COMMENTARY

The omnipresent process of sex

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Keywords:

evolution;
mutation load;
mutational deterministic hypothesis;
recombination.

West, Lively and Read (1999) (hereinafter 'the authors') note that there are upwards of 20 hypotheses for the evolutionary advantages of sexual reproduction and argue that more than one may be correct. In particular, they suggest that environmental and mutational mechanisms may both be applicable and that interactions between them could be important. I like the suggestion of a pluralistic approach. The area of interactions between different mechanisms is, as the authors say, largely unexplored. I have no criticisms of the article, only a few comments.

The quotation from Havelock Ellis, which I chose as a title, fortuitously points up the problem. I do not find it surprising that a plethora of hypotheses have been presented. It almost appears that, with each new molecular discovery, there comes another hypothesis. Is a sufficient explanation to be found among these? I suspect that among them, singly or in combination, lies the answer. But who can be sure that the happy thought that will provide a really satisfying answer will not appear. Then everyone would immediately accept the idea and say 'How obvious, why didn't I think of it?'. Welcome as this would be, it seems unlikely, and we shall continue to have a diversity of views and an increasing number of hypotheses. Yet, I suppose there is always room for one more hypothesis. Many of the newer hypotheses strike me as, if not wrong, applicable only to such special circumstances as to lack generality. I am tempted to quote Laplace: 'Sire, I have no need of that hypothesis'.

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There indeed *is* a problem, however. The evolutionary advantage of sex cannot be marginal, it must be large. The standard two-fold cost is a proper target for a quantitative assessment. But, let me emphasize that it is not alone. Here are some of the disadvantages (Crow, 1994):

- Sexual reproduction is not a very efficient means of reproduction. Meiosis and fertilization are unnecessarily complicated if reproduction is the sole objective. Asexual spores or meiosis-bypassing apomixis would appear to be far more efficient.
- The aforementioned two-fold cost. As an alternative to separate sexes, a clone of parthenogenetic females could dispense with males, with a 50% saving.
- With separate sexes, sexual selection leads to traits that are poorly adapted, such as peacock tails and destructive competition for mates.
- Sexual species cannot perpetuate what are often fitness-improving types, such as triploids, aneuploids and translocation heterozygotes.
- Species with separate sexes have to find mates, or in planktonic populations sperms have to find eggs, which can be a severe disadvantage in sparse populations.
- Sexual species are prone to sexually transmitted diseases and provide an easier opportunity for selfish DNA elements to spread.
- Sexual reproduction opens the way for 'cheating' DNA, such as meiotic drive, and for possibly adverse gametic competition.
- Short-term selection is often slower in sexual species, in which selection acts on only the additive component rather than the total genetic variance.
- The Sewall Wright dilemma. With a complex fitness surface a sexual species may not be able to cross a valley to get to a higher fitness peak.

These and other disadvantages present a formidable challenge. I believe the variety of these supports the

authors' view that there are multiple mechanisms offering an advantage to sexual reproduction. I think that research based on the two-fold cost is the best way to proceed, the other disadvantages of sex being more difficult to quantify.

I share the authors' preference for considering hypotheses that are deterministic and do not require special circumstances, such as small or structured populations. They are searching for the most generally applicable theories, and this seems to me to be the way to go.

I have long liked the mutational deterministic hypothesis. Alexey Kondrashov makes the valid point that this can be falsified by finding that mutation rates are small, say less than one per diploid genome per generation. Certainly, falsifiability is one desideratum for a scientific hypothesis. Yet, a great deal of evolutionary research – good evolutionary research – does not fit the Popper paradigm. Considering the mutation hypothesis as one that is not sufficient by itself lowers the required mutation rate and makes it less falsifiable. But the possibility of interaction among mechanisms is appealing and, in my view, can offset any loss of possible falsifiability.

The most serious problem for the mutational hypothesis arises in species with limited reproductive capacity. Most animal and plant species have high enough reproductive rates to tolerate a high mutation load and still survive. A critical place to look is in species with low rates of reproduction. Until recently there was no information on the genomic rate of deleterious mutations in any mammal. This is no longer true (Keightley, personal communication). The estimated rate for the human species is about two per diploid genome per generation. For a number of reasons, this is a minimum estimate, so a realistic range is from 2 to 5. This is high enough to require some mechanism for mutation elimination; simple exponential survival and fertility will not work.

Epistasis is regularly invoked as a means of mutation-load reduction. Yet the level of epistasis observed for quantitative traits is usually slight. I suspect, as many have suggested, that some form of rank-order selection imposes the necessary epistasis. This epistasis is a property of the way selection works rather than a function of gene interaction. No one expects nature to truncate strictly. Yet, a crude approximation, quasi-truncation selection, has almost as great a mutation-reducing effect. This was perhaps apparent to many, but my realization came with a paper by Milkman (1978), which we worked out in more detail (Crow & Kimura, 1979). All species produce more progeny than would be required to maintain the population if all survive. It seems eminently reasonable that some density-dependent selection follows and that this may be sufficiently like rank-order selection to have very similar properties. In particular, I would argue that the human species has survived, despite what increasingly seems to be a very high deleterious mutation rate and a rather low reproductive potential.

The mutation hypothesis has several advantages. All species produce deleterious mutations and selective adjustment of mutation rates is slow and inefficient. The hypothesis involves no stochastic assumption and works in all but quite small populations. It imposes no requirement for environmental fluctuations or other specialized environmental situations (e.g. parasites).

The best test of this hypothesis would be to compare deleterious mutation rates in otherwise comparable sexual and asexual species. But 'otherwise comparable' populations may be difficult to identify. The best opportunities may be in plants or perhaps some lower vertebrates. Yet, even with good data there are conceptual difficulties, as the authors have discussed.

Environmental hypotheses are more difficult to quantify and more difficult to test in ways that have general applicability. Yet there is no question of their plausibility, and the advantages of sexual reproduction in a parasite-infested world seems entirely reasonable. There are abundant observations that offer correlational support for these hypotheses, but they are rarely, if ever, capable of discriminating among rival hypotheses.

The authors emphasize that environmental hypotheses such as the Red Queen work best with strong epistasis. It is therefore inviting to regard epistasis, particularly that brought about by approximate rank-order selection, as improving the status of both hypotheses. The intriguing suggestion that there may be interactions between the two remains to be tested rigorously. A difficulty of the pluralistic approach is that it is less testable. We are giving away testability to gain plausibility and generality. And it will surely be difficult to measure interactions when the main effects are so difficult to quantify.

I think the authors are correct in emphasizing the mechanisms currently maintaining sex; these may be different from those involved in the origin of sexual mechanisms, recombination for example. I also agree that it is important to measure the magnitude of the advantage of sex for all relevant hypotheses, even though they may not individually be sufficient to balance a two-fold cost. Finally, estimation of parameters is useful even for the study of separate mechanisms, but is of special importance if they are to be considered simultaneously.

I was particularly intrigued by the possibility discussed under 'Synergism at the empirical level' by the possibility that both the parasite model and the mutation model work best under truncation selection. Each may enhance the approach to truncation selection (or quasi-truncation selection) in the other. If this turns out to be correct when specifically modelled, it will provide an excellent reason to support the authors' pluralistic view. In any case, who can object to obtaining better estimates of the relevant parameters?

I believe that the authors have emphasized the most promising hypotheses. But is there room for others? I think there is, although I would regard them as ancillary. Whether they would interact with the ones just discussed remains to be seen.

Some stochastic hypotheses certainly deserve our continued recognition. One of these is Muller's ratchet. In particular, the trade-off between this and the deterministic mutation hypothesis as population size changes is important, especially if this is combined with a model of environmental fluctuation.

Another class of hypotheses includes those that depend on individual favourable mutations sweeping through the population. In my view, these are a less likely reason for recombination than traits that depend on multiple genes (at least in multicellular eukaryotes). Yet, we know from the study of molecular evolution that favourable mutations have been incorporated in the phylogeny of various species. The well-known Fisher–Muller idea offers the possibility of incorporating favourable mutations that arise in separate individuals. Surely, there are circumstances where this would be important, but such circumstances may be rare. I suspect that Fisher's other argument is the more important. He notes that in an asexual population, in addition to the stochastic loss in the early generations (which is essentially the same in sexual or asexual species), a slightly beneficial mutation has very little chance. In Fisher's (1958) elegant prose: 'If we consider the prospect of a beneficial mutation occurring at any instant, ultimately prevailing throughout the whole group, and so leading to evolutionary progress, it is clear that its prospect of doing so will depend upon its chance of falling, out of the whole population, upon the one individual whose descendants are destined ultimately to survive.' The mutation may help that one individual, but only if the mutational effect is large, or the population is very homogeneous. But it can be very homogeneous only if the mutation rate, and therefore the chance of a favourable mutation, is small.

Data from molecular evolution are becoming more and more abundant. It should be possible eventually, perhaps soon, to compare the rate of incorporation of favourable mutations in sexual and asexual species.

In summary, I am generally supportive of the authors' views. The most fruitful approach, I believe, lies in the study of existing hypotheses, and in various combinations. The old question, 'Is Sex Necessary' (Thurber & White, 1929), is not likely to have a single answer.

Finally, let me note that it has been a great pleasure and opportunity for one who was once very closely associated with this subject, but who has fallen badly behind, to tune in again. My long association with the mutational deterministic hypothesis has been a source of much personal satisfaction. I should like to mention two items. First, Kimura and Maruyama, both now deceased, wrote their paper at a time when both were working in my lab and we were conversing regularly. Second, the fact that Alexey Kondrashov and I had each thought of this brought us together, first by correspondence and later in person during two periods in Wisconsin. The daily discussions were great.

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