Understanding Biparental Sex Through the Absence of Triparental Sex

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Abstract

In the spirit of Fisher (1930), we propose that a theory of sex must, for reasonable parameter values, be capable of predicting that sexually produced offspring have only two parents, not three or more. As an example of the power of this approach, it is shown that the range of mutation rates that support the mutational deterministic (MD) hypothesis may, in fact, be small enough to cast doubt on it as a primary explanation of the ubiquity of biparental sex.

Keywords: Biparental sex; Triparental sex; Purpose of sex; Twofold cost of sex; Deleterious mutations.

1. Introduction

Understanding the purpose of sex is one of the most important problems in evolutionary biology. To date, theories of sex have focused on explaining why genetic mixing is sufficiently beneficial that biparental sex overcomes the twofold cost of males it suffers relative to asexual reproduction (Maynard Smith, 1978).[1] No theory of sex would be viable if it were unable to do so. Thus, explaining why biparental sex dominates asexual reproduction is rightly considered to be a fundamental and *necessary* feature of any theory of sex. But is it *sufficient*?

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[1] The two-fold cost of sex arises because there are as many males as there are females. That this is so reflects the game theoretic setting for sex. Indeed, Fisher's (1930) explanation for this equality is often cited as the first instance of an "evolutionarily stable equilibrium."

Consider, for example, two competing theories, each correctly predicting the superiority of biparental sex over asexual reproduction. In addition, suppose that one of the theories predicts that biparental sex is inferior to triparental sex (i.e., where offspring are composed of the genetic material of three parents), while the other theory predicts that biparental sex is evolutionarily superior to all other sexual systems, asexual, triparental, quadriparental, etc. Surely the latter theory should then be rejected in favor of the former?

Two cases can be distinguished. Suppose first, and entirely hypothetically, that triparental sex is known to have occurred in nature and that evolutionary/microbiological pathways from biparental to triparental sexual reproduction and vice versa have been plausibly worked out. In this case, the offending theory—and only the offending theory—fails in a key respect since it fails to explain why triparental sexual reproduction has failed to displace the biparentals. Serious doubt should be cast upon this theory relative to the other, a conclusion which, we presume, is uncontroversial.

In the more realistic case however, there is no evidence of the existence, past or present, of any species that reproduces through triparental sex, and no evolutionary/microbiological pathways from either of the two systems of reproduction, biparental or triparental, to the other have been worked out.[2] The central question is, should the fact that one theory, but not the other, predicts a fitness advantage of triparental sex over biparental sex lead us to reject, or at least cast serious

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[2]There are known instances of triparental reproduction in viruses, bacteria, and yeast, but these would not typically be considered sexual reproduction. (See Bresch, 1959, Clark and Adelberg, 1962, and Bethke and Golin, 1994, respectively, for example.)

doubt upon, the one theory in favor of the other?

The answer, of course, is not entirely clear cut. If the predicted fitness advantage is very small, then even a small additional cost (several are considered below) of triparental sex over biparental sex would be enough to explain the absence in nature of a triparental sexual species and the predicted fitness advantage of triparental sex would not be problematic for the offending theory. On the other hand, if the predicted fitness advantage were very large, then dismissing the problem would require assuming a correspondingly large additional cost of triparental sex over biparental sex.[3] Such attempts to rescue the offending theory become less and less tenable then, as the theory's predicted fitness advantage to triparental sex increases.

The idea that a deeper understanding of the observed natural world can be obtained from consideration of *carefully circumscribed* unobserved phenomena— e.g., triparental sex here—is not new. Indeed, R. A. Fisher (1930, p. ix), on the separate issue of the number of mating compatibility classes, eloquently concludes:

> "No practical biologist interested in sexual reproduction would be led to work out the detailed consequences experienced by organisms having three or more sexes, yet what else should he do if he wishes to understand why the sexes are, in fact, always two?"

A legitimate concern to permitting the consideration of unobserved phenomena is that it may open a Pandora's box of infinite possibilities with no guidance as to

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[3]Including, for example, the cost of developing the necessary genetic machinery

which of them to consider. Would accepting this approach compel one to seriously consider, for example, a question such as, "Why do turtles have no wings?"

The answer is, "No." The questions one must consider will very often be suggested by the central question of interest. To be concrete, suppose that some quantifiable feature exhibited by various species in nature is always found to take on the particular numerical value x^*. If one wishes to understand *why* this is so from an evolutionary perspective, then the deepest explanation will arise from considering the possibility that the feature *could have taken on any other numerical value*, but that evolution favors the value that is observed over all others.[4]

Why is it that little or no attention has been paid to whether a theory of biparental sex inadvertently confers an advantage to, say, triparental sex? Perhaps it is because one is tempted to dismiss triparental sex altogether on the grounds that the associated costs—be they the cost of unproductive males, mating coordination costs, or the cost of developing the requisite genetic machinery—are prohibitive. But, insofar as such arguments have been provided at all, they are unpersuasive. For example, they fail to take into account the key point that any argument against the transition from biparental sex to triparental sex may be even more persuasive for ruling out the transition from asexual reproduction to biparental sex. Several such arguments are considered below.

Insisting that a theory of sex predict the evolutionary success of biparental sex

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[4]For example, the depth and completeness of our understanding of the evolutionary determinants of the sex ratio is due to the consideration of a model within which *all sex ratios are possible*, the vast majority of which have never been observed in Nature. Among all possible sex ratios the model predicts that evolutionary forces will select a unique sex ratio. This uniquely selected ratio coincides with the ratio observed in Nature.

over all other sexual systems places stringent demands on the theory. On the one hand, genetic mixing must be sufficiently beneficial to overcome the twofold cost of biparental sex over asexual reproduction, yet on the other hand genetic mixing must not be so beneficial that a further increase in fitness would be obtained from even more of it through triparental sex or quadriparental sex, etc. A viable theory of sex, therefore, must strike a delicate balance—genetic mixing must be advantageous, but not too advantageous. The latter demand—that sex not be too advantageous—has been overlooked in the literature.

As an example of the power of this approach, we consider whether the mutational deterministic (MD) hypothesis (Kondrashov, 1982, 1988) for the maintenance of biparental sex predicts the absence of triparental sex for most parameter values. Under the MD hypothesis, we find that, after considering its costs and benefits, triparental sex has a net fitness advantage over biparental sex for all parameter values considered. Moreover, this advantage can be substantial when the mutation rate is high enough to permit biparental sex to overcome its twofold cost. That is, in environments conducive to biparental sex, the MD hypothesis predicts even greater, and often by a substantial margin, evolutionary success to triparental sex. Given the range of mutation rates observed in nature[5], this casts some doubt on whether the MD hypothesis can be the primary explanation for the ubiquity of biparental sex.

The case against the MD hypothesis would be even stronger if there were a

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[5]See, for example, Drake *et al* (1998), Lynch *et al* (1999), Keightly and Eyre-Walker (2000) and (2001), and Kondrashov (2001).

competing theory that succesfully predicts the superiority of biparental sex over all other possibilities. Whether any of the other current theories of biparental sex, when extended to allow multiparental sex of any order, will predict the superiority of biparental sex is therefore an important open question.

2. Triparental sex

Triparental sex will be said to occur when each cell of an offspring contains genetic material from three parents—one mother and two fathers. For example, each parent might contribute an equal share of the offspring's genes. But this is just one possibility. Another possibility is that the mother contributes one-half of the offspring's genes and the two fathers each contribute one-quarter. In theory, there are infinitely many triparental sexual systems.

We next discuss several of the costs that might be associated with triparental sex.

First, there is the obstacle of developing the requisite genetic machinery for combining the genetic material of more than two parents. Providing a plausible and detailed microbiological mechanism through which triparental sex might operate, and determining the maintenance cost of such a mechanism (over and above the biparental mechanism's maintenance cost), is well beyond the scope of this paper. The fact that nature has produced asexual as well as biparental sex should generate skepticism that the cost of developing the requisite genetic machinery for triparental sex would be overwhelming. The fitness advantage we obtain for triparental sex over biparental sex must exclude these particular costs.

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However, the higher is the advantage we obtain, the more likely it is to outweigh these unknown genetic costs.

Although we cannot address the genetic machinery issue directly, a related empirical fact should be kept in mind. While triparental sex has never been observed, triparental recombination is well known to occur in viruses, where offspring DNA are routinely a combination of the DNA of two, three or more parents (Stent 1963, Bresch, 1959, and Munz, Young and Young 1983, for example).[6] Thus, nature has produced genetic machinery to carry out triparental recombination. If the MD hypothesis is correct, implying a large advantage to triparental sex over biparental sex, this forcefully calls into the question the assumption that nature could never adapt the viral triparental recombination technology into an advantageous triparental sexual mechanism.

Second, one might argue that the social costs of coordinating the mating of three individuals over just two outweigh the potential benefits (Power, 1976). To be taken seriously, such an argument must carefully consider the additional benefits and coordination costs incurred not only in the transition from biparental to triparental sex, but also in the transition from asexual reproduction to biparental sex. A serious difficulty for any such argument is that while there are clearly significant additional coordination costs involved in the transition from asexual to biparental sex—e.g., a technology for locating mates must be developed and

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[6]According to Bresch (1959), "In a 'triparental' cross, for instance, the [host] cells will be infected by the [viral] phage types ab^+c^+, a^+bc^+, and a^+b^+c. In this case one finds triparental recombinants abc among the progeny, i.e., particles with a marker from each of the three parental types."

maintained—the ample empirical evidence for sperm competition (Parker, 1970) implies that the additional coordination cost of triparental sex over biparental sex is negligible for a large number of species. Indeed, as the following quote explains, the prevelance of sperm competition implies that biparental mating behavior routinely brings together, within a single female, genetic material from multiple males.

> A common assumption about reproduction is that the spermatozoa in the vicinity of ova around the time of fertilization are from a single male. However, for a wide range of organisms, both internal and external fertilizers, this assumption is almost certainly wrong. It is wrong because among internal fertilizers, females typically copulate with more than one male during a single reproductive cycle, and among externally fertilizing animals, often several males simultaneously release spermatozoa near a spawning female. When the ejaculates from two or more males compete to fertilize the ova of a particular female, the process is referred to as sperm competition. Sperm competition is virtually ubiquitous and its biological consequences are considerable. (Birkhead, 1998.)

Sperm competition occurs, for example, in birds (Goetz *et al.*, 2003; Parrott, 2005), ants and bees (Hölldobler and Wilson, 1994), shrimp (Bilodeau *et al.*, 2004), snails (Evanno *et al.*, 2005), snakes (Garner *et al.*, 2002), tortoises (Roques *et al.*, 2004), and fruit-flies (Bressac and Hauscheteck-Jungen, 1996). In all these

cases, which are by no means exhaustive, triparental sex—e.g., where the sperm of two distinct males fertilize a single egg—would entail negligible additional social coordination costs over biparental sex.

Third, there is the "cost of sex." A biparental sexual population with a one to one ratio of unproductive males to females produces half as many offspring as an equally-sized asexual population (Maynard Smith, 1978). One might then expect triparental sex—involving two unproductive males and one female—to display a threefold cost of males relative to asexual reproduction. But, in fact, the cost of males depends upon which of the infinitely many triparental systems is in force. There is one particular triparental system that, on the one hand, generates more genetic mixing than biparental sex, yet, on the other hand, entails *no additional cost of males* relative to biparental sex. It is the system in which the offspring receives one-quarter of its genes from each of its two fathers, and one-half of its genes from its mother, a system that we will henceforth refer to as $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ triparental sex, or simply $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ sex. We now explain why $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ sex entails the same twofold cost of males as biparental sex.

Because the cost of males is determined not by the ratio of males to females in each mating instance but, rather, by the *population* ratio of males to females, determining the population ratio is central. We therefore turn to Fisher's celebrated equilibrium argument (Fisher, 1930). Applying the same logic to $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ sex, we note first that the total reproductive value of all of the males in any generation is precisely equal to that of all of the females in that generation. This is because, under $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ sex, all of the females supply half of the genes of all future generations.

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But then the remaining half must be supplied by all of the males. Consequently, as Fisher argued, equilibrium requires the offspring sex ratio to equate parental expenditure on male and female offspring. Maintaining the usual assumption that offspring of either sex are equally costly to raise to maturity, we conclude that the equilibrium sex ratio must be one—each male therefore mates with two females and vice versa. But this means that the cost of males is twofold—there is no additional cost of males over biparental sex.

Summing up, (i) given the existence in nature of triparental recombination in bacteria, for example, developing genetic machinery may not be an insuperable barrier to triparental sex, (ii) the additional coordination costs to triparental sex over and above those of biparental sex are negligible in many species, and (iii) $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ sex entails no additional cost of males relative to biparental sex.

Our next step is to compare the fitness—net of costs—of triparental sex versus biparental sex under the MD hypothesis. In the standard MD model, with the exception of the cost of unproductive males, *all* costs of biparental sex—including coordination costs—are ignored. To provide an appropriate comparison, genetic machinery maintenance costs and coordination costs will therefore be ignored here as well. While ignoring maintenance costs may bias the results against the MD hypothesis because it may understate the relative cost of triparental sex, ignoring coordination costs will bias the results in favor of the MD hypothesis because it will understate the relative cost of biparental sex if—see (ii) above—the cost of coordinating biparental sex over asexual reproduction is large relative to the additional cost of coordinating triparental sex over biparental sex, something that

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seems likely to hold in nature. This bias in favor of the MD hypothesis is discussed further following the MD analysis below.

Thus, in the following section, we compare the fitnesses of biparental and triparental populations under the MD hypothesis maintaining the literature's standard assumption of zero mating coordination costs and zero costs to maintaining the requisite genetic machinery. Under these assumptions it is shown that $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ triparental sex has a uniform fitness advantage, which is often substantial, over biparental sex.

What about the fitness consequences of $\frac{1}{3}$-$\frac{1}{3}$-$\frac{1}{3}$ triparental sex, where each parent contributes equally to the offspring? This sexual system provides even more mixing than $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ sex, and can be shown to yield an even greater *gross* increase in fitness under the MD hypothesis. However, Fisher's argument establishes that $\frac{1}{3}$-$\frac{1}{3}$-$\frac{1}{3}$ sex entails a threefold cost of males over asexual reproduction. On balance, for all parameter values considered here the population grows faster under $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ sex than under $\frac{1}{3}$-$\frac{1}{3}$-$\frac{1}{3}$ sex.

3. The mutational deterministic hypothesis

A leading explanation for the maintenance of sex in large populations is the mutational deterministic hypothesis in which sex is advantageous because it halts the otherwise steady accumulation of harmful mutations (Kondrashov, 1982, 1988). The first theory of this kind is due to Muller, but relies upon a finite population (Muller, 1932, 1964).

Kondrashov (1982) assumes the following. An individual's genome has infi-

nitely many loci between which there is no linkage. Mutations at all loci are equally harmful. An offspring with $i < K$ mutations survives with probability $s_i = 1 - (\frac{i}{K})^\alpha$. Offspring with K or more mutations are not viable. Finally, as individuals develop into adults, they independently receive additional mutations according to a Poisson distribution with mutation rate u, where the probability that any particular locus receives a mutation is zero. These additional mutations do not affect survival, but may be passed on to one's offspring, affecting its survival.

Kondrashov's analysis of a biparental sexual population is as follows. The life-cycle is mutations-recombination-selection-mutations. Individuals live for a single generation. Let q_i denote the fraction of individuals in a given generation with i mutations after selection. After mutations arrive according to the Poisson process, the fraction of individuals with i mutations is

$$q_i' = e^{-u} \sum_{j=0}^{i} q_j \frac{u^{i-j}}{(i-j)!}. \tag{1}$$

Now, because it is assumed that no two matched individuals have more than one mutation in total at each locus, the frequency with which an offspring from parents having n and m mutations has i mutations is $\binom{n+m}{i}(\frac{1}{2})^{n+m-i}(\frac{1}{2})^i$. Consequently, the fraction of offspring having i mutations after recombination is,

$$q_i'' = \sum_{n+m \geq i} q_n' q_m' \binom{n+m}{i} \left(\frac{1}{2}\right)^{n+m}.$$

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Finally, since offspring with $i < K$ mutations survive with probability s_i and only offspring with fewer than K mutations survive, the fraction of individuals with $i < K$ mutations after selection is,

$$q_i''' = \frac{s_i q_i''}{s_0 q_0'' + ... + s_{K-1} q_{K-1}''}, \tag{2}$$

where $s_0 q_0'' + ... + s_{K-1} q_{K-1}''$ is the fitness of the population, or equivalently, the fraction of surviving offspring. The equilibrium distribution of mutations is characterized by the additional condition that $q_i = q_i'''$ for $i = 0, 1, ..., K - 1$, from which one can also obtain the population's equilibrium fitness.

Let us now adapt Kondrashov's biparental analysis to a triparental $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ sexual population. As in the biparental case, the life cycle is mutations-recombination-selection-mutations, and we again let q_i denote the fraction of individuals with i mutations after selection. As before, after mutations arrive, the fraction of individuals with i mutations is q_i' given by equation (1).

Consider a triparental match in which the mother has m mutations and the two fathers have n total mutations. The offspring can have i mutations if for some $m' \le m$ and some $n' \le n$, it receives m' from the mother and n' from the fathers, where $m' + n' = i$. Adapting the Kondrashov model, it is assumed that the three parents have no more than one mutation in total at each locus. Consider a locus where there is a mutation. Saying that sex is $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ means that if the mutation belongs to the mother it is inherited with probability one-half, and if it belongs to one of the fathers it is inherited with probability one-quarter. Hence, because

there is no linkage, the frequency with which their offspring have i mutations is,

$$r_{m,n}^i = \sum \binom{m}{m'}\binom{n}{n'}\left(\frac{1}{2}\right)^m \left(\frac{1}{4}\right)^{n'}\left(\frac{3}{4}\right)^{n-n'},$$

where the sum is over $m' \le m$ and $n' \le n$ such that $m' + n' = i$. Consequently, the fraction of offspring having i mutations after recombination is,

$$q_i'' = \sum_{n+m \ge i} q_m' \left(\sum_{j=0}^{n} q_j' q_{n-j}'\right) r_{m,n}^i.$$

Finally, the fraction of individuals having $i < K$ mutations after selection is q_i''', which as before, is related to q_i'' through equation (2).

The equilibrium distribution of mutations is again characterized by the additional condition that $q_i = q_i'''$ for $i = 0, 1, ..., K-1$, from which one can also obtain the population's equilibrium fitness.

Let us now compare the equilibrium fitness of a $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ sexual population with that of a biparental population. The values of $\alpha = 1, 2, \infty$ and $K = 5, 20, 60, 80$ considered here are taken from Kondrashov (1982) and Howard (1994).

Table 1 shows the advantage of $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ sex over biparental sex. Each entry in the table is the percentage amount by which the equilibrium fitness of a $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ sexual population exceeds that of a biparental population for a particular vector of parameters, (u, K, α). Maintaining Kondrashov's assumption that the only cost of sex is the cost of males, there is no additional cost to $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ sex over biparental sex. Consequently, each entry is also the percentage amount by which the growth

rate of the triparental population exceeds that of the biparental population. An asterisk indicates that biparental sex fails to overcome its twofold cost relative to asexual reproduction in that cell.

u	$K = 5$	$K = 20$	$K = 60$	$K = 80$	α
	2.1	1.0	0.4	0.3	∞
1	2.3*	1.6*	0.7*	0.5*	2
	2.0*	1.4*	0.6*	0.5*	1
	4.8	3.0	1.4	1.1	∞
2	4.8	4.2	2.3	1.8	2
	4.4*	4.1	2.2	1.7	1
	7.4	5.6	2.8	2.2	∞
3	7.1	7.0	4.3	3.6	2
	6.7	7.1	4.3	3.6	1
	9.8	8.6	4.5	3.6	∞
4	9.3	10.1	6.6	5.6	2
	8.8	10.2	6.7	5.7	1
	14.2	15.3	8.9	7.3	∞
6	13.2	16.7	11.8	10.2	2
	12.6	16.8	12.0	10.4	1
	17.8	22.7	14.4	11.9	∞
8	16.5	23.7	17.7	15.5	2
	15.9	23.7	18.0	15.7	1

Table 1: % Advantage of Triparental Sex

Every entry in Table 1 is positive, indicating that a $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ sexual population always grows faster than a biparental population. Moreover, when biparental sex overcomes its twofold cost—indicated by cells without asterisks—the advantage to triparental sex can be substantial. For example, with intermediate selection (i.e., $\alpha = 2$) and a mutation rate of 2, a $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ population grows between 1.8% and 4.8% faster than a biparental population, implying a relative doubling time of between 14 and 39 generations. The MD hypothesis therefore does not provide an

explanation for both the presence of biparental sex and the absence of triparental sex.

Also, the higher is the mutation rate, the larger is the advantage to $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ sex. With intermediate selection, for example, a mutation rate of 3 is sufficiently high to imply that a $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ sexual population grows 3.6% to 7.1% faster than a biparental population, implying a relative doubling time of between 10 and 20 generations. Thus, contrary to current thinking, not only do low mutation rates—e.g., below 1-2 (Kondrashov, 1988; Charlesworth, 1990; and Howard, 1994)—constitute evidence against the MD hypothesis, but *high* mutation rates too constitute evidence against it. And indeed, genomic mutation rate estimates of between 3 and 6 have been found, for example, in chimpanzees (Keightley and Eyre-Walker, 2000).

This also shows how a large but ignored coordination cost to biparental sex over asexual reproduction, together with a small additional cost to triparental sex would bias our results. A large coordination cost from asexual to biparental sex would *increase* the mutation rate at which biparental sex dominates asexual reproduction—from 1-2 mutations per genome per generation to, possibly, 3-4— while a small coordination cost from biparental to triparental sex would have little impact on our relative fitness figures in Table 1. Thus, the entries in Table 1 would be essentially unchanged, but more of them would be marked with an asterisk— e.g. only mutation rates above 3 or 4, say, might be consistent with biparental sex dominating asexual reproduction. But for these high mutation rates, triparental sex has a substantial advantage over biparental sex and the case against the MD hypothesis would be even stronger.

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To permit a direct comparison with the literature, we have presented in Table 1 the relative *equilibrium* fitnesses of triparental and biparental populations. However, to further illustrate the advantage of triparental sex under the MD hypothesis, we also establish that a small fraction of triparental females introduced into an equilibrated biparental population will eventually take over.

An equilibrated biparental population is seeded with a small fraction of females each possessing one copy of a dominant triparental gene for $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ sexual reproduction. Their distribution of mutations is that of the biparental population. Males can mate with biparental and triparental females. The triparental gene is expressed only in females, although males can pass it on to male and female offspring, the latter then reproducing triparentally through $\frac{1}{4}$-$\frac{1}{4}$-$\frac{1}{2}$ sex.

In all runs, the fraction of triparental females—i.e., those with at least one copy of the triparental gene—increases with each generation, and *the biparental population is driven to extinction*. A particular example of one of our runs is shown in Figure 1, where f denotes the initial number of females, as a fraction of the population, possessing a single copy of the triparental gene. In contrast, when a triparental sexual population is in equilibrium, biparental sex cannot invade.

4. Discussion.

There are two major classes of theories on the maintenance of sex, those based upon the purging of deleterious mutations, and those based upon adaptation to the environment.

In the deleterious mutation model analyzed here, the post-sex variance of the

Figure 0.1: Figure 1: $f = 0.001$, $u = 3$, $K = 20$, $\alpha = 2$

distribution of mutations is the average of the pre-sex mean and variance. Therefore if, in a biparental-sex equilibrium, the post-sex mean number of mutations exceeds its variance (as it does for all parameter values considered), additional (pre-selection) sex *increases* the variance. Combined with the tendency of selection exhibiting synergistic epistasis to favor mean-preserving increases in variance, this explains why triparental sex dominates biparental sex for all parameter values considered.

Because many deleterious mutation models incorporate synergistic epistasis (Charlesworth, 1990; Howard 1994; Kondrashov, 1982, 1988), triparental sex may be expected to dominate biparental sex in these models as well. A possible exception arises in a model of mutational meltdown in finite populations with zero epistasis (Lynch and Gabriel, 1990). Because reducing epistasis to zero eliminates a potential advantage of triparental sex over biparental sex, such a model may be consistent with the absence of triparental sex.

We next consider three subclasses of theories based upon adaptation to the environment. In directional selection models, sexual reproduction increases genetic and phenotypic variance and can permit a species to better track the optimum phenotype in a changing environment (Charlesworth, 1976; Crow, 1992; Maynard Smith, 1980, 1988; Waxman and Peck, 1999). When conditions are favorable for biparental sex, additional genetic mixing—as would occur under triparental sex— may increase genetic variance further and be even more favored. If so, directional selection hypotheses would fail to predict the absence of triparental sex.

Host-parasite coevolution models can yield an advantage to biparental sex

when selection effects are sufficiently strong (Hamilton, 1980; Hamilton *et al.*, 1990; Jaenike, 1978; Otto and Nuismer, 2004; Peters and Lively, 1999). Whether triparental sex would appreciably increase this advantage is unclear and must await further study.

A third subclass of environmental models are those based upon the Hill-Robertson effect (Barton and Otto, 2005; Felsenstein, 1974; Felsenstein and Yokoyama, 1976; Hill and Robertson, 1966; Martin *et al.*, 2006; Otto and Barton, 1997, 2001; Iles *et al.*, 2003). In these models, sex and recombination permit the species to improve faster when the fixation effect of selection without sex (or with low levels of recombination) leads to negative linkage disequilibrium. Importantly, this effect is present even under zero epistasis (Otto and Barton, 1997). Once again, because zero epistasis eliminates a potential source of advantage of triparental sex over biparental sex, hypotheses based upon the Hill-Roberston effect with zero epistasis may be consistent with the absence of triparental sex.

Finally, there are hybrid models involving both deleterious mutation effects and coevolution effects (Howard and Lively, 1994, 1998; West *et al.* 1999). Because these hybrid models can explain biparental sex under a wider range of parameter values than any of the individual models taken separately, it would be of interest to compare triparental and biparental sex in such hybrids.

We have shown here that under the MD hypothesis, triparental sex always dominates biparental sex, that the advantage is significant at modest genomic mutation rates, and that higher mutation rates only serve to increase this advantage. With all three options—asexual, biparental, triparental—available, fitness

would be highest either under asexual reproduction or under triparental sex. Accordingly, biparental sex should not be observed, contrary to fact. Thus the MD hypothesis fails to predict the absence of triparental sex and the range of parameter values under which biparental sex has a significant fitness disadvantage against either asexual reproduction or triparental sex is large, casting doubt on the MD hypothesis as a primary explanation for the ubiquity of sex.

According to Hurst and Peck, 1996, p.51, "One of the great struggles in the evolution-of-sex literature is to find a prediction that is truly discriminating between hypotheses." Is the prediction that sexual reproduction is always biparental, and not triparental or more, "truly discriminating among hypotheses?" While a definitive answer awaits further study, it is suggested here that theories relying upon synergistic epistasis are less likely to be consistent with the prediction than those permitting zero epistasis.

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