Evolution of sex and deterministic mutation assignment

In studying evolution, there has been much debate over the origins and evolutionary maintenance of sex. This represents a great challenge in evolution as it appears that the vast majority of animals and plants reproduce sexually. One component compounding the mystery is the two fold cost of sex, that is, there is a cost to producing males. Where an asexual species can double its population each generation, the sexual species will remain at a constant population if both populations produce 2 offspring per generation.

An added cost of sexual reproduction can be that there is a time investment in finding mates, as well at the potential for sexual selection which can lead to the selection of unfavorable traits. There have been a number of hypotheses for how sex is maintained. Some of these ideas include speed in creating novel genotypes, the red queen hypothesis and resistance to parasites, and being better at removing deleterious mutations. The answer to the problem of sex may be related to one or all of these hypotheses, and the maintenance of sex in each taxa may be accomplished by different means.

One subset of models are those that deal with removal of deleterious genes. The fundamental reasoning in these models is that deleterious mutations can build up in a lineage such that it decreases an organism’s overall fitness. Sex is then thought to be more efficient at removing deleterious mutations from the genome through recombination. An asexual lineage would have to rely on a reversal mutation to remove deleterious alleles. Two models in this subset are Muller’s ratchet hypothesis, and the deterministic mutation model, that I will discuss in more detail.

Muller’s ratchet hypothesis considers an asexual population to act as a ratchet. When mutations arise in the least mutated individuals in a population, further generations cannot have fewer mutations in that population, provided that back mutations don’t exist. This hypothesis is built under the assumption that the population size is at least occasionally small enough that the least deleterious mutation-loaded individuals are lost due to sampling. After the least loaded class is removed, the new least loaded class may also be eliminated due to sampling.

Sex is then considered to neutralize the ratchet as it can recreate good genotypes that are lost because of genetic drift. A very controversial hypothesis for the maintenance of sex based on removal of deleterious genes was proposed by Kondrashov (1988) called the deterministic mutation model. Unlike Muller’s ratchet hypothesis, this model does not require finite population sizes. It is instead based on an infinite population model. Also, this model requires that the mutation rate (U) for diploid species is greater than one, as the advantage of sex will theoretically increase with the mutation rate.

It also assumes synergistic epistasis, meaning that even between two weakly deleterious mutations the net negative effect is greater than the sum of the two individual deleterious mutations. Therefore it is most agreeable to have a low number of mutations than to have many mutations that are individually less severe. The thinking here is that sex will allow recombination to produce individuals with large amounts of mutations, and individuals with few mutations. The individuals with few mutations have the preferable phenotype and therefore have a selective advantage.

Although inconclusive, the deterministic mutation model may be a mechanism for the maintenance of sex. There is some good evidence for the ratchet hypothesis, such as a study done by Lambert and Moran (1998) in which stabilities of the domain 1 of 16SrRNA were found to be lower in small non-recombining populations. Another study by Shabalina et al. (1997) also showed operation of the ratchet in Drosophilla populations. The success of Muller's ratchet at least gives some evidence that the removal of deleterious mutations is a good evolutionary reason for the maintenance of sex.

There is less evidence supporting the deterministic mutation model. To begin, the assumption of U being greater than one is not clearly shown. In general, U is estimated to be variable, sometimes within the same species (Drake et al. , 1998). For instance, E-coli and Drosophilla have a mutation rate that is much less than one, while influenza A and humans have mutation rates greater than 1, and are likely candidates for the deterministic mutation hypothesis. Kondrashov (2001), points out that the low estimates for U in drosophila (done by Keightley and Eyre-Walker) may be due to selection at synonymous sites.

He suggests that the best way to measure the mutation rate is to do so shortly after the mutation emerges, as has been done with humans and C. elegans, which have estimates of U greater than one. In a response by Keightley and Eyre-Walker (2001), the deterministic mutation model was challenged, and they claimed that they had indeed measured selection at synonymous sites. They also argue that the mutation rate is small in coding sites, but large in noncoding regions of the genome. Since selection will tend

to act on the coding regions, this was not a favorable result for the deterministic mutation model.

The arguments by Kondrashov, Keightley and Eyre-Walker also highlight the general lack of consistency in measuring U. Additionally, comparisons among three related species: C. elegans (asexual), C. briggsae (asexual), and C. remanei (sexual) where shown to have insignificantly different mutation rates (Cutter, 2003). This does not support the deterministic mutational model as you would expect the asexual species to have lower mutational rates than the sexual ones. The authors conclude that this clade does not show evidence for conforming to any mutational model to explain sexual recombination.

Synergistic epistasis was also a major prediction of the deterministic mutation hypothesis. It has been suggested that genome architecture may be organized such that it favors synergistic negative epistasis, based on an an artificial gene network model (Azevedo, 2006). This model predicts that recombination selects for genome robustness, and that negative synergistic epistasis evolves as a consequence of genome robustness, thus sexual reproduction selects for its own upkeep. Other evidence for synergistic epistasis comes from de Visser et al. 1997), who used the sexual algae, Chlamydomonas moewusii, to show that synergistic epistasis existed between pre-existing and new mutations. This study used r and K measurements to measure fitness. They compared the log of the fitness to investigate how the genes interact, and argued that their results based on K support the deterministic mutation model. They also proposed that their evidence may give some clue as to why K-selected environments tend to

favor sexual reproduction. West et al. , (1998) have criticized the methods used by some researchers for testing synergistic epistasis.

According to these authors, the best way to determine synergistic epistasis is to cross different lineages with varying numbers of mutations and then compare fitness of offspring and parents. They re-analyzed the data on Chlamydomonas moewusii, and disagreed with the finding that there was synergistic epistasis upon re-analysis of the data. Elena and Lenski (1997) used mutated strains of E-coli to test for synergistic epistasis. In their experiment they generated E-coli mutants carrying one, two or three mutations using a Tn10 transposon to create the new mutations.

They compared the fitness of their 225 mutants to the fitness to other E-coli that were not mutated. Their finding was that there is a log-linear relationship between fitness and number of mutations, showing that there is an additive, but not multiplicative, interaction between these mutations. They also looked at 27 recombinant genotypes with known individual and combined mutation effects from single mutant strains. They found interaction of some pairs, suggesting epistasis, however they found only three synergistic interactions and four antagonistic interactions.

The remainder of the recombinant genotypes did not appear to interact. The authors concluded that the deterministic mutational model was not supported by their data. They do show that in some cases synergistic epistasis does exist. In general, evidence for negative synergistic epistasis is unclear as the sign (positive or negative) of the epistasis is different among organisms and varieties of mutations (de Visser, 2007). Also when the

epistasis is negative, it is often the case that it is not in a range that will support sexual reproduction.

The theoretical work underlying the deterministic mutational model is yet another example of progress that has been made in the pursuit of understanding the evolutionary role of sex. The conditions of negative synergistic epistasis and U less than one have left the validity of this model to be uncertain, although not necessarily always wrong. It has been shown that estimates of U are variable . Also, the recent development suggesting that genetic architecture and sex are interrelated suggests that recombination could lead to negative epistasis.

While neither synergistic epistasis nor U > 1 has been shown to be definitively true, they remain possible, and thus the deterministic mutational model may still have some explanatory power in solving the problem of sex in evolution. References Kondrashov, A. S. 1988 Deleterius mutations and the evolution of sexual reproduction. Nature 336, 435???-440. Lambert, J. D. , and Moran, N. A. , 1998, Deleterious mutations destabilize ribosomal RNA in endosymbiotic bacteria. Proceedngs of the National Academy of Sciences USA, 95: 4458-4462.