2sW/(S + 2sW) \)...

The text was incorrect and should have read:

However, when the effects of loss of complementation are considered, the proportion of asexual females will increase, in one generation, from \( s/(S + s) \) to \( 2sW/(S + 2sW) \)...

We apologize for this error.

Reference