# ON THE EVOLUTIONARY GENETIC STABILITY OF AN EVEN SEX RATIO IN TWO LOCUS, AUTOSOMAL SYSTEMS OF SEX DETERMINATION

by

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Abstract

It is shown that in a two locus dyploid system of autosomal sex determination, like in one locus systems, the even sex ratio is the only one with the property of (long term) Evolutionary Genetic Stability (E.G.S.). This in contrast to models of internal two locus stability, that are likely to lead to different sex ratios.

suggested by Eshel and Feldman (1982 a). Following Hamilton's concept of an Unbeatable Strategy (Hamilton 1967) and Maynard Smith and Price's (1973) concept of an Evolutionarily Stable Strategy (E.S.S), it has been shown that, concerning a one locus autosomal control of the sex (either of the carrier or of his offspring), the 1:1 sex ratio is the only one with the property of Evolutionary Genetic Stability (E.G.S.), namely: (i) A sex ratio of 1:1 is the only one that can be stable against new, autosomal mutation. (ii) Moreover, a new autosomal mutation, introduced into any internally stable equilibrium determining a sex-ratio different from 1:1 will increase in frequency if and only if it render the sex ratio closer to 1:1, at least initially (see for comparison Eshel and Feldman 1984 for E.G.S. of viability E.S.S.'s in general two locus systems, Eshel 1975 for E.G.S. of Mendelian segregation under control of non-linked modifiers, Weinshall and Eshel 1988 and Eshel and Weinshall 1988 for E.G.S. of the rate of sexual reproduction). It was further proved by Karlin and Lessard (1983, 1984) that, moreover, a new mutation, once stabilized in the system, will determine a new stable equilibrium which is closer to 1:1.

In this case, however, when modifiers of the sex ratio are assumed to appear at one locus only the difference between the predictions of the two population dynamics (namely the relatively short-term dynamics of changes in genotype-frequencies and the rather long-term dynamics of allele-substitution due to introduction of ever new mutation) is not very drastic, at least on a qualitative level. This is not the case as we see when more than one locus is involved.

Analyzing the population dynamics of changes in genotype frequencies in several models involving two loci or more, Karlin and Lessard (1986) have concluded that, in this case, a sex ratio of 1:1 is most unlikely to be stably maintained by the system and, in fact, any sex ratio between 0 and 1 can be stable, depending on the parameters of the model. As usually is the case in multilocus systems, this finding stands in contrast to the intuitive game theory argument of maximization of grandoffspring number. As they have maintained: "This result contrast sharply to Theorem 3.5 for exact sex determination at one locus, where only an even sex-ratio equilibrium can be stable."

In this work I show that the situation is essentially different when one asks about the long-term evolution of the sex ratio, namely about the slower dynamics of ever introduction of random new mutation into internally stable genetic equilibria in two locus as well as in one locus systems.

## 2. Introduction of new alleles into a two locus sex-determination system

Consider an infinite size, two-sex dyploid population at which males and females mate at random. The sex of an individual is determined, at least probabilistically, by alleles $A_1, \ldots, A_n$ carried at one locus and alleles $B_1, \ldots, B_m$ carried at another locus. Thus, the probability that a genotype $A_iB_k/A_jB_l$ will be a male is $M_{ijkl}$ and we assume $0 \leq M_{ijkl} \leq 1$, $M_{ijkl} = M_{jikl} = M_{ijlk} = M_{jilk}$. This includes, as a special case, the situation where $M_{ijkl}$ are either 1 or 0 (full genetical sex determination, special subcase of which being treated by Karlin and Lessard (1986)). Another, important, special case is the XY system of sex determination with both sex linked $X^{(1)} \ldots X^{(n)}$ and autosomal modifiers $B_1, \ldots, B_m$ of sex determination, provided they only change the chance of an XX individual being a female (but not modifiers of sex-linked miotic drive, see for example Maffi and Jayaker 1981).

Denote by $X_{ik}$ and $Y_{ik}$ the relative frequencies of the chromosome $A_iB_k$ ($i=1, \ldots, n$; $k=1, \ldots, m$) passed to the offspring by adult males and females of the first generation respectively (after recombination). The relative frequency of the double homozygotes $A_iB_k/A_iB_k$ among all newborn offspring (males and females) is $X_{ik}Y_{ik}$ whereas the relative frequency of $A_iB_k/A_jB_l$ when $i \neq j$ or $k \neq l$ is $X_{ik}Y_{jl} + X_{jl}Y_{ik}$. Hence, the frequency of males in the population will be

$$M = \sum_{ijkl} X_{ik}Y_{jl}M_{ijkl}. \qquad (1)$$

The frequency of the double homozygote $A_iB_k/A_iB_k$ among newborn males will, therefore, be $(1/M)X_{ik}Y_{ik}M_{iikk}$ whereas this of the

heterozygote (at least at one locus) $A_iB_k/A_jB_l$ will be $(1/M)(X_{ik}Y_{jl} + X_{jl}Y_{ik})M_{ijkl}$. The relative frequency of the chromosome $A_iB_k$ among newborn males will, therefore, be

$$\tilde{X}_{ik} = \frac{1}{2M} \sum_{jl} (X_{ik}Y_{jl} + X_{jl}Y_{ik})M_{ijkl} .$$

Allowing for a rate $0 < r \leq \frac{1}{2}$ of recombination at the stage of meiosis, the relative frequency of $A_iB_k$ among chromosomes passed by males of the next generation to their offspring is readily shown to be:

$$X'_{ik} = \frac{1}{2M} \sum_{jl} [(1-r)(X_{ik}Y_{jl} + X_{jl}Y_{ik}) + r(X_{il}Y_{jk} + X_{jk}Y_{il})]M_{ijkl} . \qquad (2)$$

In the same way, the relative frequency of $A_iB_k$ among all chromosomes passed by females of the next generation is

$$Y'_{ik} = \frac{1}{2(1-M)} \sum_{jl} [(1-r)(X_{ik}Y_{jl} + X_{jl}Y_{ik}) + r(X_{il}Y_{jk} + X_{jk}Y_{il})](1-M_{ijkl}) . \qquad (3)$$

From (2) and (3) it immediately follows that

$$Y'_{ik} = \frac{1}{2(1-M)} \sum_{jl} [(1-r)(X_{ik}Y_{jl} + X_{jl}Y_{ik}) + r(X_{il}Y_{jk} + X_{jk}Y_{il})] - \frac{M}{1-M} X'_{ik} . \qquad (4)$$

Denote by

$X_i = \sum_{n=1}^{m} X_{ik}$ The frequency of $A_i$ among males (5a)

$$Y_i = \sum_{n=1}^{m} Y_{ik} \qquad \text{The frequency of } A_i \text{ among females} \qquad (5b)$$

$$U_k = \sum_{i=1}^{n} X_{ik} \qquad \text{The frequency of } B_k \text{ among males} \qquad (5c)$$

$$V_k = \sum_{i=1}^{n} Y_{ik} \qquad \text{The frequency of } B_k \text{ among females.} \qquad (5d)$$

(4) becomes:

$$2MX'_{ik} + 2(1-M)Y'_{ik} =$$

$$= (1-r)(X_{ik} + Y_{ik}) + r(X_iV_k + Y_iU_k) \cdot \qquad (6)$$

Inserting $X'_{ik} = X_{ik}$ ; $Y'_{ik} = Y_{ik}$ we get at (internal) equilibrium

$$(M - \tfrac{1}{2})(X_{ik} - Y_{ik}) = r(X_iV_k - X_{ik} + Y_iU_k - Y_{ik}) \qquad (7)$$

for all $i = 1, \ldots, n$; $k = 1, \ldots m$.

Note that $\sum_k X_{ik} = X_i = \sum_k X_iV_k$ and $\sum_k Y_{ik} = Y_i = \sum_k Y_iU_k$. Thus, summing (7) over $K$ we get

$$(M-\tfrac{1}{2})(X_i-Y_i) = 0 \qquad \text{for all } i=1, \ldots,n \cdot \qquad (8)$$

In the same way, summing over $i$ we get

$$(M-\tfrac{1}{2})(U_k-V_k) = 0 \qquad \text{for all } K=1, \ldots, m. \qquad (9)$$

Corollary

If, in a two locus (internal) equilibrium, the sex ratio is different from 1:1 (say $M \neq \frac{1}{2}$) then the allele-frequencies at each locus (but not necessarily the chromosome-frequencies) are equal in male and in females (for a comparison with one locus counterparts of this corollary see Eshel 1975, Uyenoyama and Bengtsson 1979, Eshel and Feldman 1982).

Assume now any equilibrium with a sex ratio different from 1:1 and let a new mutation, say $A_{n+1}$, enter the system at one of the two loci, so that the relative frequency of males among newborn individuals of the heterozygote mutant genotype $A_{n+1}B_k/A_jB_l$ is $M_{n+1,j,k,l}$.

Let the relative frequency of the mutant chromosome $A_{n+1}B_k$ among chromosomes passed by male to the next generation be $\epsilon_k \geq 0$, and let the relative frequency of $A_{n+1}B_k$ among female chromosomes passed to the next generation be $\delta_k \geq 0$ where $\epsilon_k$ and $\delta_k$ are small numbers, part of which being strictly positive. Denote

$$\epsilon_k = \epsilon \quad \text{and} \quad \delta_k = \delta \tag{10}$$

the relative frequency of males among newborn mutant individuals is:

$$M_{n+1} = \frac{1}{\varepsilon+\delta} \sum_{jkl} (\epsilon_k Y_{jl} + \delta_k X_{jl})$$

$$M_{n+1,j,k,l,} + O(\delta, \epsilon) . \qquad (11)$$

As a special case of (2) we get (ignoring terms of order) $o(\epsilon, \delta)$:

$$\epsilon_k' = \frac{1}{2M} \sum_{jl} [(1-r)(\epsilon_k Y_{jl} + \delta_k X_{jl}) +$$

$$+ r(\epsilon_l Y_{jk} + \delta_l X_{jk})] M_{n+1,j,k,l} . \qquad (12)$$

Summing over K, one readily gets

$$\epsilon' = \frac{1}{2M} \sum_{jkl} (\epsilon_k Y_{jl} + \delta_k X_{jl}) M_{n+1,j,k,l} . \qquad (13)$$

Thus from (11) and (13) it follows that

$$\epsilon' = \frac{\varepsilon+\delta}{2} \cdot \frac{M_{n+1}}{M} \qquad (14)$$

In the same way

$$\delta' = \frac{\varepsilon+\delta}{2} \cdot \frac{1+M_{n+1}}{1-M} . \qquad (15)$$

Now from (12) and (15) it follows that the linear approximation matrix of the transformation $(\underline{\epsilon}, \underline{\delta}) \rightarrow (\underline{\epsilon}', \underline{\delta}')$ is non negative. Moreover, with $r > 0$ and with all alleles $A_1, \ldots, A_n; B_1, \ldots, B_m$ present in the population, it is easy to see that for all $j, k$ either $X_{jk} > 0$ or $Y_{jk} > 0$ (or both), hence it is not difficult to establish that the second power of the matrix of linear approximation is strictly positive. From the

Perron-Frobenius theorem it, therefore, follows that the matrix has a leading positive right eigenvector, corresponding to a positive eigenvalue $\lambda > 0$. The population is stable against the mutation $A_{n+1}$ if $\lambda < 1$ (and only if $\lambda \leq 1$).

Assuming $(\underline{\epsilon}, \underline{\delta})$ in the direction of the main right eigenvector of the transformation we have $\epsilon'_k = \lambda\epsilon_k$ , $\delta'_k = \lambda\delta_k$. Hence, employing (11) we get $M'_{n+1} = M_{n+1} + 0(\epsilon, \delta)$ i.e.: The frequency of males among mutants is virtually constant $M_{n+1} \equiv M^*_{n+1}$ in the direction of the main eigenvector.

Employing (14) and (16) we get

$$\epsilon' + \delta' = \lambda(\epsilon+\delta) = \frac{\varepsilon+\delta}{2}\left[\frac{M^*_{n+1}}{M} + \frac{1-M^*_{n+1}}{1-M}\right]$$

$$= (\epsilon+\delta)\left[1 + \frac{(1/2 - M)(M^*_{n+1} - M)}{M(1-M)}\right]$$

thus

$$\lambda = 1 + \frac{(1/2 - M)(M^*_{n+1} - M)}{M(1-M)} \qquad (16)$$

and $\lambda > 1$ if either $M < \frac{1}{2}$ and $M^*_{n+1} > M$ or $M > \frac{1}{2}$ and $M^*_{n+1} < M$.

We therefore get:

Theorem

In a two locus, random mating autosomal system of sex determination in equilibrium, if the sex ratio is not 1:1 , a new mutation will successfully enter the system if and only if it innitially renders the sex ratio closer to 1:1 , at least when in the direction of the leading eigenvector.

Remark

Starting from small enough values $\epsilon_k$ and $\delta_k$, we know that, exept for a singular (measure 0) direction, the vector $(\underline{\epsilon}, \underline{\delta})$ will approach the direction of the main eigenvector, if converging, and get as close to its direction as one wishes (provided of how small the initial values $\epsilon_k$, $\delta_k$ are) if diverges.

Note that a sex ratio of 1:1 is stable against new mutation at each locus, at least when determined by monomorphic fixation (because the problem is then reduced to a one locus stability, see for example Eshel 1975, Eshel and Feldman 1984).

This, together with the theorem proved in this section means that the even sex ratio 1:1 has the property of autosomal two locus Evolutionary Genetic Stability (E.G.S. See Eshel and Feldman 1982b, 1984, Eshel 1985, Eshel and Matessi 1988), i.e.:

1. The only possible sex ratio, (determined by any genetic equilibrium) which is stable against any mutation at the two autosomal loci is 1:1.

2. Any internally stable equilibrium at the two loci, determining a sex ratio different from 1:1 is stable in face of new mutation that initially render the sex ratio further apart from 1:1 and unstable in face of new mutation initially rendering the sex ratio closer to 1:1, at least in the direction of the main eigenvector.

## 3. Summary and Discussion

Natural genetic systems are, generally, complicated and modifier genes can appear in more than one locus. The effect of natural selection, however, operating through changes in genotype frequencies is, sometimes, qualitatively different for one-locus and for multilocus systems. Thus, while Fisher's fundamental law of natural selection is valid for one locus viability selection in which the average fitness always increases (except in equilibrium) it is well established that this is not the case in multilocus systems. As it appears, the same is true for the evolution of sex-determination and sex-ratio. While autosomal one locus systems of sex-determination modifiers always tend to evolve toward an even sex ratio (e.g. Eshel and Feldman 1982b and references there) it has been demonstrated by Karlin and Lessard (1986) through various examples that any sex ratio can be stabilized by two locus (or multilocus) systems of self determination. Moreover, an even sex ratio is then not likely to evolve, even when feasible.

The situation appears to be different if one asks about the long-term process of evolution, in which new mutations are always introduced into internally stable equilibria (e.g. See Hamilton 1967, Maynard Smith and Price 1973). In a different paper (Eshel and Feldman 1984) it has been shown that although viability selection does not generally increase the population average viability, a new mutation, introduced into any two locus equilibrium can increase in frequency if and only if the weighed average fitness of its carriers surpasses this of the population at equilibrium, weights being proportional to those of the leading right eigenvector of the transformation in mutant frequences. In this sense it can be maintained that the mutant can sucessfully

enter an externally stable equilibrium if and only if it initially increases the main population viability.

In this paper it has been shown, quite similarly, that a new sex determination modifier, introduced into any two locus equilibrium of sex-determination will increase in frequency if and only if the average sex-ratio among its carriers, average calculated in the direction of the main eigenvestor, diverges from the population sex-ratio in the direction of 1:1.

For a discussion on the role of sex in the qualitative difference between short term evolution, based on changes in genotype frequencies and long term evolution, based on selective gene-substitution, the reader is referred to Eshel 1988.

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