The Accumulation of Sexually Antagonistic Genes as a Selective Agent Promoting the Evolution of Reduced Recombination between Primitive Sex Chromosomes

William R. Rice


Stable URL: http://links.jstor.org/sici?sici=0014-3820%28198707%2941%3A4%3C911%3ATAOSAG%3E2.0.CO%3B2-U

*Evolution* is currently published by Society for the Study of Evolution.

---

Your use of the JSTOR archive indicates your acceptance of JSTOR's Terms and Conditions of Use, available at http://www.jstor.org/about/terms.html. JSTOR's Terms and Conditions of Use provides, in part, that unless you have obtained prior permission, you may not download an entire issue of a journal or multiple copies of articles, and you may use content in the JSTOR archive only for your personal, non-commercial use.

Please contact the publisher regarding any further use of this work. Publisher contact information may be obtained at http://www.jstor.org/journals/ssevol.html.

Each copy of any part of a JSTOR transmission must contain the same copyright notice that appears on the screen or printed page of such transmission.

---

JSTOR is an independent not-for-profit organization dedicated to and preserving a digital archive of scholarly journals. For more information regarding JSTOR, please contact support@jstor.org.
THE ACCUMULATION OF SEXUALLY ANTAGONISTIC GENES AS A SELECTIVE AGENT PROMOTING THE EVOLUTION OF REDUCED RECOMBINATION BETWEEN PRIMITIVE SEX CHROMOSOMES

WILLIAM R. RICE
Department of Biology, University of New Mexico, Albuquerque, NM 87131

Received August 4, 1986. Accepted February 17, 1987

The evolution of dimorphic sex chromosomes is generally thought to proceed in two stages: first a breakdown in recombination between the primitive X and Y chromosomes (W and Z in a WZ system), followed by the loss of function of most Y-linked genes (for reviews, see Mittwoch [1967], Ohno [1979], and Bull [1983]). By primitive X and Y sex chromosomes, I mean homologous chromosomes that are differentiated only by the alleles (x or y; note that lower case symbols refer to genes, and upper case symbols refer to entire chromosomes) that they carry at a single sex-determining locus.

Fisher (1931) was the first to suggest that linkage to a sex-determining locus facilitates the accumulation of genes that are selectively favored in males (more generally, the heterogametic sex) but selected against in females. This idea was extended to the case of chromosomal translocations by Charlesworth and Charlesworth (1980). Close linkage to the y allele causes male-benefit/female-detriment genes to be transmitted more frequently to sons, where they are selectively favored. If such sexually antagonistic genes were to accumulate in linkage with a y allele, they would cross over onto the primitive X chromosome and reduce the average fitness of females. This crossover of male-benefit/female-detriment genes from y- to x-linkage produces natural selection for both reduced recombination in the heterogametic sex and also sex-specific gene expression.

Bull (1983, pp. 265–269) partially quantified Fisher's verbal model by considering two special cases: when the allele with sex-specific fitness is unlinked to the sex-determining locus, and when it is completely linked. He concluded that linkage between a sex-determining locus and a sexually antagonistic locus facilitates the maintenance of polymorphisms for alleles with opposing fitness effects in the two sexes.

The work by Fisher (1931), Charlesworth and Charlesworth (1980), and Bull (1983) demonstrates that tight linkage between the sex locus and the sexually antagonistic locus facilitates the initial increase and maintenance of y-linked male-benefit genes when they are detrimental to females. An important question that remains is how tight linkage must be in order to promote the accumulation (to substantial frequency) of male-benefit/female-detriment genes, especially when the disadvantage to females is high. That is, what are the "linkage constraints" (Charlesworth and Charlesworth, 1980) for the buildup of y-linked sexually antagonistic genes? The answer to this question is crucial, because the feasibility of breakdown in X-Y recombination via the accumulation of sexually antagonistic genes depends critically on the "genetic opportunity" for such genes to evolve. The looser the requisite linkage, the larger the pool of genetic variability that could be selected in a sex-specific manner, and the more feasible the model.

Here, I address this question by solving for the equilibrium frequency of sexually antagonistic genes as a function of their recombinational distance from the sex locus. I conclude that very tight linkage is not required for the accumulation of genes that are lethal or semi-lethal to the homogametic sex.

The Model

Consider a large population with genic sex determination. Males are assumed to be the heterogametic sex. The male-determining gene is designated y and assumed to be dominant and epistatic to all other sex determining genes. Thus males have genotype xy and females xx. The sex chromosomes are assumed to be undifferentiated except at the sex-determining locus. A second locus (the A locus) is initially monomorphic for allele A, which produces unit fitness (viability) in both sexes. Mutation recurrently introduces a second allele (A,) which increases male fitness by an increment S when homozygous and hS when heterozygous (see Table 1). In females the A, allele reduces fitness by a decrement T when homozygous and hT when heterozygous. The coefficient h indicates dominance, with h = 0 for a fully recessive and h = 1 for a fully dominant A, allele. The A locus is located R recombinational units away from the sex determining locus.

Will the A, allele increase when rare? In a previous paper examining a different aspect of sex-chromosome evolution (Rice, 1986), I determined, to a conservative approximation, that A, will increase when rare whenever R < hS/(1 + hS). This result, however, tells us little about the generation of selection for reduced recombination between the sex chromosomes, since a trivial accumulation of A, alleles will have virtually no impact.

Here, I ask how tight linkage must be for an A, allele to accumulate to substantial frequency in linkage with the y gene. To answer this question, I first consider the analytically tractable case of a completely dominant A, allele (h = 1) that is beneficial to males (S > 0) and lethal to females (T = 1) (see fitness model in Table 1). In the model, it is assumed that the life cycle is discrete and that the population is censused at the adult stage. The A locus influences fitness by modifying zygote-to-adult survivorship.
Table 1. The fitness model. In the analytical model \( h = 1 \) and \( T = 1 \), so that the frequencies \( a, c, f, \) and \( g \) are necessarily equal to 0. In the simulation model, \( h \) and \( T \) are unconstrained. In both models, \( p = a + b \) is the fraction of \( Y \) chromosomes carrying the \( A_2 \) allele.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Frequency (adults)</th>
<th>Genotype</th>
<th>Fitness (viability)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MALE</td>
<td>a</td>
<td>( y-A_2/x-A_2 )</td>
<td>( 1 + S )</td>
</tr>
<tr>
<td></td>
<td>b</td>
<td>( y-A_2/x-A_1 )</td>
<td>( 1 + hS )</td>
</tr>
<tr>
<td></td>
<td>c</td>
<td>( y-A_1/x-A_2 )</td>
<td>( 1 + hS )</td>
</tr>
<tr>
<td></td>
<td>d</td>
<td>( y-A_1/x-A_1 )</td>
<td>( 1 )</td>
</tr>
<tr>
<td>FEMALE</td>
<td>e</td>
<td>( x-A_1/x-A_1 )</td>
<td>( 1 )</td>
</tr>
<tr>
<td></td>
<td>f</td>
<td>( x-A_1/x-A_2 )</td>
<td>( 1 - hT )</td>
</tr>
<tr>
<td></td>
<td>g</td>
<td>( x-A_2/x-A_2 )</td>
<td>( 1 - T )</td>
</tr>
</tbody>
</table>

When \( h = 1 \) and \( T = 1 \), then \( p = b \) and,

\[
\Delta p = \frac{p(1 - R)(1 + S)}{p(1 - R)(1 + S) + pR + d} - p. 
\]

For \( \Delta p > 0 \),

\[
R < \frac{S(1 - p)}{1 + S(1 - p)}. 
\]

I specifically solve for the fraction \( (\hat{p}) \) of primitive \( Y \) chromosomes that carry the \( A_2 \) allele (designated by the haplotype \( y-A_2 \)). The equilibrium frequency of \( y-A_2 \) (Table 1) can be shown to be:

\[
\text{freq}[y-A_2] = \hat{p} = 1 - \frac{R}{S(1 - R)} . 
\]

Equation (1) was used to construct Figure 1. This figure illustrates that dominant \( A_2 \) alleles with a lethal effect in females can accumulate to high frequency even when the advantage to males (S) is quite small. The larger the advantage to males, the looser the requisite linkage and the higher the equilibrium frequency for a specified value of \( R \). To illustrate the use of Figure 1, suppose males carrying a dominant \( A_2 \) allele had their fitness increased by 5%. If the recombinational distance between the sex locus and the \( A \) locus were 2%, then \( \hat{p} = 0.592 \). This would result in about 1.2% of females dying each generation due to recombination and expression of \( A_2 \) in females.

The sensitivity of the equilibrium values predicted from this simple genetic model to incomplete dominance and semilethality have been investigated numerically by computer simulation (see Rice [1986] for a description of the computer model). The simulations demonstrate that \( \hat{p} \) is approximately equal to or greater than \( 1 - R/[hS(1 - R)] \). Figure 2 illustrates the effect of deviations of \( h \) and \( T \) from unity. Note that when \( S > T \) the \( A_2 \) allele can increase when rare without the benefit of linkage to the \( y \) gene (see Rice, 1984). In summary, the simulations demonstrate that \( A_2 \) alleles that have low or no dominance will only accumulate in the area immediately adjacent to the sex locus, while dominant and semidominant \( A_2 \) alleles can accumulate at much more distal locations.

The analytical and simulation models illustrate how male-benefit (female-benefit in the case of female heterogamy) genes can accumulate to high frequency even when they are highly detrimental to females. The requisite linkage depends on both dominance and the benefit of the allele to males. If one concludes that a fitness advantage of 5-10% for polymorphic alleles is not uncommon in nature (e.g., see Endler, 1986 Ch. 6), then a segment of chromosome 18 centimorgans in length (±9 centimorgans about the sex locus) will potentially support the accumulation of dominant male-benefit/female-detriment genes. In the case of Drosophila melanogaster, this would encompass about 6% of the entire genome. Because such a large portion of the genome is influenced by the presence of a \( y \) gene, male-benefit/female-detriment genes need not be common in nature to be important in the evolution of reduced \( X-Y \) recombination. Nonetheless, one must ask whether or not such sexually antagonistic genes can be expected to occur in nature.

Sexually Antagonistic Alleles in Nature

The empirical studies pertaining to genes with sex-specific fitness effects have been reviewed by Bull (1983 Ch. 18). He concludes that, in the case of bright-coloration genes in poeciliid fishes, there is empirical support for the kind of sex-specific fitness presumed in the above model. Interestingly, as predicted by the model, 17 out of the 18 naturally occurring coloration genes in the guppy (Poecilia reticulata; \( 2n = 46 \)) are linked within ten centimorgans of the sex-determining locus, and all of these are dominant (Wingle, 1927). However, other well documented examples of genes with sex-specific fitness effects are uncommon in the literature (Bull, 1983).

Previously (Rice, 1984), I suggested that there "should be" natural circumstances that favor different phenotypic optima in the two sexes and that this will make the occurrence of sexually antagonistic genes inevitable. As an example, consider energy allocation in a hypothetical annual plant that has recently evolved dioecy. Suppose a particular gene increased flower production by substantially draining the energy reserves needed for later growth. Such a gene may be selectively favored in males, since growth and survival subsequent to flowering are of no consequence, but this gene would
virtually eliminate female reproductive success, since females must provision their fertilized embryos after flowering.

Is there empirical evidence for large sex-specific differences in the fitness effects of specific genes? In a survey of the hundreds of known mutants of *D. melanogaster*, Lindsley and Grell (1968) showed that genes with major fitness differences between the sexes are common. Most of these mutants produce the same, or similar, gross phenotype in both sexes (e.g., eye color, wing shape, bristle shape, etc.) but produce sterility or near sterility in only one of the sexes.

As an example of how genes highly detrimental to the homogametic sex might be selectively favored in the heterogametic sex, suppose environmental change produced selection for reduced body size in a population of *D. melanogaster*. One of the many mutants known to produce smaller body size is the gene ty(tiny). Viability of *ty ty* genotypes is high in both sexes, but females are sterile while males are fertile. If a gene such as *ty* were present in an ancestral population of *Drosophila* that had genic sex determination, and if it were located within hS/(1 − hS) centimorgans of a y gene, it would be expected to increase in frequency and thereby depress the viability of females (the homogametic sex in *Drosophila*) due to crossover between primitive X and Y chromosomes. Note that, in this case, selection for small body size is presumed to occur in both sexes. The sexual antagonism results from sex-specific pleiotropy and not from different optima in the two sexes.

Is the *ty* gene atypical? To answer this question, I surveyed all of the recorded *D. melanogaster* mutants known to produce small body size (i.e., those listed in Lindsley and Grell [1968 pp. 433–471]). I found a total of 66 genes that reduced body size. Of these, 22 (33%) produced sterility (or lethality-semilethality) in one but not both sexes. One might reasonably argue that many of these genes pleiotropically produce other detrimental effects (and thus drastically reduce fitness) and do not represent a sample of the genes that might reasonably be expected to be acted upon by natural selection.

To partially eliminate this problem, I removed from the tally of 66 small-body genes all of those that were reported to reduce viability and/or fertility or that produced major deformities in the sex not rendered sterile. Of the 20 remaining small-body genes, eight (40%) produced sex-specific sterility (or lethality-semilethality) in one but not both sexes. One might reasonably argue that many of these genes pleiotropically produce other detrimental effects (and thus drastically reduce fitness) and do not represent a sample of the genes that might reasonably be expected to be acted upon by natural selection.

To partially eliminate this problem, I removed from the tally of 66 small-body genes all of those that were reported to reduce viability and/or fertility or that produced major deformities in the sex not rendered sterile. If a gene such as *ty* were present in an ancestral population of *Drosophila* that had genic sex determination, and if it were located within hS/(1 − hS) centimorgans of a y gene, it would be expected to increase in frequency and thereby depress the viability of females (the homogametic sex in *Drosophila*) due to crossover between primitive X and Y chromosomes. Note that, in this case, selection for small body size is presumed to occur in both sexes. The sexual antagonism results from sex-specific pleiotropy and not from different optima in the two sexes.

Is the *ty* gene atypical? To answer this question, I surveyed all of the recorded *D. melanogaster* mutants known to produce small body size (i.e., those listed in Lindsley and Grell [1968 pp. 433–471]). I found a total of 66 genes that reduced body size. Of these, 22 (33%) produced sterility (or lethality-semilethality) in one but not both sexes. One might reasonably argue that many of these genes pleiotropically produce other detrimental effects (and thus drastically reduce fitness) and do not represent a sample of the genes that might reasonably be expected to be acted upon by natural selection.

To partially eliminate this problem, I removed from the tally of 66 small-body genes all of those that were reported to reduce viability and/or fertility or that produced major deformities in the sex not rendered sterile. Of the 20 remaining small-body genes, eight (40%) produced sex-specific sterility (or lethality-semilethality) in one but not both sexes. One might reasonably argue that many of these genes pleiotropically produce other detrimental effects (and thus drastically reduce fitness) and do not represent a sample of the genes that might reasonably be expected to be acted upon by natural selection.

To partially eliminate this problem, I removed from the tally of 66 small-body genes all of those that were reported to reduce viability and/or fertility or that produced major deformities in the sex not rendered sterile. Of the 20 remaining small-body genes, eight (40%) produced sex-specific sterility (or lethality-semilethality) in one but not both sexes. One might reasonably argue that many of these genes pleiotropically produce other detrimental effects (and thus drastically reduce fitness) and do not represent a sample of the genes that might reasonably be expected to be acted upon by natural selection.
vening segments of the chromosome, and a genetic chain reaction would be initiated, which should continue until the X and Y sex chromosomes fail to recombine over their entire lengths or until there is a sequence of sufficient recombinational length that fails to provide genetic variation for sexually antagonistic traits.

Conclusions

The model presented here supports the hypothesis, originally articulated by Bull (1983 Ch. 18), that the accumulation of genes with opposing fitness effects in the two sexes may be responsible for the breakdown in recombination between primitive sex chromosomes. The major finding from the model is that the requisite linkage between a sexually antagonistic locus and the sex-determining locus can be surprisingly loose for the accumulation of genes that are highly detrimental to the homogametic sex. It is also suggested that sex-specific pleiotropy may be an important genetic mechanism that is responsible for the opposing fitness effects of sexually antagonistic genes.

Acknowledgments

I thank K. Ono, L. Brooks, and J. Bull for many helpful comments on an earlier draft of this manuscript. This work was supported in part by grant BSR 8407440 from the National Science Foundation.

Literature Cited


Corresponding Editor: M. K. Uyenoyama

EGG VOLUME AND ENERGETIC CONTENT ARE NOT CORRELATED AMONG SIBLING OFFSPRING OF STARFISH: IMPLICATIONS FOR LIFE-HISTORY THEORY

Larry R. McEdward and Louise K. Coulter

Department of Zoology, University of Alberta, Edmonton, AB T6G 2E9, Canada, and Friday Harbor Laboratories, Friday Harbor, WA 98250

Received November 12, 1986. Accepted February 17, 1987

Egg size occupies a central position in the study of the ecology and evolution of marine invertebrate life histories. Egg dimensions are easily measured and frequently reported, and they show striking correlations with other life-history characters. Thorson (1936, 1946, 1950) compiled information from several marine phyla showing that egg size was correlated with fecundity, larval type (feeding or nonfeeding), larval habitat (plankton or benthos), and the duration of the larval period. Recent reviews have provided further support for these trends (see Hadfield, 1975; Hendler, 1975; Rice, 1975; Chia, 1976; Hermans, 1979; Reaka, 1979; Sastry, 1979; Hadfield and Switzer-Dunlap, 1984; Emlet et al., 1987).

Several quantitative models describing the effects of natural selection on egg size, given some reasonable assumptions about the reproductive and developmental correlates of differing parental investment per offspring, have been published (Vance, 1973a, 1973b;