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Complementation, Genetic Conflict, and the Evolution of Sex and Recombination

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Abstract

The existence of sexual reproduction is difficult to explain because the 2-fold cost of meiosis requires a compensatory 2-fold advantage that is difficult to prove. Here, I show that asexual reproduction has a short-term disadvantage due to the loss of complementation of recessive deleterious mutations, which can overcome the 2-fold cost of meiosis in one or few generations. This complementation hypothesis can also explain why most asexual species are polyploid, why only certain types of asexual reproduction exist, why meiosis is not one-step, and the origin of amphimixis. I also show that the promotion of variation by recombination is not necessary to explain the evolution of amphimixis. Instead, recombination can be the result of an intragenomic conflict between alleles that induce the initiation of crossing over and alleles that evolve to resist that initiation. Thus recombination does not require any advantage at the individual or population level.

Key words: *amphimixis, apomixis, automixis, endomitosis, asexual reproduction, complementation, deleterious mutations, gene conversion, genetic conflict, intragenomic conflict, meiosis, recombination, sexual reproduction*

Why sexual reproduction exists is perhaps the most important unsolved problem in evolutionary biology. It is relevant not only for our understanding of the evolution of life cycles but especially because it poses a fundamental problem to the theory of evolution by natural selection, a crisis that evolutionary biologists have tried to address for almost 4 decades (Maynard Smith 1971; Williams 1975; Bell 1982).

This paper suggests a possible solution that differs from those on which research has focused so far. This is a strong claim and it might sound surprising, as it seems an unquestioned belief among evolutionary biologists that, as John Maynard Smith put it (Maynard Smith J, personal communication), "we have the answers, we just can't agree on them." This new solution is based on a number of ideas I proposed recently (Archetti 2003, 2004a, 2004b). As we shall see, however, Maynard Smith himself, at the beginning of *The Evolution of Sex* (Maynard Smith 1978, p. 7–9), outlined a simple and general theory that mirrors these ideas (with one important difference). I call this the "complementation" hypothesis.

This idea has been ignored in virtually all discussions of the topic; Maynard Smith himself decided to abandon it because of a conceptual problem he could not solve (Maynard Smith 1978, p. 9, personal communication). The second purpose of this paper, therefore, is to suggest a solution to Maynard Smith's conceptual problem. I call this the "genetic conflict" hypothesis. The 2 hypotheses are related but independent.

The Problem

What Asexual Reproduction Is

The terminology used to describe asexual reproduction is particularly confused. In most discussions it is assumed that asexual simply means clonal: an individual producing exact copies of itself. This is incorrect, and it has important consequences. Therefore, a few definitions are necessary before discussing the problem. The production of asexual seeds in plants (agamospermy) was first described by Smith (1841), although the first reference to "parthenogenesis" (virgin birth) I am aware of in animals is by Owen (1849). Winkler (1908) instead used the presence or absence of "fusion" (mixis) to define reproduction as "amphimictic" (sexual: with fusion) or "apomictic" (asexual: without fusion). "Amphimixis" is often used as a synonym of "sexual reproduction"; however, sexual reproduction may be misleading because it implies the presence of morphologically different sexes or gametes, which would exclude mating types. Both parthenogenesis (a term used mainly by zoologists) and apomixis (a term used mainly by botanists) mean asexual reproduction. Although apomixis is more specific (see below), both terms are too generic to be useful

in theoretical analysis. The standard classification of the types of asexual reproduction for plants seems to be the one adopted by Asker and Jerling (1992) and Nogler (1984):

1. Vegetative propagation: a new individual formed neither through seed nor embryo
2. Apomixis (sporophytic and gametophytic):
    - 2.1 Sporophytic apomixis (adventitious embryony): embryo (sporophyte) from a somatic cell of the ovule (usually the nucellus).
    - 2.2 Gametophytic apomixis (apospory and diplospory): embryo sac (female gametophyte) from an initial unreduced embryo sac.
        - 2.2.1 Apospory: unreduced embryo sac from a somatic cell of the ovule (usually the nucellus).
        - 2.2.2 Diplospory (meiotic and mitotic): unreduced embryo sac from a generative cell (female archesporial cell, megaspore mother cell).
            - 2.2.2.1 Meiotic diplospory (Taraxacum type and Ixeris type): a modified meiosis without the first division.
            - 2.2.2.2 Mitotic diplospory (Antennaria type): a mitotic division.

This classification has 2 problems: first, it is based on embryology rather than genetics; but what matters for our argument is the genetic system (the rules by which the genetic information is transmitted from one generation to the other); second, it does not include automixis and endomitosis, which are very rare in plants but occur in animals. The classification of asexual reproduction in animals (Suomalainen 1950; Suomalainen et al. 1987) is simpler (because plants have alternation of generations and in some cases double fertilization, which can lead to very complicated life cycles). A classification based on genetic systems is the following.

1. Apomixis (Figure 1): a normal meiosis is absent
    - 1.1. Mitotic apomixis: a normal mitosis
    - 1.2. Meiotic apomixis: a meiosis in which one division is suppressed:
        - 1.2.1. Suppression of the first division
        - 1.2.2. Suppression of the second division
2. Automixis (Figure 2): a normal meiosis followed by fusion of nuclei:
    - 2.1. Cleavage nuclei (generated by the same pronuclei)
    - 2.2. Sister nuclei (generated by the same division)
    - 2.3. Nonsister nuclei (generated by the other division)
3. Endomitosis (Figure 3): a normal meiosis preceded by a replication:
    - 3.1. Sister chromosome pairing (generated by the same replication)
    - 3.2. Nonsister chromosome pairing (not generated by the same replication)

This classification includes all the possible simple types of asexual mutants arising from (2-step) meiosis, that is, those that arise by a further replication before the 2 divisions (endomitosis), by fusion of meiotic products after the 2 divisions (automixis) or by the suppression of one division (meiotic apomixis). Therefore, I have listed all plausible types including meiotic apomixis in which the second division is skipped, because it is plausible in principle, although it probably doesn't exist at all (as we shall see, according to the complementation hypothesis there is a reason why). In principle, it is possible to envisage even further types, for example, an endomitosis with many rounds of replication and division or asexual mutants derived from more complicated alternatives to 2-step meiosis (Haig 1993; Archetti 2004a); these speculative alternatives are not included in the list. I describe elsewhere why they are not likely to exist at all and how this fits with the complementation hypothesis (Archetti 2004a).

Note that vegetative propagation, sporophytic apomixis, and apospory occur in plants in the presence of normal amphimixis; they require special conditions to be triggered

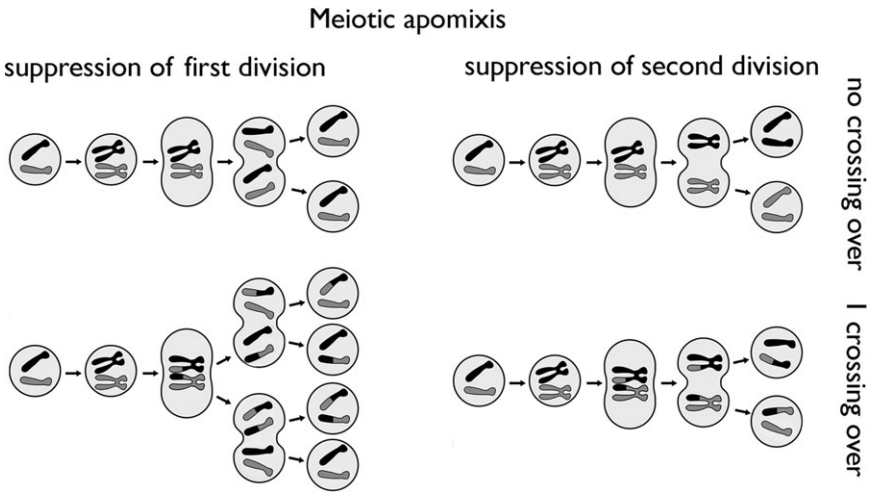

Figure 1. Meiotic apomixis with suppression of the first or second division, with or without recombination.

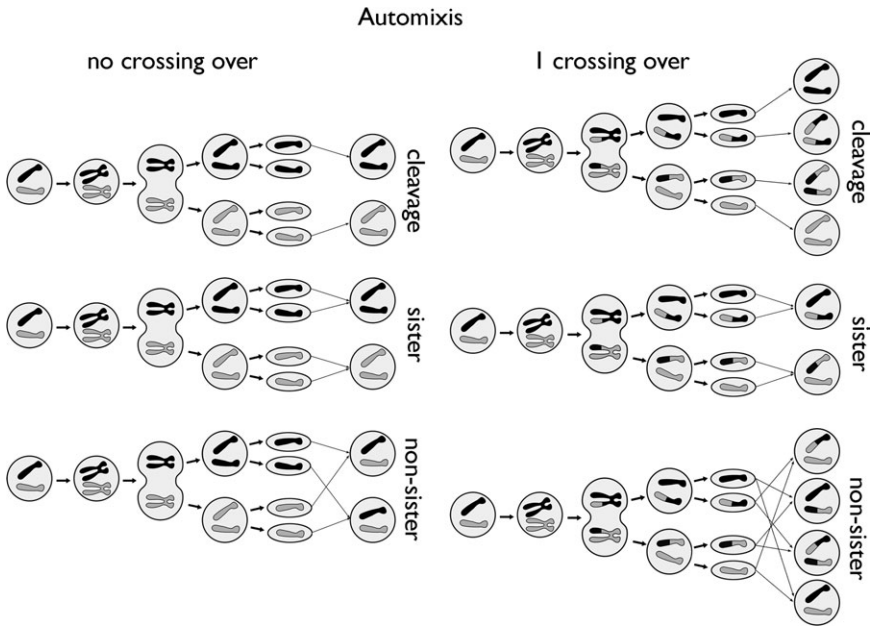

Figure 2. Automixis with fusion of cleavage nuclei, sister nuclei, or nonsister nuclei, with or without recombination.

(Nogler 1984) and can be considered an auxiliary rather than a normal mode of reproduction; they produce a continuation of the somatic line of the parents rather than new individuals. Therefore, mitotic diplospory is the only kind of mitotic reproduction that is really important for our discussion.

To complete the nomenclature it is useful to remember that normal (i.e., not sporadic) asexual reproduction can be "facultative" (mixed with amphimixis) or "obligate" (exclusively asexual); if obligate it can be either "constant" or "cyclical" (alternate with amphimixis). Facultative parthenogenesis is usually the rule in plants; cyclical parthenogenesis, on the other hand, occurs in animals (Kondrashov 1997), and it has no obvious counterparts in plants (Asker and Jerling 1992).

The 5 Problems with Sexual Reproduction

I list 5 problems that must be addressed. Clearly, this and any other classification are to some extent arbitrary. The

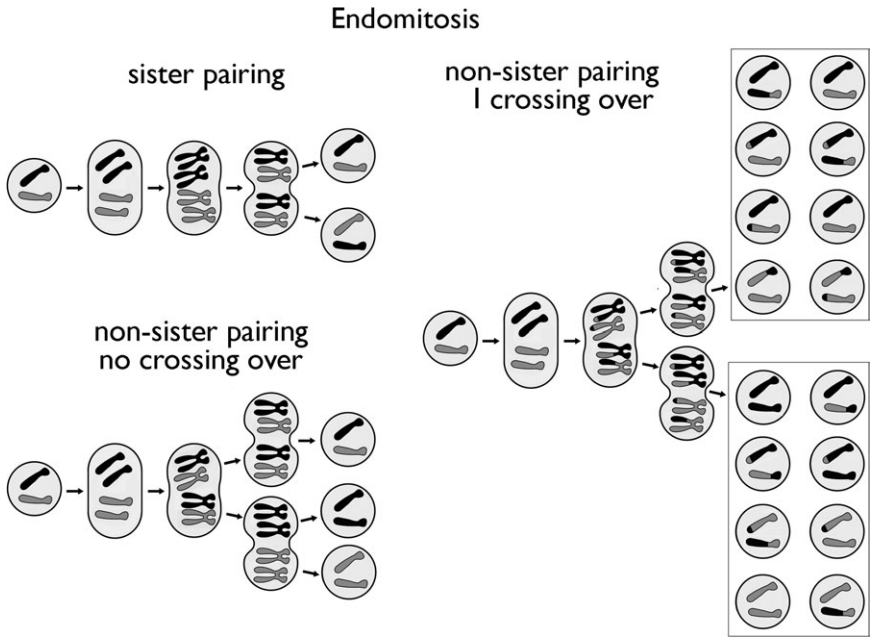

Figure 3. Endomitosis with sister chromosome pairing and with nonsister chromosome pairing, with or without recombination.

5 points below, however, seem to capture the essential facts in a simple way.

The Balance Argument

Asexual females can produce twice as many daughters as sexual females: if N_A is the number of asexual females and N_S the number of sexual individuals, in one generation the proportion of asexual females will increase from $N_A/(N_S+N_A)$ to $2N_A/(N_S+2N_A)$; therefore, the ratio of asexual to sexual individuals should, when N_A is small, double at each generation; this is the 2-fold cost of meiosis or, more properly, the cost of males (defined by Maynard Smith 1971, 1978); the cost is not always actually 2-fold and not necessarily associated with meiosis (reviewed by Lewis 1987). If sexual reproduction persists, it must have some short-term advantage that counterbalances its 2-fold cost; this is the balance argument (Williams 1975).

Polyploidy

Asexual species reproducing by apomixis (gametophytic apomixis in plants) are virtually all polyploid (usually triploid or tetraploid) even though their sexual relatives are diploid (Suomalainen et al. 1987; Asker and Jerling 1992; Kondrashov 1997). Asexual reproduction allows polyploids with a disrupted meiosis to reproduce, and this can explain the existence of asexual polyploids (Ramsey and Schemske 1998); it does not explain, however, why the polyploids replace the diploids. In other words, why are not diploid apomicts as common as polyploid apomicts? Polyploidy seems to confer some advantage to apomixis (Bicknell et al. 2000) that diploidy does not. But advantage against what? The absence of apomictic diploids is a striking fact that is usually ignored and that a general theory should be able to explain.

Types of Asexual Reproduction

Among the possible types of asexual reproduction listed above, only some types actually exist and some are very rare. For example, meiotic apomixis exists only with the suppression of the first and not the second division; automixis with fusion of cleavage nuclei is very rare. How do we explain this distribution of types? Also, how can we explain cyclical parthenogenesis? If apomixis has an advantage, why go back cyclically to amphimixis and why only for one generation?

Two-Step meiosis

If the function of meiosis is to produce haploid gametes, why begin with a replication followed by 2 divisions? In principle, the unreplicated chromosomes could simply pair with each other and move to opposite poles to produce 2 haploid nuclei (one-step meiosis—Figure 4). A general theory for the evolution of sexual reproduction cannot dismiss as irrelevant the fact that meiosis is 2-step (Maynard Smith and Szathmary 1995). Mendelian segregation relies on the very fact that meiosis is 2-step, but there is no a priori reason why it should be so.

Origin of Amphimixis

The problems listed above are relevant for the maintenance of sexual reproduction but not necessarily for the origin of amphimixis. For example, at the origin of amphimixis gametes were almost certainly isogamous and there was likely no 2-fold cost of meiosis (Lewis 1987); meiosis was probably one-step (Maynard Smith and Szathmary 1995). It is not necessary that the origin and the maintenance of amphimixis have the same explanation, but a comprehensive theory that explained both would be more parsimonious.

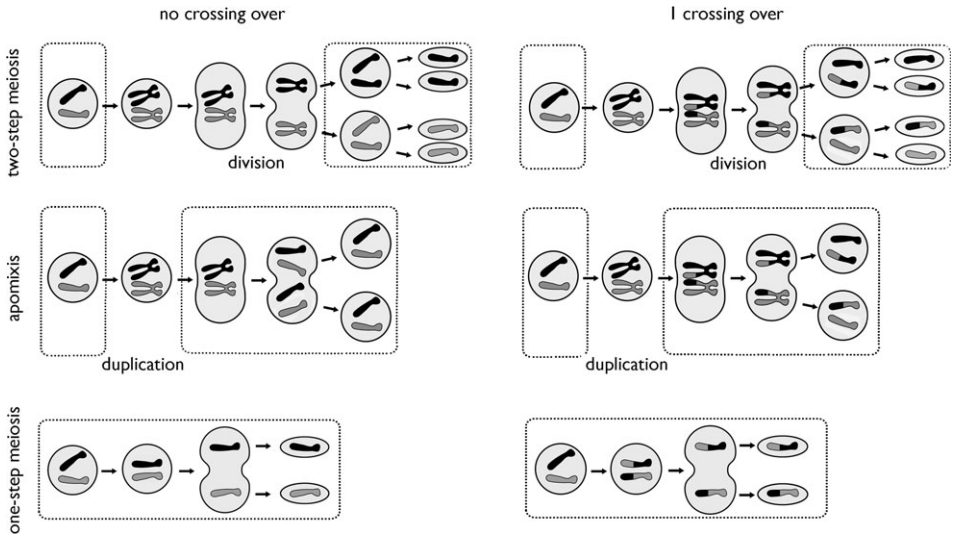

Figure 4. Comparison of 2-step meiosis, one-step meiosis, and apomixis with suppression of the first division, with or without recombination.

The Complementation Hypothesis

Loss of Complementation

The rationale of the complementation hypothesis is that with asexual reproduction the masking of recessive deleterious mutations (the adaptive value of diploidy) is lost (loss of complementation [LOC]). The details of this LOC depend on the type of asexual reproduction (Archetti 2004b).

Apomixis. Meiotic apomixis with suppression of the first division leads to LOC only with recombination (Figure 1). According to the terminology introduced by Stern (1936) for mitotic segregation, recombinants can segregate in 3 possible ways: 1) "x segregation" when recombinant chromatids segregate to opposite poles; this leads to LOC; 2) "z segregation" when both recombinants segregate in one daughter cell; there is no LOC; 3) "y segregation" when sister chromatids fail to disjoin and segregate to the same daughter cell; this also leads to LOC. Although x and z segregation usually occur with equal frequencies (except in mitotic recombination, where x segregation is more common than z segregation; Pimpinelli and Ripoll 1986), y segregation is not normally observed (not shown in Figure 1). Mitotic apomixis has the same results as meiotic apomixis with suppression of the first division. Meiotic apomixis with suppression of the second division leads to complete LOC without recombination; with recombination the results are the same as for x segregation in meiotic apomixis with suppression of the first division.

Automixis. Fusion of cleavage nuclei immediately leads to complete LOC, irrespective of recombination (Figure 2). Fusion of sister nuclei leads to the same results as apomixis with suppression of the second meiotic division. Fusion of nonsister nuclei leads to the same result as apomixis with suppression of the first meiotic division.

Endomitosis. Pairing of sister chromosomes does not lead to any LOC, irrespective of recombination (Figure 3). Pairing of nonsister chromosomes leads to LOC in 50% of the progeny if there is no recombination; with recombination LOC may occur in all the progeny. Random pairing leads to intermediate results.

Because some of the types described above have equivalent results with respect to LOC they can be grouped as follows.

Type 1: mitotic apomixis, meiotic apomixis with suppression of the first division, automixis with fusion of nonsister nuclei.
Type 2: meiotic apomixis with suppression of the second division, automixis with fusion of sister nuclei.
Type 3: automixis with fusion of cleavage nuclei.
Type 4: endomitosis.

Asexual mutants in species with complex alternatives to 2-step meiosis also have LOC (these are not discussed here: see Archetti 2004a). Asexual mutants arising from one-step meiosis are a notable exception (see below).

LOC increases with further replications. The amount of LOC after further generations depends on selection against recessive homozygous alleles because there will be variation among individuals and the ones with less LOC will be favored. The deleterious effects of mutations exposed by LOC depend on the number of lethal equivalents (LEs), defined as the number of genes (a single lethal allele or a large number of mildly deleterious alleles) that would cause on average one death if made homozygous (Morton et al. 1956; Hedrick 2002). If this cost of LOC (which is absent in sexual reproduction with outcrossing) is larger than the 2-fold cost of meiosis, parthenogenesis will not have an advantage against sexual reproduction.

The 5 Propositions

A short definition of the complementation hypothesis is the following: "Sexual reproduction persists against asexual reproduction, in spite of the 2-fold cost of meiosis, because asexual reproduction generally has a more than 2-fold cost due to loss of complementation." This definition, however, does not address all 5 problems mentioned in the introduction. Here I address these problems.

The Balance Argument

The cost of unmasking recessive deleterious mutations due to LOC (for asexual reproduction) can be greater than the 2-fold cost of meiosis (for sexual reproduction). Mutant asexuals disappear in few generations or in some cases cannot even invade (Table 1). Therefore this is a short-term disadvantage that can solve the balance argument. The number of generations required for the extinction of the asexual lineage depends on the type of asexual reproduction (Table 1). Type 1 asexuals can invade and increase in frequency at the beginning because of the 2-fold cost of meiosis, but they then decrease because of the cost of LOC (which grows with generations). With many LE's and frequent recombination, the cost of LOC may outweigh the 2-fold cost of meiosis even in the first generation, and therefore, asexuals do not even invade. With polyploidy results differ (see point 2). For Type 2 the cost of LOC outweighs the 2-fold cost of meiosis in the first generation even with a low number of LE's, irrespective of recombination. Type 3 leads to immediate complete LOC, therefore it is possible only with no LE's, irrespective of recombination. Type 4 can replace amphimixis only if the number of LE's is very low or if the number of LE's is higher, with sister chromosome pairing, irrespective of recombination.

Polyploidy

Polyploidy protects asexuals from LOC because more copies of the same gene take longer to become homozygous (see Table 1). Because polyploidy slows down LOC, the types of asexual reproduction (in particular apomixis) that cannot persist with diploidy can persist with polyploidy even with many LE's. Here, I am assuming allopolyploidy, which is usually the normal condition (Asker and Jerling 1992; Kondrashov 1997) and therefore multiple copies of each gene. The effects of tetraploidy are similar to triploidy (Archetti 2004b). It is known that polyploidy, in the long

Table 1 The number of generations required for the disappearance (in italics) or the fixation (in bold) of asexual reproduction after an asexual mutant is introduced in a sexual population (1000 individuals – average of 10 runs) with 2-fold cost of meiosis and outcrossing (for diploid types unless otherwise stated)

		LEs					
	Recombination[a]	0	0.5	1	2	4	6
Meiotic apomixis (Type 1)	0	**20**	**20**	**20**	**20**	**20**	**20**
	1	**20**	**54**	**411**	nd	nd	nd
	1.25	**20**	**62**	*215*	*179*	*3*	*2*
	1.5	**20**	**74**	*52*	*42*	*3*	*2*
	2	**20**	**192**	*25*	*15*	*1*	*1*
Meiotic apomixis (Type 1) triploid	0	**20**	**20**	**20**	**20**	**20**	**20**
	1	**20**	**25**	**27**	**30**	**30**	**31**
	2	**20**	**25**	**27**	**30**	**33**	**34**
Meiotic apomixis (Type 1) tetraploid	0	**20**	**20**	**20**	**20**	**20**	**20**
	1	**20**	**23**	**26**	**30**	**34**	**37**
	2	**20**	**24**	**29**	**31**	**38**	**41**
Endomitosis (nonsister chromosome pairing)	0	**20**	*39*	*30*	3	2	2
	1	**20**	*39*	*4*	*2*	*2*	*2*
	2	**20**	*39*	*4*	*2*	2	2
Endomitosis (random chromosome pairing)	0	**20**	**33**	**34**	**34**	*4*	2
	1	**20**	**75**	**92**	**94**	*4*	*2*
	2	**20**	**92**	**185**	**192**	*4*	2
Automixis (fusion of sister nuclei)	0	**20**	nd	*1*	*1*	*1*	*1*
	1	**20**	*92*	*5*	*2*	*2*	*2*
	2	**20**	*32*	*5*	*2*	*2*	*2*

Data from Archetti (2004b).

nd, asexual reproduction persists at very low frequency for many generations.

[a] 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%).

term, allows more deleterious mutations to persist and that therefore polyploids eventually have a higher mutation load than diploids (Otto and Whitton 2000; Otto 2007); a newly formed polyploid, however, benefits from complementation before mutant alleles reach their equilibrium frequency.

Types of Asexual Reproduction

Because the cost of LOC depends on the type of asexual reproduction, the number of deleterious recessive mutations, and ploidy level, only certain types of asexual reproduction will persist. The results described above suggest the following predictions. Type 1 is possible without recombination, with recombination and a very low number of LE, or with polyploidy; Type 2 and Type 3 are difficult: they are possible only with very few LE's. Type 4 is possible only with sister chromosome pairing, if the LE's are not too frequent or with nonsister pairing, if the LE's are few. LOC might also explain cyclical parthenogenesis: because apomixis leads to LOC after successive generations, the optimal strategy for an individual would be to reproduce asexually (to exploit the 2-fold cost of meiosis) for several generations until LOC becomes so high that it becomes convenient to switch to sexual reproduction (outcrossing) for one generation in order to restore complementation. These predictions can be tested (see next section).

Two-Step meiosis

Consider a species with a one-step meiosis. A mutant asexual could arise in 2 simple ways. First, it could arise as a replication followed by the one-step meiotic division: this would give LOC as in an endomitosis arising from 2-step meiosis without the nonrecombinant product; it could be maintained for a few generations (see previous section) before going extinct. A mutant asexual, however, could also arise via fusion of the 2 meiotic products (as in automixis): this would not have LOC, irrespective of recombination, and could invade and replace amphimixis with one-step meiosis (because the 2-fold cost of meiosis is not opposed by the cost of LOC). Therefore amphimixis will not persist with one-step meiosis (whereas, as we have seen, it can persist with 2-step meiosis except in the special cases described above: e.g., polyploidy).

Origin of Amphimixis

The complementation theory can explain the origin of amphimixis (syngamy and outcrossing) with the same logic used for its maintenance: the need for complementation. Maynard Smith (1978, p. 7–9) suggested the following scenario: first diploidy evolved in order to allow DNA repair; diploidy also allowed the masking of recessive deleterious mutations (complementation), which could therefore accumulate; now if complementation was lost for some reasons (e.g., because of recombination), syngamy

followed by outcrossing would be beneficial because it would allow complementation to be restored.

Evidence

The Balance Argument

There is no doubt that LOC is deleterious because it leads to unmasking of recessive deleterious mutations. There is also no doubt that asexual reproduction leads to LOC under the assumptions mentioned above. If the right combination of parameters exists, asexual reproduction has a more than 2-fold cost compared with sexual reproduction. These parameters are, for Type 1 asexuals: enough recombination and enough LE; more precisely, with exactly 2-fold cost of meiosis and an equal proportion of x and z segregation, >1 crossing over per chromosome per generation and >1 LE (these values are lower if x segregation is more frequent and if the cost of meiosis is less than 2-fold); for Type 2 and Type 3, even a very low number of LE's, irrespective of recombination; for Type 4 a low number of LE's or sister chromosome pairing, irrespective of recombination.

The number of LE's is critical for all types of asexual reproduction. Available data suggest that the number of LE's 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 less than 1 in embryos of many herbaceous plants, possibly more after development) and ferns (less than 1.3) (Lynch and Walsh 1998). We need more data. An indirect way to test the complementation hypothesis, in the absence of data on LEs, could be to test whether the transition from sexual to asexual reproduction occurred more frequently in taxa with reproductive strategies that allow less LEs to persist, that is, selfing, inbreeding or alternation of haploid, and diploid phases with an extended haploid phase.

Recombination requires a longer discussion. It seems a common misconception that recombination is absent in asexual reproduction; this is wrong. First, there is no reason why a mutant asexual arising from a sexual should suppress recombination; in fact, even putative ancient asexuals have functional genes for recombination, although these genes may be used in cryptic sexuality (Schurko and Logsdon 2008).

Recombination rates in automixis and endomitosis are similar to the rates in amphimixis; in fact, in endomitosis recombination can be even more frequent (Macgregor and Uzzell 1964). This is not surprising, for both automixis and endomitosis include a normal meiosis and the only difference with amphimixis is the addition of one replication (in endomitosis) or one fusion of meiotic products (in automixis).

In meiotic apomixis recombination rates are also similar to meiosis; this is not surprising either, for pairing of chromosomes occurs, and the only difference with a normal meiosis is the suppression of one (normally the first) division. Darlington already knew that aberrations in plants reproducing by what he named "subsexual reproduction" (Darlington 1937; Darlington and Mather 1952) were caused by LOC (due to recombination in apomixis). In *Taraxacum*, for example, the number of chiasmata in the asexuals is about 3 per chromosome per replication (Van Baarlen et al. 2000), which is lower than in meiosis but still significant. Omilian et al. (2006) report much lower rates of recombination in apomictic *Daphnia*, but because they estimate recombination rates by measuring LOC after about a 100 generations of selection, they presumably measure only individuals whose ancestors have never recombined or recombined only marginally, for those with recombination have more LOC and therefore were lost during selection (Archetti 2004b; Cristescu M, personal communication). Recombination rates should be measured in the offspring before selection against LOC can occur.

For mitotic apomixis, Schoustra et al. (2007) show that in fungi with parasexual reproduction, mitotic recombination occurs at a very high rate and suggest that this may apply also to yeast, algae, and mosses (and that mitotic recombination causes extensive LOC with important evolutionary consequences). High homozygosity (possibly due to mitotic recombination and LOC) is also shown by Butler et al. (2009) in 8 *Candida* species. Chapman et al. (2004) show extensive recombination in triploid *Hieracium*, which reproduces by mitotic diplospory. Recombination in mitotic apomixis, therefore, is not as rare as in mitotic somatic recombination (where it is very rare). This is reasonable because recombination is necessary to repair double-strand chromosome breaks (DSBs). Therefore, although DSB repair might not be necessary for somatic cells (mitotic pairing and recombination in somatic cells may be absent), a reproductive lineage cannot infinitely persist without DSB repair and therefore cannot forgo pairing and recombination (Bernstein et al. 1988; Archetti 2003). Therefore, obligate apomixis without recombination is probably impossible; note that mitotic diplospory is usually facultative.

Recombination therefore probably occurs at nearly normal rates in automixis, endomitosis, and apomixis, but we need more data to test whether the combination of LE's, recombination rates, and ploidy level of asexual species corresponds to the parameters predicted by the theory (Table 1). I should point out again that for Type 2 and Type 3 the only relevant parameter is the number of LE's. Recombination is necessary only for Type 1 asexuals. For Type 4 what matters is the type of chromosome pairing; there seems to be no compelling reason why nonsister pairing should be more likely than sister pairing; with exclusive sister pairing indeed, DSBs cannot be repaired because there is no template to carry out the repair (Bernstein et al. 1988), therefore random pairing is probably the rule in endomitosis.

It is also important to notice that high LE and recombination rates are expected to occur in mutant asexuals arising from current sexual species, rather than in species that have been asexual for a long period, because in the asexuals there will have been selection to reduce recombination rates (to reduce LOC). In fact asexual species are predicted to persist only if they have few LE's and low recombination rates.

A critical test could come from cyclical parthenogenesis. As explained before, it would be optimal to reproduce asexually until the cost of LOC becomes too high: the optimal number of asexual replications before fitness decays to below 0.5 (assuming a perfectly 2-fold cost of meiosis) can be calculated as a function of recombination rates and LE's, and this theoretical prediction could be tested in cyclical parthenogenetic species. Certain species of *Daphnia*, for example, reproduce asexually about 5 to 10 times a year and once sexually: these values would be optimal with 2 LEs and 1.5 crossing overs per chromosome or 1 LE and 2 crossing overs; this is within the range of actual values (1–2 crossing overs in the sexual forms), but precise data are needed. Other species are obligate asexuals: these species are predicted to have a lower number of LEs.

Polyploidy

As predicted, polyploidy is the normal condition associated with gametophytic apomixis and with endomitosis (Nogler 1984; Asker and Jerling 1992; Kondrashov 1997; Otto and Whitton 2000; for an exception see Thompson and Ritland 2006; the situation is less clear for automixis). Although it is possible that this is due to the difficulty of actually recognizing diploid apomicts, the reason is probably that polyploidy confers an advantage against LOC (Otto and Whitton 2000; Otto 2007). Note that polyploidy does not necessarily lead, per se, to asexual reproduction; in fact autotetraploids or colchicin-induced tetraploids are not usually apomictic (Asker and Jerling 1992) and most polyploids are not apomictic (Otto and Whitton 2000).

Types of Asexual Reproduction

The complementation hypothesis predicts that only asexual reproduction of Type 1 will be common. I am not going to make an extensive description of the distribution of asexual reproduction—good reviews can be found in Asker and Jerling (1992), Kondrashov (1997), and Suomalainen et al. (1987)—but I will discuss this prediction briefly. More data are needed.

Type 2 is very rare (meiotic apomixis with suppression of the second division does not seem to exist at all). Type 3 is known (Nur 1971) only in few species (automixis with fusion of cleavage nuclei) derived from haplo–diploid arrhenotokous ancestors that have arguably no LE's (because recessive deleterious alleles have been eliminated in the haploids). Type 4 (endomitosis) is known, in plants, only in 2 species of *Allium* (Nogler 1984) and in animals in 5 genera of lizards and some insects (Maynard Smith 1978; Vrijenhoek et al. 1989); in *Cnemidophorus tesselatus*, there is evidence of nonsister pairing and recombination (Parker and Selander 1976).

Type 1 is much more common: apomixis with suppression of the first division is widely distributed in animals (where it is usually obligate) and plants (although strictly it is always facultative but usually more than 99% of the individuals reproduce by apomixis—Nogler 1984; Asker and Jerling 1992). Mitotic apomixis is common in plants and fungi; I am not aware of mitotic apomixis in animals. Automixis with fusion of nonsister nuclei occurs in ciliates and insects; it is very rare in plants and occurs in algae, fungi, bryophytes, and pteridophytes. As predicted, therefore, Type 1 is common, whereas the other types are rare or do not exist at all.

Two-step Meiosis

One-step meiosis may exist in Archezoans, Dinozoa, Sporozoa, and Parabasalia, although all these cases are uncertain (Cavalier-Smith 1981; Raikov 1982; Haig 1993; Cavalier-Smith 1995; Maynard Smith and Szathmary 1995; Kondrashov 1997). In Pyrsonymphida (Cleveland 1947; Raikov 1982, 1995), conjugation may protect from invasion by asexual mutants (Archetti 2004a) and may explain why one-step meiosis persists in that case.

Origin of Amphimixis

Evidence for the origin of amphimixis is clearly speculative. It seems plausible, however, that the alternation of generations was initially due to endomitosis rather than syngamy (Cleveland 1947; Maynard Smith and Szathmary 1995) and that syngamy and outcrossing evolved only afterward, presumably as an adaptation to maintain complementation (Maynard Smith and Szathmary 1995; Wilkins and Holliday 2009).

It seems also clear that recombination already existed before the origin of amphimixis, for recombinational capacity is found throughout the prokaryotes and therefore must considerably predate eukaryotes and meiosis (Levin 1988; Cavalier-Smith 2002; Marcon and Moens 2005; Wilkins and Holliday 2009). In particular, a crucial set of molecules for genetic recombination, the recA family of proteins, is utilized for recombination in both prokaryotes and eukaryotes (Schurko and Logsdon 2008). The very reason for the origin of diploidy is probably the advantage of being able to repair DNA through recombinational repair (Bernstein et al. 1988). Therefore, the hypothesis (Maynard Smith 1978) that recombination led to LOC in a primitive asexual seems plausible.

The problem with this hypothesis is: why give up complementation? Maynard Smith abandoned his idea because it seemed to argue in a circle: first evolve diploidy for the benefit of complementation, then give up complementation for the benefit of recombination (variation), then evolve syngamy to restore complementation. This was Maynard Smith's dilemma (Maynard Smith 1978, p. 7–9). In the next section, I will argue that this problem can be solved if one consider recombination as an intragenomic conflict rather than as an adaptation for the benefit of the organism. Therefore, recombination in a primitive asexual might have evolved not because of the benefits of genetic variation for the organism or the population but because of the benefits of recombination to the recombinogenic genes themselves.

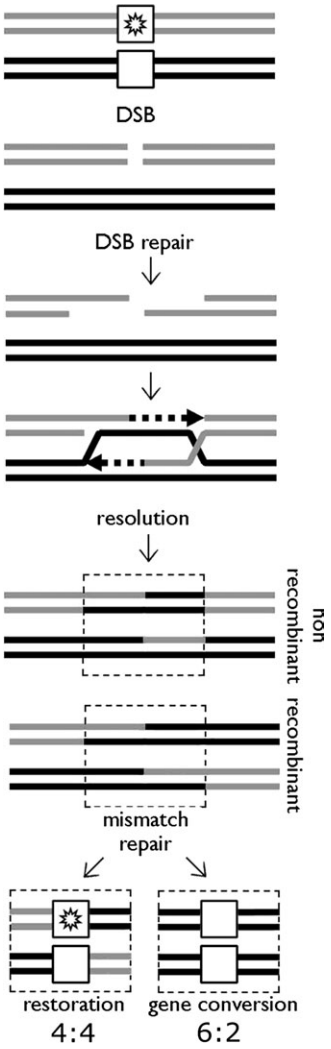

Figure 5. The Double Strand Break Repair model of recombination (Szostak et al. 1983). The 2 chromatids participating in crossing over are each shown with a double DNA strand, one in gray, one in black; squares show the 2 alleles at the site of the initiation of recombination (only in the first and final step for clarity); the allele where the DSB occurs is indicated by a star (see Figure 6 for possible different types). The DSB is repaired using the other allele as a template. Resolution of the Holliday junction leads to recombinant or nonrecombinant products (with respect to flanking markers) and to the formation of a heteroduplex at the site of initiation (shown within the dotted box); the heteroduplex is processed (mismatch repair) by restoration of the original alleles or by gene conversion, which leads on average to a 5:3 segregation in favor of the allele on which the DSB did not occur.

The Genetic Conflict Hypothesis for Recombination

First, I will describe how recombination occurs at the molecular level and the genetic conflict hypothesis. Then, I will explain how this provides an explanation for the maintenance of recombination in current amphimixis. Finally, I will explain how this is relevant for the origin of amphimixis and Maynard Smith's dilemma. I must stress the fact that the genetic conflict hypothesis is relevant not only for the origin of amphimixis but more in general for the maintenance of recombination.

Molecular Mechanism of the Initiation of Recombination. The Genetic Conflict Hypothesis

The initiation of recombination (Figure 5) is due to a DSB on one of the chromatids. DSB's are induced by Spo11, a topoisomerase whose function is to promote chromosome pairing and segregation by inducing transient cleavages in the chromosome. The allele with the DSB is then repaired by the molecular machinery for DNA repair using the other allele as a template; the template therefore is overtransmitted with a 5:3 ratio to the next generation by gene conversion (Szostak et al. 1983, Figure 5).

An allele can influence the probability of a DSB on itself or on the opposite chromosome through its interaction with Spo11, and it can actually increase the probability of DSB's on the homolog (Archetti 2003 and references therein). Therefore, an allele that is able to induce Spo11 to produce a DSB preferentially on the homolog can increase its own frequency by gene conversion, even if this gives no advantage to the individual or to the population, indeed even if this is deleterious for the individual. This is the genetic conflict hypothesis for the evolution of recombination (Archetti 2003).

The Maintenance of Recombination. A Solution to the Hotspot Paradox

The genetic conflict hypothesis implies that DSB's are induced in *trans* (Archetti 2003), that is on the homolog, rather than in *cis*. There is evidence that an allele can induce DSBs in *trans*: Xu and Kleckner (1995) showed that changes at a particular locus can influence DSBs at the corresponding locus of the homolog; Keeney and Kleckner (1996) showed that chromatin structure (which influences the likelihood of DSBs) can be influenced in *trans* and suggest that such effects might be important even with partial or transient homologs pairing (e.g., in mitosis). The problem with a *trans*-inducer is that there is evidence that, in the presence of a hot and a cold allele ("hot" alleles induce higher recombination rates than "cold" alleles in homozygotes) the allele that is lost preferentially in heterozygotes is the hot one; this does not seem to fit with the data because with a *trans*-inducer the allele that is lost preferentially in heterozygotes is the cold one (Pineda-Krch and Redfield 2005).

Induction in *cis* is compatible with the fact that the allele that is lost preferentially in heterozygotes is the hot one; however, if an allele induces a DSB on itself, how can recombination persist? This is the "hotspot paradox" (Boulton et al. 1997). It has been shown that drift may allow *cis*-inducers to persist (Calabrese 2007; Coop and Myers 2007; Peters 2008), especially if the inducer overlaps

only partially with the cut region and that reduced Hill–Robertson interference helps the inducer to persist (Friberg and Rice 2008). Some data, however, are not compatible with a *cis*-inducer (Neumann and Jeffreys 2006; Baudat and De Massy 2007).

Another problem for both *cis*- and *trans*-inducers is that recombination hotspots seem to be short lived, and their position within the chromosome not conserved between closely related species (Jeffreys and Neumann 2002; Jeffreys et al. 2004; Kauppi et al. 2004; Jeffreys and Neumann 2005). An inducer in *cis* would lead to the disappearance of recombination because the hotspots destroy themselves (Boulton et al. 1997; Pineda-Krch and Redfield 2005); an inducer in *trans* would not lead to changes in the position of hotspots (Archetti 2003). Neither *cis*- nor *trans*-inducers alone therefore can explain the available data.

In the rest of this section, I will argue that more complex models based on coevolution between inducers and resistance can explain the hotspot paradox (a problem for the *cis*-inducer model), the fact that the hot allele is lost preferentially in heterozygotes (a problem for the *trans*-inducer model), and the fact that recombination hotspots are short lived (a problem for both *cis*- and *trans*-inducers). These new models are based on coevolution of inducers in *trans* (or *cis–trans*) and resistance in *cis* (Figure 6). The co-occurrence of *cis–trans* inducers and *cis* resistors has been actually observed by Baudat and De Massy (2007). Figure 6 shows the possible cases.

Trans inducer–*Cis* resistance. Imagine first a *trans*-inducer allele, fixed in the population. If a resistance in *cis* evolves, it will quickly go to fixation, and the cold allele will be the one that is lost in the heterozygotes, as observed. This case

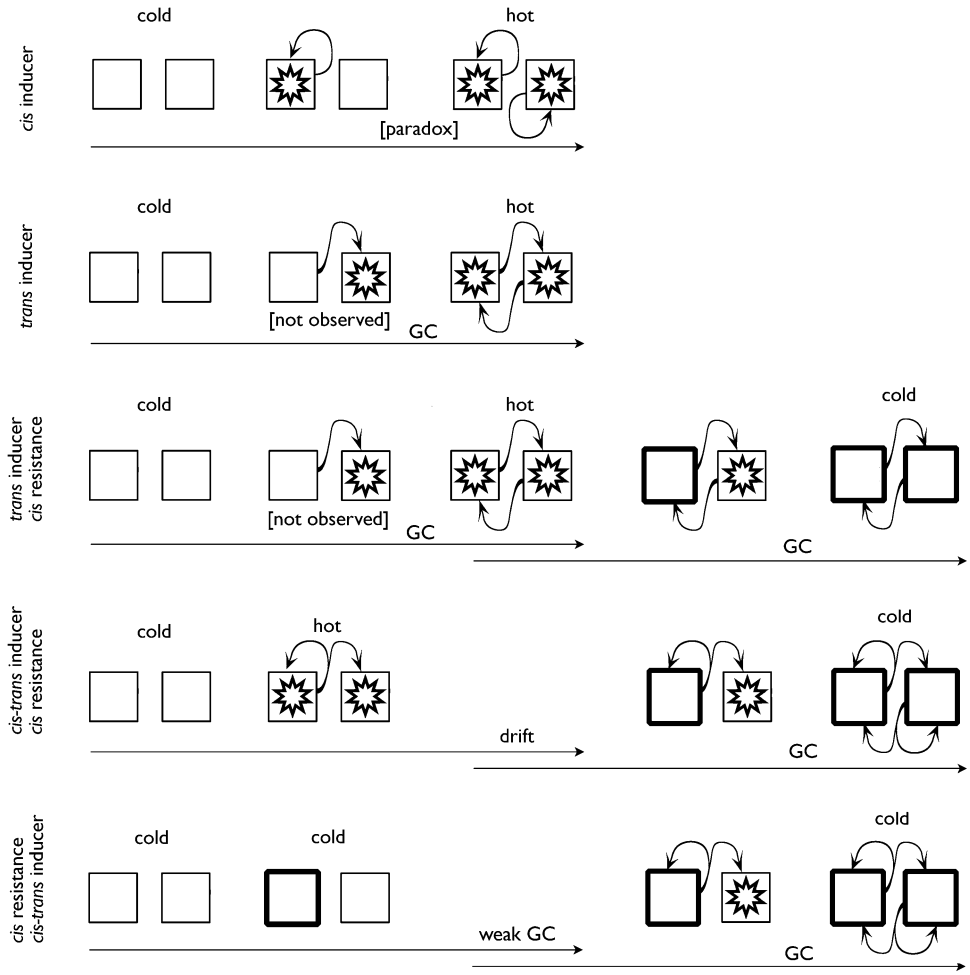

Figure 6. Birth and death of recombination hotspots when recombination is due to a self-promoting allele that induces a DSB in *cis* or *trans* opposed by resistance in *cis*. Pairs of squares show the 2 homologous alleles at the site of the initiation of recombination, as in Figure 5. Inducer mutants are indicated by an arrow pointing at the same allele (*cis*) or the homolog (*trans*) or both. Mutations for higher resistance are indicated by a thick square. The allele where high levels of DSB occur is indicated by a star. Hot and cold indicate the frequency of recombination (respectively high and low) in homozygotes. Gene conversion (GC) in heterozygotes leads to the quick fixation of *trans*-inducers and *cis* resistance; when resistance is fixed the process can start again with a new, stronger inducer or resistance.

leaves unexplained the fact that, before resistance arises, it is the cold allele that is lost preferentially in heterozygotes. However, it is still possible that these heterozygotes are not observed because without resistance an inducer can increase recombination rates by 2000 times (Baudat and De Massy 2007) and would go to fixation in a few generations by gene conversion (Archetti 2003), whereas heterozygotes in the second stage (with resistance) would persist for longer if resistance reduces the overall recombination rate at the hotspot, and therefore would be observed more frequently.

Cis resistance–*Trans* inducer. Resistance could evolve before inducers. In this case resistant alleles would be favored because of the background recombination the locus experiences (even without being a hotspot) making them increase in frequency by gene conversion. One would observe only cold homozygotes (both with and without the inducers) and high recombination rates only in the heterozygotes.

Cis-Trans inducer–*Cis* resistance. In this case the inducer would have no advantage due to gene conversion but could initially increase by drift, and eventually (it is not necessary that it goes to fixation) might be coupled with an inducer that, even if partially in *cis*, would lead to its fixation.

Cis resistance–*Cis-Trans* inducer. This would be similar to *cis* resistance–*trans* inducer, although recombination rates in heterozygotes would be lower because opposed in part by resistance.

In all these cases, when resistance is fixed the process can start again with a new, stronger inducer or resistance. Therefore intragenomic conflict between inducers (in *trans* or in *cis–trans*) and resistance can explain both why that the hot allele is lost preferentially in heterozygotes and the persistence and change in position of hotspots. It is also consistent with evidence showing that transmission distortion is observed in some hotspots but not in others (Jeffreys and Neumann 2002; Jeffreys et al. 2004; Jeffreys and Neumann 2005). More in general, this genetic conflict hypothesis can explain why recombination occurs without invoking any advantage for the individual or the population.

The Origin of Amphimixis. A Solution to Maynard Smith's Dilemma

The genetic conflict hypothesis is relevant for the maintenance of recombination, as explained above; gene conversion, however, does not require syngamy and outcrossing, therefore it could also occur with asexual reproduction, and it may be relevant for the origin of amphimixis. A selfish allele that induced recombination in a primitive asexual could evolve simply because of the advantage due to gene conversion: it would not spread to other individuals in the population, but it would replace its homolog; it would also, however, produce LOC and therefore a conflict with the rest of the genome; this conflict could be solved by the evolution of syngamy and outcrossing, which would restore complementation (and would also allows the selfish gene to spread in the population—Archetti 2003). This can solve Maynard Smith's dilemma because it does not require any advantage at the individual or population level (like the creation of variation) for recombination.

I want to stress again that the complementation hypothesis (for amphimixis) and the genetic conflict hypothesis (for recombination) are separate hypotheses; they overlap (and require each other) only in the explanation for the origin of amphimixis. Even if recombination was not due to genetic conflict, the first 4 propositions of the complementation hypothesis relevant for the maintenance of amphimixis would be unaffected. And even if LOC was not the cause if the spread of recombinogenic genes at the origin of amphimixis, the genetic conflict hypothesis would still be relevant for the maintenance of recombination in current sexual reproduction.

Conclusion

The many explanations suggested for why sexual reproduction is maintained (Kondrashov 1993; Barton and Charlesworth 1998; Otto and Lenormand 2002) derive, in different ways, from Weismann's idea that sexual reproduction increases the variation on which natural selection can act (Burt 2000): ecological models ("Red Queen") suggest that this variability allows sexual species to coevolve with parasites; mutation-based models suggest that variability allows to get rid of deleterious mutations more efficiently. These and other hypotheses suggest that, although sexual reproduction has no immediate advantage to balance the 2-fold cost (problem 1) the variability produced by sexual reproduction allows sexual populations to persist, whereas asexual populations go extinct. Even the synergistic epistasis theory (Kondrashov 1982, 1988, 1994) requires a period of time of the order of 100 generations (Charlesworth 1990). These hypotheses do not explain the prevalence of polyploidy in asexuals (problem 2); nor why only certain kinds of asexual reproduction exist (problem 3); nor the rarity of one-step meiosis (problem 4)—indeed, if the evolutionary value of amphimixis is the promotion of genetic variability, then a one-step meiosis should be favored because with the same number of crossing over events a 2-step meiosis produces less variability (Archetti 2004a); finally, the production of variability cannot be an explanation for the origin of amphimixis (problem 5) but only for its maintenance.

The complementation hypothesis described here provides a stronger short-term advantage for amphimixis (one or a few generations), and it could solve all 5 problems. It can be disproved as explained above by measuring LE's and recombination rates. The complementation hypothesis already seems to be the standard accepted explanation for the maintenance of amphimixis against some kinds of asexual reproduction, namely automixis; this was clearly stated by Maynard Smith in his discussion on automixis with fusion of cleavage nuclei (Maynard Smith 1978). It seems easy to extend it to the other types of asexual reproduction.

Meiotic apomixis (with suppression of the first division), mitotic apomixis, and automixis with fusion of nonsister nuclei requires more data. I would like to encourage those studying species with these types of asexual reproduction to measure the number of LEs and recombination rates to test whether they match the predictions discussed here.

If these predictions are valid, asexual reproduction has a short-term disadvantage due to the LOC that can overcome the 2-fold cost of meiosis in one or few generations. LOC can also explain why most asexual species are polyploid, why only certain types of asexual reproduction exist, why meiosis is usually 2-step, and the origin of amphimixis. Moreover, recombination can be the result of an intragenomic conflict between alleles that induce the initiation of crossing over and alleles that evolve to resist that initiation; therefore, recombination does not require any advantage at the individual or population level. These 2 ideas, the complementation hypothesis for the evolution of sex and the genetic conflict hypothesis for the evolution of recombination, are related but independent and could provide a new explanation for the long-standing problems of the evolution of sex and recombination.

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References

Archetti M. 2003. A selfish origin for recombination. J Theor Biol. 223:335–346.

Archetti M. 2004a. Loss of complementation and the logic of two-step meiosis. J Evol Biol. 17:1098–1105.

Archetti M. 2004b. Recombination and loss of complementation: a more than twofold cost for parthenogenesis. J Evol Biol. 17:1084–1097.

Asker SE, Jerling L. 1992. Apomixis in plants. Boca Raton (FL): CRC Press.

Barton NH, Charlesworth B. 1998. Why sex and recombination? Science. 281:1986–1990.

Baudat F, De Massy B. 2007. Cis- and trans-acting elements regulate the mouse Psmb9 meiotic recombination hotspot. PLoS Genetics. 3:1029–1039.

Bell G. 1982. The masterpiece of nature: the evolution and genetics of sexuality. London: Croom Helm.

Bernstein H, Hopf FA, Michod RE. 1988. Is meiotic recombination an adaptation for repairing DNA, producing genetic variation or both? In: Michod RE, Levin BR, editors. The evolution of sex. Sunderland (MA): Sinauer. p. 139–160.

Bicknell RA, Borst NK, Koltunow AM. 2000. Monogenic inheritance of apomixis in two *Hieracium* species with distinct developmental mechanisms. Heredity. 84:228–237.

Boulton A, Myers RS, Redfield RJ. 1997. The hotspot conversion paradox and the evolution of meiotic recombination. Proc Natl Acad Sci U S A. 94:8058–8063.

Burt A. 2000. Sex, recombination and the efficacy of selection—was Weismann right? Evolution. 54:337–351.

Butler G, Rasmussen MD, Lin MF, Santos MA, Sakthikumar S, Munro CA, Rheinbay E, Grabherr M, Forche A, Reedy JL, et al. 2009. Evolution of pathogenicity and sexual reproduction in eight *Candida* genomes. Nature. 459:657–662.

Calabrese P. 2007. A population genetics model with recombination hotspots that are heterogeneous across the population. Proc Natl Acad Sci U S A. 104:4748–4752.

Cavalier-Smith T. 1981. The origin and early evolution of the eukaryotic cell. In: Carlile MJ, Collins JF, editors. Molecular and cellular aspects of microbial evolution. Cambridge: Cambridge University Press. p. 33–84.

Cavalier-Smith T. 1995. Cell cycles, diplokaryosis and the archaezoan origin of sex. Arch Protist. 145:187–207.

Cavalier-Smith T. 2002. Origins of the machinery of recombination and sex. Heredity. 88:125–141.

Chapman H, Robson B, Pearson ML. 2004. Population genetic structure of a colonising, triploid weed, *Hieracium lepidulum*. Heredity. 92:182–188.

Charlesworth B. 1990. Mutation-selection balance and the evolutionary advantage of sex and recombination. Genet Res. 55:199–221.

Cleveland LR. 1947. The origin and evolution of meiosis. Science. 105:287–289.

Coop G, Myers SR. 2007. Live hot, die young: transmission distortion in recombination hotspots. PLoS Genet. 3:377–386.

Darlington CD. 1932. Recent advances in cytology. 2nd ed. London: Churchill (UK).

Darlington CD, Mather K. 1952. The elements of genetics. London: George Allen and Unwin Ltd.

Friberg U, Rice WR. 2008. Cut thy neighbor: cyclic birth and death of recombination hotspots via genetic conflict. Genetics. 179:2229–2238.

Haig D. 1993. Alternatives to meiosis: the unusual genetics of red algae, microsporidia, and others. J Theor Biol. 163:15–31.

Hedrick PW. 2002. Lethals in finite populations. Evolution. 56:654–657.

Jeffreys AJ, Holloway JK, Kauppi L, May CA, Neumann R, Slingsby MT, Webb AJ. 2004. Meiotic recombination hot spots and human DNA diversity. Philos Trans R Soc Lond B Biol Sci. 359:141–152.

Jeffreys AJ, Neumann R. 2002. Reciprocal crossover asymmetry and meiotic drive in a human recombination hotspot. Nat Genet. 31:267–271.

Jeffreys AJ, Neumann R. 2005. Factors influencing recombination frequency and distribution in a human meiotic crossover hotspot. Hum Mol Genet. 14:2277–2287.

Kauppi L, Jeffreys AJ, Keeney S. 2004. Where the crossovers are, recombination distribution in mammals. Nat Rev Genet. 5:413–424.

Keeney S, Kleckner N. 1996. Communication between homologous chromosomes: genetic alterations at a nuclease-hypersensitive site can alter mitotic chromatin structure at that site both in cis and in trans. Genes Cells. 1:475–489.

Kondrashov AS. 1982. Selection against harmful mutations in large sexual and asexual populations. Genet Res. 40:325–332.

Kondrashov AS. 1988. Deleterious mutations and the evolution of sexual reproduction. Nature. 336:435–441.

Kondrashov AS. 1993. Classification of hypotheses on the advantage of amphimixis. J Hered. 84:372–387.

Kondrashov AS. 1994. Sex and deleterious mutations. Nature. 369:99–100.

Kondrashov AS. 1997. Evolutionary genetics of life cycles. Ann. Rev. Ecol. Syst. 28:391–435.

Levin BR. 1988. The evolution of sex in bacteria. In: Michod RE, Levin BR, editors. The evolution of sex. Sunderland (MA): Sinauer. p. 194–211.

Lewis WM. 1987. The cost of sex. In: Stearns SC, editor. The evolution of sex and its consequences. Basel (Switzerland): Birkhauser Verlag. p. 33–57.

Lynch M, Walsh B. 1998. Genetics and analysis of quantitative traits. Sunderland (MA): Sinauer.

Macgregor HC, Uzzell TM. 1964. Gynogenesis in salamanders related to *Ambystoma jeffersonianum*. Science. 143:1043–1045.

Marcon E, Moens PB. 2005. The evolution of meiosis: recruitment and modification of somatic DNA-repair proteins. Bioessays. 27:795–808.

Maynard Smith J. 1971. What use is sex? J Theor Biol. 30:319–335.

Maynard Smith J. 1978. The evolution of sex. Cambridge: Cambridge University Press.

Maynard Smith J, Szathmary E. 1995. The major transitions in evolution. Oxford: W.H. Freeman.

Morton NE, Crow JF, Muller HJ. 1956. An estimate of the mutational damage in man from data on consanguineous marriages. Proc Natl Acad Sci U S A. 42:855–863.

Neumann R, Jeffreys AJ. 2006. Polymorphism in the activity of human crossover hotspots independent of local DNA sequence variation. Hum Mol Genet. 15:1401–1411.

Nogler GA. 1984. Gametophytic apomixis. In: Johri BM, editor. Embryology of angiosperms. Berlin (Germany): Springer Verlag. p. 475–518.

Nur U. 1971. Parthenogenesis in coccids (Homoptera). Am Zool. 11:301–308.

Omilian AR, Cristescu MEA, Dudycha JL, Lynch M. 2006. Ameiotic recombination in asexual lineages of *Daphnia*. Proc Natl Acad Sci U S A. 103:18638–18643.

Otto SP. 2007. The evolutionary consequences of polyploidy. Cell. 131:452–462.

Otto SP, Lenormand T. 2002. Resolving the paradox of sex and recombination. Nat Rev Genet. 3:252–261.

Otto SP, Whitton J. 2000. Polyploidy incidence and evolution. Ann Rev Genet. 34:401.

Owen R. 1849. On parthenogenesis or the successive production of procreating individuals from a single ovum. London: Van Voorst.

Parker ED Jr., Selander RK. 1976. The organization of genetic diversity in the parthenogenetic lizard *Cnemidophorus tesselatus*. Genetics. 84:791–805.

Peters AD. 2008. A combination of cis and trans control can solve the hotspot conversion paradox. Genetics. 178:1579–1593.

Pimpinelli S, Ripoll P. 1986. Nonrandom segregation of centromeres following mitotic recombination in *Drosophila melanogaster*. Proc Natl Acad Sci U S A. 83:3900–3903.

Pineda-Krch M, Redfield RJ. 2005. Persistence and loss of meiotic recombination hotspots. Genetics. 169:2319–2333.

Raikov IB. 1982. The protozoan nucleus. Vienna: Springer-Verlag.

Raikov IB. 1995. Meiosis in protists: recent advances and persisting problems. Eur J Protist. 31:1–7.

Ramsey J, Schemske DW. 1998. Pathways, mechanisms, and rates of polyploid formation in flowering plants. Ann Rev Ecol Syst. 29:467–501.

Schoustra SE, Debets AJ, Slakhorst M, Hoekstra RF. 2007. Mitotic recombination accelerates adaptation in the fungus *Aspergillus nidulans*. PLoS Genet. 3:4.

Schurko AM, Logsdon JM Jr. 2008. Using a meiotic toolkit to investigate ancient asexual "scandals" and the evolution of sex. Bioessays. 30:579–589.

Smith J. 1841. Notice of a plant which produces seeds without any apparent action of pollen. Trans Linn Soc. 18.

Stern C. 1936. Somatic crossing over and segregation in *Drosophila melanogaster*. Genetics. 21:625–730.

Suomalainen E. 1950. Parthenogenesis in animals. Adv Genet. 3:193.

Suomalainen E, Saura A, Lokki J. 1987. Cytology and evolution in parthenogenesis. Boca Raton (FL): CRC Press.

Szostak JW, Orr-Weaver TL, Rothstein RJ, Stahl FW. 1983. The double-strand-break repair model for recombination. Cell. 33:25–35.

Thompson SL, Ritland K. 2006. A novel mating system analysis for modes of self-oriented mating applied to diploid and polyploid arctic Easter daisies (*Townsendia hookeri*). Heredity. 97:119–126.

Van Baarlen P, Van Dijk PJ, Hoekstra RF, de Jong JH. 2000. Meiotic recombination in sexual diploid and apomictic triploid dandelions (*Taraxacum officinale* L.). Genome. 43:827–835.

Vrijenhoek R, Dawley R, Cole C, Bogart J. 1989. A list of known unisexual vertebrates. In: Dawley R, Bogart J, editors. Evolution and cytology of unisexual vertebrates. New York State Museum, Albany, NY: University State of New York. p. 19–23.

Wilkins AS, Holliday R. 2009. The evolution of meiosis from mitosis. Genetics. 181:3–12.

Williams GC. 1975. Sex and evolution. Princeton (NJ): Princeton University Press.

Winkler H. 1908. Über parthenogenesis und apogamie im pflanzenreiche. Prog Rei Bot. 2:293.

Xu L, Kleckner N. 1995. Sequence non-specific double-strand breaks and interhomolog interactions prior to double-strand break formation at a meiotic recombination hot spot in yeast. EMBO J. 14:5115–5128.

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