Evolutionary dynamics of sex determination
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Sexually antagonistic genes and the evolution of sex determining mechanisms

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Abstract

Sexually antagonistic (SA) alleles, beneficial to one sex but detrimental to the other, seem to be common in species in which there were looked for. Theory, supported by experimental data, predicts that SA variation is especially prone to accumulate on sex chromosomes. Accumulation of SA alleles close to sex determining (SD) genes may in turn facilitate reduced recombination and eventually differentiation between sex chromosomes. Although sex determining systems strongly influence the pattern of SA variation little theoretical work has been done on how SA variation can influence the evolution of sex determination. Here, we present a model to investigate the conditions under which new SD factors can spread in response to accumulation of SA variation on the original sex chromosomes. We start with a XY system and let the sex chromosomes accumulate SA variation, and then introduce new male- or female-determining genes to see if they can spread in the population. We investigate the effect of sex chromosome differentiation, dominance effect of different SA alleles and linkage of new SD factors with SA loci on the outcome of the evolutionary dynamics. Our results show that for the system with undifferentiated sex chromosomes (both X and Y chromosome posses homologous SA locus) a new male-determining factor never has a fitness advantage. A new female-determining factor can spread only if it can accumulate SA variation and female-beneficial alleles are dominant or SA alleles show sex-specific dominance. If sex chromosomes are differentiated and only X possesses an SA locus, the conditions under which new SD factors can spread are much less restrictive and new SD factors can spread even if they are not linked with SA alleles, although linkage facilitates their spread. After their initial spread new SD alleles can reach fixation leading to a switch to a new male or female heterogametic SD system. In some cases a new SD factor does not spread to fixation, but a SD system polymorphic on multiple loci is maintained.
Introduction

It is becoming broadly accepted that conflict has a strong impact on male and female co-evolution (Partridge & Hurst 1998; Chapman et al. 2003; Arnqvist & Rowe 2005). The two sexes have different roles in reproduction, rooted in anisogamy (Chapman et al. 2003). Simplifying, males often increase their fitness by mating with as many females as possible, but females are limited in their reproductive fitness by the number of eggs they lay and usually prefer much fewer matings, since matings may decrease their fitness (for example, due to increased predation rate). Therefore, adaptations increasing the fitness of one sex may lead to a decrease in fitness in the other sex, thus causing sexual conflict. This process has been extensively studied, both theoretically and empirically, although many issues still remain unresolved (Rice 1996b; Cordero & Eberhard 2003; Arnqvist & Rowe 2005).

Many male- and female-beneficial adaptations are located on different loci which results in so-called intragenomic (Rice & Chippindale 2001) or interlocus (Chapman et al. 2003) conflict. However, sexual conflict can be present even at a single locus (intralocus conflict; Chapman et al. 2003; or intersexual ontogenetic conflict; Rice & Chippindale 2001). For example if males have a higher optimal weight than females, alleles increasing weight will be beneficial for males, but detrimental for females, and the other way round for alleles decreasing weight. Alleles whose fitness effects in one sex are negatively related to their fitness effects in the other sex are called sexually antagonistic (SA) alleles (Rice 1992). Sexual antagonism may result not only from sex-specific optima, but also from sex-specific pleiotropy (Rice 1987).

There is increasing experimental evidence that SA genes are common in genomes of a number of species (Forsman 1995; Vieira et al. 2000; Chippindale et al. 2001; Rice & Chippindale 2001; Gibson et al. 2002; Fedorka & Mousseau 2004; Kozielska et al. 2004). Theory predicts that SA genes will be especially prone to accumulate on sex chromosomes. Autosomes are present equally in both sexes and therefore autosomal SA genes can increase and then fixate only if the advantage to one sex overcompensate the disadvantage to the other sex (Rice 1984). In contrast, the segregation of sex chromosomes is biased towards one sex (males for Y chromosome and females for X) facilitating the accumulation of SA genes (Rice 1984, 1987). For example, a recessive male-beneficial SA allele on the X chromosome will spread when rare, since it is expressed in hemizygous males, but not in females (where it initially only occurs in heterozygous state). With the increase in frequency of SA alleles, homozygous females will be produced preventing the allele from fixating and polymorphism will be maintained. A similar rationale applies to a dominant female-beneficial allele, since it will be initially present (and expressed) two times as often in females as in males, leading to its spread when rare (for details see Rice 1984). These theoretical results are supported by the profound sexually antagonistic variation present on the Drosophila X chromosome (Gibson et al. 2002).
Additionally, a chromosome restricted only to one sex (Y in XY system and W in ZW system) is expected to accumulate SA alleles beneficial to the sex they are present in, even if they are potentially detrimental if expressed in the other sex (e.g. Rice 1996a). This has been confirmed by artificial selection in *Drosophila*, where autosomes were artificially made to segregate in one sex. After a number of generations this sex had higher fitness than controls, but when the autosomes were expressed in the other sex, it resulted in lower fitness (Rice 1992, 1998).

Sex chromosomes not only facilitate the accumulation of SA genes, but their evolution is believed to be strongly influenced by the SA genes themselves. Suppression of recombination is expected to evolve between the sex determining factor and SA genes with alleles beneficial to the heterozygous sex, leading to a gradual increase of Y-(or W-) specific regions and eventually degradation of this chromosome (Charlesworth 1991; Rice 1996a; Charlesworth *et al.* 2005).

Sex determining mechanisms strongly influence the pattern of SA variation that can accumulate, but can SA variation also lead to changes in the sex determining system? Although this idea was already put forward two decades ago (Rice 1986), only very few studies have so far investigated it (Rice 1986; van Doorn & Kirkpatrick 2007). Rice (1986) showed that linkage with a SA locus may lead to the spread of a new sex determining factor and a switch from polygenic sex determination to a one-locus SD system. Van Doorn and Kirkpatrick (2007) showed that SA variation on autosomes can facilitate the spread of a new (autosomal) sex determining factor, leading to a change from an XY system to an autosomal system. Both of these studies focused on the scenario in which a new SD factor was linked to a SA locus. They also allowed for only one SA allele per locus.

We take a different approach and concentrate on the case where a new SD factor is not linked with fitness affecting genes. We start with an XY system and let the sex chromosomes accumulate SA variation introduced by mutation. Then we introduce a new autosomal male or female sex determining factor and investigate whether it can spread in the population. For completeness, we also investigate how linkage with a SA locus influences the chance for a new SD factor to spread.

Since it is known that the dominance of SA alleles strongly influences their chance to spread (Rice 1984), we also investigate the effect of dominance of SA alleles on the outcome of the evolutionary dynamics of the SD system. Additionally, we study the effect of sex chromosome differentiation on the dynamics of the system. We consider undifferentiated chromosomes with a SA locus present on both X and Y (Rice 1987; van Doorn & Kirkpatrick 2007), and differentiated chromosomes with a SA locus present only on the X chromosome (Rice 1984; Charlesworth *et al.* 1987).
The model

**Sex determination**: Since the number of different sex determining (SD) mechanisms seems limitless (Bull 1983), we decided to base our model on a relatively generic sex determining (SD) mode. We consider a sex determining system consisting of three independent gene loci (on three different chromosomes), each locus having two alleles. The first locus corresponds to the standard XY sex determining system with two basic alleles: a male-determining Y allele and a sex-neutral X allele. We will refer to the chromosomes possessing these alleles as the X and the Y chromosome, respectively, or together as sex chromosomes. The second locus harbours a male-determining M allele and a standard m allele. The third locus has a female-determining F allele and a standard f allele. The F allele is dominant over M, meaning that the presence of F always leads to female development, even if both Y and M are present in homozygous state. If F is absent, but at least one male-determining factor, either Y or M, is present in the genotype, individuals become males, otherwise (no Y or M) they become females. We arbitrary start with the XY system, as most of the studies on SA variation have been done in species with male heterogamety (Rice & Chippindale 2001; Fedorka & Mousseau 2004). The results of the model will also apply to the ZW systems, assuming that SD factors have opposite effect on sexual differentiation.

**Sexually antagonistic (SA) genes**: On each chromosome there is also a tightly linked locus that can potentially accumulate sexually antagonistic alleles. We will assume that there is no recombination between the SA gene and the sex determining locus on a given chromosome. For simplicity, we also assume that SA genes directly affect viability and that the positive effect on male viability is equal to the negative effect on female viability. We assume that the value of an allele corresponds to viability in males, meaning that if an allele is expressed in males their fitness is equal to the value of the allele. If an allele is expressed in females, their fitness equals one minus the value of the alleles.

We consider four different dominance scenarios for SA alleles (Table 5.1). a) There is no dominance and viability is dependent on the average of the allele values. b) Male-favouring alleles are dominant, meaning that the allele with the higher value is expressed. c) Female-favouring alleles are dominant, meaning that the allele with the lower value is expressed; d) There is a sex specific dominance, meaning that the allele conferring the higher fitness for a given sex is expressed. This scenario may be interpreted as sex specific expression or sex specific pleiotropy, for example, the situation where the SA alleles interact with both male- and female-specific hormones and a better interaction with male-specific hormones in males results in a worse interaction with female-specific hormones in females. Table 5.1 shows some examples of the fitness of males and females with different genotypes under different dominance scenarios.
In our model SA alleles can take any value between zero (maximizing female viability) and one (maximizing male viability). At the beginning of the simulation SA genes start at the value of 0.5 (the same fitness in males and females) and every generation with the chance of 0.01 an allele at each locus can mutate. Mutation adds a value from a normal distribution with mean zero and standard deviation 0.005 to the value of the allele. Genes located on different chromosomes act multiplicatively.

**X and Y chromosome differentiation:** We look at two scenarios for the differentiation between sex chromosomes and the location of SA genes on X and Y chromosomes. First, we assume that there is little differentiation between X and Y and that the SA locus is common for both chromosomes. Accordingly, both males and females are diploid at the SA loci (Rice 1987; van Doorn & Kirkpatrick 2007). Second, we assume strong differentiation between the sex chromosomes, i.e. the Y is degenerated and does not possess SA genes or it is even absent. Therefore, SA genes are located only on the X chromosome (Rice 1984; Charlesworth *et al.* 1987). XX individuals have two alleles and their fitness depends on the dominance scenario (Table 5.1), and XY individuals are hemizygous and the SA allele is always expressed.

**Simulation:** We use individual-based simulations to model the evolution of the sex determining system. We assume discrete non-overlapping generations and a fixed population size of \( N = 10,000 \) diploid individuals. We started each simulation with the standard XY system (all females are \( XX; \, mm; \, ff \) and all males: \( XY; \, mm; \, ff \)). SA genes located on each chromosome started with the value of 0.5. \( N \) new individuals were generated each generation using the following algorithm: first we assign one random male to each female in the population and then draw with replacement a female; given her genotype and a genotype of her pre-assigned partner create an offspring genotype by drawing random chromosomes from both parents; let the SA

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**Table 5.1. Illustration of the sex-dependent viability effects of different genotypes under four dominance scenarios.** For a given genotype male and female viabilities are shown. Here we assume that the values of sexually antagonistic alleles are \( x_1=0.9 \) and \( x_2=0.3 \). Alleles are encoded by the viability effect they have in males homozygous for this allele. The viability of homozygous females equals one minus the allele values. The viability of heterozygous individuals depends on the dominance scenario for the SA gene (see the model section for details).

<table>
<thead>
<tr>
<th>Dominance scenario</th>
<th>( x_1x_1 )</th>
<th>( x_1x_2 )</th>
<th>( x_2x_2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. No dominance (additivity)</td>
<td>0.9</td>
<td>0.6</td>
<td>0.3</td>
</tr>
<tr>
<td>2. Male-beneficial alleles dominant</td>
<td>0.9</td>
<td>0.9</td>
<td>0.3</td>
</tr>
<tr>
<td>3. Female-beneficial alleles dominant</td>
<td>0.9</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>4. Sex specific dominance</td>
<td>0.9</td>
<td>0.9</td>
<td>0.3</td>
</tr>
</tbody>
</table>

In our model SA alleles can take any value between zero (maximizing female viability) and one (maximizing male viability). At the beginning of the simulation SA genes start at the value of 0.5 (the same fitness in males and females) and every generation with the chance of 0.01 an allele at each locus can mutate. Mutation adds a value from a normal distribution with mean zero and standard deviation 0.005 to the value of the allele. Genes located on different chromosomes act multiplicatively.
genes mutate (equivalent to mutations during gametogenesis; see above for details); then based on the offspring genotype on SA loci determine offspring viability; draw a random number between zero and one to decide whether an offspring actually survives; if it does not (random value above viability value) draw a new mother and start again, otherwise continue: determine the offspring’s sex based on its genotype on sex determining loci; add the offspring to the next generation; repeat until N new individuals have been created. Simulations are run for sufficiently many generations until equilibrium values of the SA genes appear to have been reached. At this point an M allele is introduced in males at the frequency of 0.05. Simulations are run until a new equilibrium is reached and then F is introduced in females at the frequency of 0.05. Simulations are run till a new equilibrium is reached. We also examine an alternative scenario in which F is introduced before M.

For each of the scenarios we look first at the situation where SA genes can evolve only on sex chromosomes, but not on any of the autosomes. We investigate whether autosomal SD factors can invade the system and what the resulting SD mechanism is. Additionally, we compare these results with the situations in which SA genes can evolve on one or both autosomes. For each case we investigate the effect of dominance of SA alleles and the order of introducing new SD factors (see above) on the dynamics of the system. For each set of parameters we run 25 duplicate simulations.

**Results**

We analyze the effect of sex chromosome differentiation, mode of dominance of SA alleles and linkage of new SD factors with SA alleles on the resulting SD system. We categorize the outcomes into five main categories. 1) A new SD factor has a selective disadvantage, does not invade and there is no change in the SD system. 2) A new SD factor always invades, leading to a change in the SD system. For M this means that it replaces Y (Fig. 5.1A) and for F that its frequency in females reaches 0.5 and the SD system switches to female heterogamety (Fig 5.1B). 3) A new SD factor invades in some simulation runs leading to a change in the SD system, but it disappears for others. This suggests a new factor has only a low fitness advantage and it can be lost by drift. 4) A new SD factor appears to be selectively neutral and its frequency seems to be governed by random drift. It can persist in the population for many generations with strong fluctuations in frequency, which may eventually lead to its loss or fixation (Fig 5.1C). In this case the frequency of the factor is highly variable between different simulation runs. 5) A new SD factor invades the population and does not reach fixation, but some intermediate stable frequency. Stable polymorphism is maintained (Fig 5.1D).

A summary of the results for different conditions is given in Table 5.2 and 5.3. In short, switches to new SD systems are easier if SA variation accumulates only on X (differentiated sex chromosomes) and if new SD genes are linked to SA loci.
Below we present some more details on the dynamics of the system for different scenarios. We concentrate on the case in which new SD factors are not linked with a SA locus and only briefly mention other scenarios. We often attempt to explain the observed evolutionary patterns, however, it should be noted that it is often speculative and more detailed analysis is needed to more reliably explain the observed patterns.

Figure 5.1. Examples of different SD systems evolved after the introduction of new SD factors to a standard XY system. (A) After introduction (generation 10000) M invades the population replacing Y; the SD system switches from male heterogamety for Y to male heterogamety for M. (B) F invades, leading to a switch to female heterogamety and fixation of Y. (C) F is neutral when introduced (generation 15000) to the system with male heterogamety for M (M introduced in generation 15000 replaced Y). F frequency fluctuates over time and it may be eventually lost or fixate; SD system is in a neutral polymorphism. (D) Protected polymorphism-F invades the system with male heterogamety for M (M introduced in generation 15000 replaces Y), but it does not reach fixation. The system polymorphic for F and M is stable. Results on all panels were obtained with the scenario for differentiated sex chromosomes. The other parameters were as follows: panels A and C – additivity of SA alleles, SA variation only on X chromosome; B – dominance of male-beneficial alleles, SA variation only on X chromosome; D – sex-specific dominance, SA variation on each chromosome.

Below we present some more details on the dynamics of the system for different scenarios. We concentrate on the case in which new SD factors are not linked with a SA locus and only briefly mention other scenarios. We often attempt to explain the observed evolutionary patterns, however, it should be noted that it is often speculative and more detailed analysis is needed to more reliably explain the observed patterns.
1. Undifferentiated sex chromosomes: SA genes on a homologous locus on both X and Y chromosome. The results for the different dominance scenarios are given in the rows, both for the case when M was introduced before F (M, F) and the other way around (F, M). In the columns the scenarios for presence of SA genes on different chromosomes are given, as indicated in the upper row: XY – on sex chromosomes; M – on autosome with M/m locus; F – on autosome with F/f locus. For each scenario fate of M and F sex determining factors are given in separate cells and is indicated by different colours: white – a new sex determining factor is selected against; dark grey and white stripes – a new factor invades in less than 50% of cases leading to a switch to a new SD system; light grey – a new factor invades, but there is no full switch to a new system: N – a new factor seems to be neutral, and its frequency is governed by drift; P – protected polymorphism – a new factor reaches a stable frequency. See text and Fig 5.1 for details.

Table 5.2. Summary of the results for undifferentiated sex chromosomes (SA locus present both on X and Y chromosome, at homologous locus). The results for the different dominance scenarios are given in the rows, both for the case when M was introduced before F (M, F) and the other way around (F, M). In the columns the scenarios for presence of SA genes on different chromosomes are given, as indicated in the upper row: XY – on sex chromosomes; M – on autosome with M/m locus; F – on autosome with F/f locus. For each scenario fate of M and F sex determining factors are given in separate cells and is indicated by different colours: white – a new sex determining factor is selected against; dark grey and white stripes – a new factor invades in less than 50% of cases leading to a switch to a new SD system; light grey – a new factor invades, but there is no full switch to a new system: N – a new factor seems to be neutral, and its frequency is governed by drift; P – protected polymorphism – a new factor reaches a stable frequency. See text and Fig 5.1 for details.

<table>
<thead>
<tr>
<th>Dominance scenario</th>
<th>Order of introduction</th>
<th>XY</th>
<th>XY,M</th>
<th>XY,F</th>
<th>XY,M,F</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. No dominance (additivity)</td>
<td>M,F</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>F,M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Male-beneficial alleles dominant</td>
<td>M,F</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>F,M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Female-beneficial alleles dominant</td>
<td>M,F</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>F,M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Sex specific dominance</td>
<td>M,F</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>F,M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 5.3. Summary of the results for differentiated sex chromosomes (SA genes are present only on the X chromosome). The setup and the meaning of the colours is identical to table 5.2 with additional dark grey – a new factor always invades leading to the switch to a new SD system.

<table>
<thead>
<tr>
<th>Dominance scenario</th>
<th>Order of introduction</th>
<th>X</th>
<th>X,M</th>
<th>X,F</th>
<th>X,M,F</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. No dominance (additivity)</td>
<td>M,F</td>
<td></td>
<td>N</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>F,M</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Male-beneficial alleles dominant</td>
<td>M,F</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>F,M</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Female-beneficial alleles dominant</td>
<td>M,F</td>
<td>N</td>
<td>N</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>F,M</td>
<td>N</td>
<td></td>
<td>N</td>
<td></td>
</tr>
<tr>
<td>4. Sex specific dominance</td>
<td>M,F</td>
<td>N</td>
<td></td>
<td></td>
<td>P</td>
</tr>
<tr>
<td></td>
<td>F,M</td>
<td></td>
<td></td>
<td>N</td>
<td></td>
</tr>
</tbody>
</table>
and the sex ratio in the population is female biased. However, the masculinizing factor $M$ cannot invade since it would lead to the creation of XX males which have very low viability. $F$ does not invade either, since it would initially lead to an even more female biased sex ratio and the production of low viability XY females.

**b) Dominance of male-beneficial alleles:** As above alleles on $Y$ increase to one and alleles on $X$ decrease to zero. However, since male-favouring alleles are dominant, males and females both have maximal fitness and the sex ratio is equal to 0.5. New sex determining factors do not invade, since they would lead to suboptimal, in terms of fitness, genotypes (as above).

c) **Dominance of female-beneficial alleles:** The value of SA alleles on $Y$ increases to one, but there is great variation of SA alleles on $X$ ranging roughly from 0.2 to 1.0, with an average higher than 0.5 (favourable for males) in both sexes (Fig 5.2). The resulting sex ratio equals 0.5. $F$ invades the system only if it is linked with the SA locus which possesses SA variation allowing $F$ to be linked with genes beneficial for females. Eventually, alleles linked with $F$ evolve towards a value of zero. The frequency of $F$ increases to 0.5 in females, but since $Y$ possesses alleles detrimental for females it does not fixate and polymorphism for the $X$ and $Y$ chromosomes is maintained (Fig 5.2). The population sex ratio is equal to 0.5. $M$ never has a fitness advantage, but can be neutral if $F$ is present in the population.

d) **Sex specific dominance of SA alleles:** In this scenario the allele beneficial for a given sex is expressed. SA alleles on $X$ evolve towards zero and the alleles on $Y$ towards values of one, leading to maximal viability in both sexes and a 1:1 sex ratio. Since $Y$ strongly increases male fitness $M$ can never replace it. $F$ invades if it is linked with a SA locus, but a full switch to female heterogamety and fixation of $Y$ chromosome is impossible since it has accumulated alleles detrimental to females. As a result a polymorphic system for both $X$ and $Y$, and $F$ and $f$ is stable (Fig 5.3).

2. **Differentiated sex chromosomes:** Under this scenario SA alleles are present only on the $X$ chromosome. Table 5.3 shows a summary of the results.

a) **Additivity of SA alleles:** As predicted by theory (Rice 1984) not much SA variation accumulates on the $X$ chromosome and the average value of SA alleles in both males and females and the population sex ratio equals 0.5. $M$ can invade the system and can replace $Y$ (fig 5.1A), but positive selection for $M$ seems to be weak. This may be caused by the fact that the presence of $M$ decreases variation in male fitness. Invasion is facilitated by linkage of SA genes with $M$. Then $M$ replaces $Y$ and accumulates SA alleles favourable for males and $m$ accumulates SA alleles favourable for females. The sex ratio becomes female biased. If $F$ is introduced after $M$, it is favoured if it is linked with the SA locus, but $M$ is not. If $F$ is introduced first it can spread even without linkage with SA genes. When $F$ invades, the SD system switches to female heterogamety, with either $M$ or $Y$ fixating in the population (depending on which one was already present).

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Figure 5.2. Dynamics of the SD system and alleles on SA loci for the scenario with undifferentiated sex chromosomes and female-beneficial alleles dominant. The panels on the left concern males and those on the right females. (A) and (B): distribution of SA alleles on sex chromosomes. The higher the frequency of the allele with a given value the darker the point. In males the SA alleles located on the Y chromosome have the highest value. (C) and (D): distribution of SA alleles on locus linked with $F/f$ locus. (E) and (F). Sex ratio, frequency of different SD factors and average value of SA alleles in males and females, respectively. SA-Y denotes SA alleles linked with Y, etc. Initially a standard XY system is present, $F$ is introduced at generation 20000 and spreads leading to a female heterogametic system with polymorphism for X and Y chromosome. Polymorphism on the X linked SA locus decreases and the average allele value is almost zero. The value of the SA alleles linked with $F$ decreases to zero and the value of SA alleles linked with $f$ increases to 1.
b) Dominance of male-beneficial alleles: As expected (Rice 1984) there is very little variation of the SA locus on the X chromosome. M always invades since homozygosity for X in males increases their fitness, due to the higher chance of the expression of more favourable alleles, especially since in XY system average the value of SA alleles evolves towards a female optimum. For that reason F can also invade if it is introduced in the system without M, since hemizygous XY females will have higher fitness than XX females in which there is a higher chance that male-beneficial alleles will be expressed.

c) Dominance of female-beneficial alleles: The X chromosome accumulates SA variation (similar to situation in 1c; Fig 5.2A and 5.2B), since both dominant female-beneficial alleles as well as recessive male-beneficial ones can spread (Rice 1984). M never invades since homozygosity for X in males is not beneficial due to the increased chance that female-beneficial alleles will be expressed. F can invade only if

![Figure 5.3. Dynamics of the SD system and average value of SA loci for the scenario with undifferentiated sex chromosomes and sex-specific dominance of SA alleles. Shown are sex ratio, frequency of different SD factors and average value of SA alleles in males (A) and females (B). Initially a standard XY system is present, the SA alleles located on the X chromosome decrease in value to zero and the alleles located on Y increase to one. F is introduced at generation 20000 and increases in frequency, but does not spread to fixation. A system polymorphic for two SA loci is maintained: X and Y, and F and f.](image-url)
it can accumulate SA alleles, leading to a switch to female heterogamety and fixation of Y. F accumulates female-beneficial and f - male-beneficial alleles.

d) **Sex specific dominance of SA alleles:** As above the X chromosome accumulates SA variation. However, now M always invades if it is introduced first, since homozygous XX males (out of two alleles the more beneficial one is expressed) have higher fitness than XY males (also female-beneficial, male-harmful alleles are expressed). F is favoured only if it can accumulate female-beneficial alleles. However, it does not fixate if M has already accumulated male-beneficial alleles. In that case polymorphism on both the M/m and F/f locus is maintained (Fig. 5.1D).

**Discussion**

We showed that sexually antagonistic variation on sex chromosomes may facilitate the spread of new sex determining factors and the switch to a new sex determining system, even if new SD factors are not linked with SA genes. However, this is only the case if sex chromosomes are differentiated and SA genes located only on the X chromosome. In most cases the presence of SA alleles on autosomes in close linkage to a new SD factor facilitates the switch to a new SD system.

Previously, Van Doorn & Kirkpatrick (2007) made an analytical model to investigate how SA variation on sex chromosomes and autosomes influences the invasion of a new autosomal male-determining factor. Their model corresponds to our scenario with undifferentiated sex chromosomes and invasion of M, although they considered only one SA allele at each locus. They showed that, all else being equal, SA variation on autosomes facilitates, but SA variation on sex chromosomes hampers the spread of a new SD factor. This is consistent with our results, where sex chromosomes accumulate SA variation, but variation on autosomes is absent or low, and the M factor does not invade. However, when sex chromosomes are differentiated and SA genes located only on X, conditions for invasion of new autosomal SD genes are much less restrictive, although still presence of SA variation on autosomes helps new SD factors with establishing in the population. We do not expect much variation of SA genes on autosomes, since alleles having a net advantage averaged over both sexes should spread to fixation (Rice 1984). However, some SA variation can be maintained by mutation (as we saw in our simulations), migration, frequency-dependent selection or be transient during the process of fixation of new alleles (Rice & Chippindale 2001; van Doorn & Kirkpatrick 2007).

It has to be noted that in our model we assumed that the lack of either an X or Y chromosome does not have any negative fitness effects (except for the ones potentially caused by SA alleles). This may be true when sex chromosomes are not yet strongly differentiated. However, differentiation of sex chromosomes may on the one hand lead to degeneration of the Y chromosome and the presence of vital genes only on the X chromosome (Charlesworth 1996), or on the other hand, genes necessary
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for male fertility may accumulate on the Y chromosome (Roldan & Gomendio 1999). Differentiation of sex chromosomes may also lead to the evolution of dosage compensation (Charlesworth 1996) and result in the unviability of individuals with novel genotypes (Schütt & Nöthiger 2000). All of these processes may lead to lethality of YY individuals or sterility of XX males and hamper the change of the sex determining system. Therefore, some differentiation of sex chromosomes facilitates changes in SD systems (compare Tables 5.2 and 5.3), but stronger differentiation may in turn prevent them. However, there are species that have morphologically differentiated chromosomes, but the fitness of males and females with unusual genotypes is not lower (Bull 1983; Dübendorfer et al. 2002) and SD systems in those species might be especially prone to changes. One could even expect cycles of co-evolution between SA genes and sex chromosomes: the chromosome with the SD factor accumulates SA alleles, which favours reduced recombination and differentiation of sex chromosomes (Rice 1996a; Charlesworth et al. 2005). This facilitates the accumulation of SA variation on the X chromosome (Rice 1984), which in turn may lead to the invasion of a new SD factor and the beginning of a new cycle of sex chromosome evolution.

We showed that the mode of expression of SA genes has a profound effect on the fate of new SD factors (Table 5.2 and 5.3). When both the X and Y chromosome possess an SA locus, the condition promoting the highest variation (dominance of female-beneficial alleles) allows the invasion of new SD factors (although only if they are also linked with the SA locus; Table 5.2). The opposite effect is seen in cases where only the X chromosome possesses an SA locus, under dominance of female-beneficial alleles, conditions for the invasion of new SD factors are more restrictive than for other modes of allele dominance (Table 5.3).

Not much is known about the expression of SA genes in nature, but it seems that some of them are at least partly dominant, since their effect can be detected in heterozygous females (Gibson et al. 2002). There is no a priori reason to assume that all genes show the same pattern of dominance. It is often believed that new deleterious mutations are recessive, but some of them may be also at least partly dominant (Oliver & Parisi 2004). However, SA alleles by definition are deleterious for one sex, and we can imagine that both male- and female- beneficial mutations can be dominant. SA variation seems to be most easily maintained if female-beneficial alleles are dominant and male-beneficial alleles are recessive (Rice 1984). However, polymorphism at SA loci should also be present if alleles have different patterns of dominance, either only transiently during the process of replacement of one SA allele by another (Rice & Chippindale 2001) or when maintained by migration and mutation (van Doorn & Kirkpatrick 2007). Little is known about the patterns of dominance of SA alleles and more empirical research is necessary to estimate what is (if any) the most common pattern for SA genes dominance.