THE THEORETICAL GENETICS OF THE SEX RATIO[1, 2]

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Received May 10, 1957

SEX ratios different from one half are found from time to time in animal populations and in families within populations. It is often supposed that these ratios are due to genes affecting the primary sex ratio, that is to say the sex ratio at fertilization. In certain cases the existence of such genes has been demonstrated. In several species of Drosophila there is an X-linked gene causing males which carry it to produce almost all daughters (MORGAN, BRIDGES and STURTEVANT 1925; GERSHENSON 1928). In *Drosophila affinis* NOVITSKI (1947) has found an autosomal gene which, in the presence of this X-linked gene, leads to the production of almost all sons. In both these cases it appears that only one kind of sperm cell is produced.

If you consider all the imaginable modes of action for genes affecting the sex ratio it is clear that there are two categories.

The Drosophila type just mentioned may be called a type I sex ratio gene and occurs in connection with an X-Y system of sex determination. This type of gene operates either by causing an unequal production of the two gametes in the heterogametic sex or by causing non random fertilization.

The other kind of gene is a type II sex ratio gene. It occurs where there is no chromosomal sex determination and can best be understood by considering the simplest example. Suppose there are two alleles, A and a; and that an AA individual is a male and an aa one a female. If the heterozygote is always of the same sex, say a male, only one homozygote is possible, and we have a backcross or X-Y type of sex determination. On the other hand if the heterozygote is a hermaphrodite or if it has a certain probability of developing into either a male or a female then both homozygotes as well as the heterozygote can remain in the population. The sex ratio in the population will depend upon the gene frequencies of these two alleles. Under the same general scheme a polygenic system would be possible. In any case a type II sex ratio gene is distinguished by acting as a sex determining factor in development while a type I sex ratio gene determines the frequencies with which XX and XY zygotes are formed.

An example of type II sex ratio genes is perhaps afforded by the isopods of DE LATTIN (1952). DE LATTIN claims that in his material sex is determined by autosomal genes only. In many cases of what is called environmental sex determination, type II sex ratio genes may also play a role of greater or lesser importance.

[1] Adapted from the author's Ph.D. thesis in Zoology, University of California.

[2] Part of the printing cost of the accompanying figures has been paid by the GALTON AND MENDEL MEMORIAL FUND.

That is to say there may be a joint determination of sex by genes and environment.

Since certain of the possible kinds of sex ratio genes have been discovered and others may reasonably be anticipated to exist, I propose to examine their expected behavior. A variety of genes differing in their mode of inheritance and effect on fitness will be considered in detail. The kind of selection each gene is subject to and consequently the effect which the presence of such a gene would have on the sex ratio of a population will be determined.

Some facts are already known about the population behavior of sex ratio genes and are set forth by GERSHENSON (1928), FISHER (1930), and SHAW and MOHLER (1953).

GERSHENSON considered the sex-linked sex ratio gene of the type found in Drosophila and which causes males carrying it to produce only daughters. He explains that such a gene should tend to increase in frequency. Experiments by WALLACE (1948) show that the effects on fitness produced by the *sex ratio* factor in *Drosophila pseudoobscura* are also important in determining the population behavior of this gene.

FISHER dealt with the relationship between parental care and the sex ratio. His discussion is difficult to paraphrase and should be consulted in the original. He is mainly concerned in showing that with parental care and a difference in viability between the sexes before they leave the care of the parents, the primary sex ratio will be adjusted to yield an excess of the less viable sex. This principle merits special attention since it may hold for man. Nevertheless, it cannot be considered here. In the examples to be given parental care is assumed to be absent or to play a negligible role.

It would seem to follow from FISHER's treatment that where there is no parental care or where offspring of the two sexes are equally viable the sex ratio will be adjusted to one half. This is the conclusion that MOHLER and I came to using a different approach. The conclusion is broadly applicable to the sex ratio insofar as it is determined by autosomal genes.

An approach different from any of the previous ones is used here. If it is assumed that the sex ratio is under the control of a given genetic mechanism, the successive frequencies of the genotypes present can be calculated, and so can the sex ratio of the population in each generation. Iterative calculations of this type are known to every geneticist. What follows is only a method for facilitating this kind of generation-by-generation calculation.

The figures for these calculations are written as matrices. The term "matrix" merely means a rectangular array of numbers and is legitimately used here even though no matrix algebra is employed.

Definitions:

a) The genotypes among the males are designated 1, 2, 3 . . . i . . . n, and among the females 1, 2, 3 . . . j . . . k.

b) The probability of genotype i among the males is z_i and of j among the females z_j.
c) The fitness of genotype i is w_i, a value such that rw_i gives the expected number of zygotes which will be produced by an individual (zygote) of genotype i. The factor r is a constant. The fitness of a female, w_j, is defined in the same fashion.
d) The initial number of male zygotes in the population is M and that of female zygotes, F.

Derivation:

Given the values of z_i and z_j in the parental generation we can find the corresponding values in the offspring generation.
1) The parental zygotes of genotype i, taken collectively and over their whole lives, are expected to produce rw_iMz_i offspring zygotes.
2) The probability that a zygote selected at random from the offspring generation is from an i father and also from a j mother, under the assumption of random mating, is

$$\frac{rw_iz_iM}{\Sigma\, rw_iz_iM} \cdot \frac{rw_jz_jF}{\Sigma\, rw_jz_jF}$$

$$= \frac{w_{ij}z_{ij}}{\Sigma\Sigma\, w_{ij}z_{ij}}$$

3) The probability that a zygote is i given that its parents are ij may be designated $s^{(i)}{}_{ij}$ and the probability that it is j, $s^{(j)}{}_{ij}$. (No summation applies to the (i) or (j) superscripts unless explicitly indicated, as for example, by $\sum_{(i)=1}^{n}$.)

4) The probability in the offspring generation of an individual which is both i and from ij parents is

$$\frac{(zw)_{ij}}{\Sigma\Sigma\,(zw)_{ij}} \cdot s^{(i)}{}_{ij} = \frac{(zws^{(i)})_{ij}}{\Sigma\Sigma\,(zw)_{ij}}$$

5) The probability of genotype i is the sum of the above or

$$[\Sigma\Sigma\,(zw)_{ij}]^{-1}\,\Sigma\Sigma\,(zws^{(i)})_{ij} \cdot$$

6) The probability of a male zygote given that the parents are ij may be defined as m_{ij}, and the probability of a female zygote as f_{ij}. (Note that the matrices $[m_{ij}]$ and $[f_{ij}]$ can be gotten as the sums of certain other matrices since they are the same as $\sum_{(i)=1}^{n} s^{(i)}{}_{ij}$ and $\sum_{(j)=1}^{k} s^{(j)}{}_{ij}$).
7) The probability of a male zygote in the offspring generation is

$$\frac{(zw)_{ij}}{\Sigma\Sigma\,(zw)_{ij}} \cdot m_{ij} = [\Sigma\Sigma\,(zw)_{ij}]^{-1}[\Sigma\Sigma\,(zwm)_{ij}]$$

8) The probability of genotype i among the offspring males is

$$z'_i = \frac{P\{i\}}{P\{\delta\}}$$

$$= \frac{[\Sigma\Sigma\,(zw)_{ij}]^{-1}[\Sigma\Sigma\,(zws^{(i)})_{ij}]}{[\Sigma\Sigma\,(zw)_{ij}]^{-1}[\Sigma\Sigma\,(zwm)_{ij}]}$$

$$z'_i = \frac{\Sigma\Sigma\,(zws^{(i)})_{ij}}{\Sigma\Sigma\,(zwf)_{ij}}$$

and likewise for the females

$$z'_j = \frac{\Sigma\Sigma\,(zws^{(j)})_{ij}}{\Sigma\Sigma\,(zwf)_{ij}} \cdot$$

Remember that z'_i and z'_j represent the zygotic frequencies in the succeeding generation of the various genotypes and that i and j indicate the arbitary number given to each genotype for identification. The iterative use of these equations will give the successive genotype frequencies for any desired number of generations.

A slight improvement in computation can be effected by multiplying the two equations together to give

$$z'_{ij} = \frac{\Sigma\Sigma\,(zws^{(i)})_{ij}\ \Sigma\Sigma\,(zws^{(j)})_{ij}}{\Sigma\Sigma\,(zwm)_{ij}\ \Sigma\Sigma\,(zwf)_{ij}} \cdot$$

Directions for computing an actual example will now be given in order to show more concretely what the various symbols mean and how a numerical result is obtained. Suppose that the sex ratio is influenced by a certain locus and that the recessive gene a causes males to produce all sons rather than half sons and half daughters. The matrix for the probability of an aa male is

$[s^{(i)}{}_{ij}] =$

♂ ♂ \ ♀ ♀	AA	Aa	aa
AA	0	0	0
Aa	0	⅛	¼
aa	0	½	1

This matrix gives the probability, for each different possible parental combination, of an offspring that is aa and a male. The letter s is an appropriate symbol

for this type of matrix because its elements are probabilities due to *segregation.* The superscript is given as $(i) = 1$ in accordance with the assignment of numbers to the genotypes and could also be written $(i) = aa$. All the matrices of this kind are written out below but without the complete labelling for parental combinations.

$$[s_{ij}{}^{(i)=1}] = \begin{matrix} \\ \\ \\ \end{matrix} \begin{matrix} \text{♂ ♂} \\ \end{matrix} \begin{bmatrix} \frac{1}{2} & \frac{1}{4} & 0 \\ \frac{1}{4} & \frac{1}{8} & 0 \\ 0 & 0 & 0 \end{bmatrix} \qquad [s_{ij}{}^{(j)=1}] = \begin{matrix} \\ \\ \\ \end{matrix} \begin{matrix} \text{♀ ♀} \\ \end{matrix} \begin{bmatrix} \frac{1}{2} & \frac{1}{4} & 0 \\ \frac{1}{4} & \frac{1}{8} & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

$$[s_{ij}{}^{(i)=2}] = \begin{bmatrix} 0 & \frac{1}{4} & \frac{1}{2} \\ \frac{1}{4} & \frac{1}{4} & \frac{1}{4} \\ 1 & \frac{1}{2} & 0 \end{bmatrix} \qquad [s_{ij}{}^{(j)=2}] = \begin{bmatrix} 0 & \frac{1}{4} & \frac{1}{2} \\ \frac{1}{4} & \frac{1}{4} & \frac{1}{4} \\ 0 & 0 & 0 \end{bmatrix}$$

$$[s_{ij}{}^{(i)=3}] = \begin{bmatrix} 0 & 0 & 0 \\ 0 & \frac{1}{8} & \frac{1}{4} \\ 0 & \frac{1}{2} & 1 \end{bmatrix} \qquad [s_{ij}{}^{(j)=3}] = \begin{bmatrix} 0 & 0 & 0 \\ 0 & \frac{1}{8} & \frac{1}{4} \\ 0 & 0 & 0 \end{bmatrix}$$

$$[m_{ij}] = \begin{bmatrix} \frac{1}{2} & \frac{1}{2} & \frac{1}{2} \\ \frac{1}{2} & \frac{1}{2} & \frac{1}{2} \\ 1 & 1 & 1 \end{bmatrix} \qquad [f_{ij}] = \begin{bmatrix} \frac{1}{2} & \frac{1}{2} & \frac{1}{2} \\ \frac{1}{2} & \frac{1}{2} & \frac{1}{2} \\ 0 & 0 & 0 \end{bmatrix}$$

If we suppose that *aa* females have a fitness of one half while the other genotypes are unaltered in fitness, the matrix for fitness is

$$[w_{ij}] = \begin{bmatrix} 1 & 1 & \frac{1}{2} \\ 1 & 1 & \frac{1}{2} \\ 1 & 1 & \frac{1}{2} \end{bmatrix}$$

Finally suppose that the three genotypes occur in frequencies 0.3, 0.3, 0.4 in the males and 0.3, 0.4, 0.3 in the females. Then the z matrix together with its marginal totals, which are given for clarity, is

$$[z_{ij}] = \begin{matrix} \\ \\ \\ \\ \end{matrix} \begin{matrix} \\ \\ \\ \\ .30 \end{matrix} \begin{matrix} \\ \\ \\ \\ .40 \end{matrix} \begin{matrix} \\ \\ \\ \\ .30 \end{matrix} \begin{bmatrix} .09 & .12 & .09 \\ .09 & .12 & .09 \\ .12 & .16 & .12 \end{bmatrix} \begin{matrix} .30 \\ .30 \\ .40 \end{matrix}$$

For ease in calculation it is desirable to combine the w matrix with each of the segregation matrices by multiplying corresponding elements. Whether this is done or not the formula

$$z'_{ij} = \frac{\Sigma\Sigma\,(zws^{(i)})_{ij}\ \Sigma\Sigma\,(zws^{(j)})_{ij}}{\Sigma\Sigma\,(zwm)_{ij}\ \Sigma\Sigma\,(zwf)_{ij}}$$

can now be applied. The first step is to calculate the denominator for which there is only one value. Next calculate the numerator for all the values of i and j and arrange the figures in their proper order in an i by j matrix. Multiply each element of the matrix by the reciprocal of the denominator (because with a desk calculator this is easier than dividing). The result is the matrix z'_{ij} for the succeeding generation. The frequencies of the various genotypes are gotten from this simply by taking the marginal totals. This can be done at each generation, at intervals of several generations, or only for the final generation.

Examples:

Various examples will now be considered. Each of these is given as a figure captioned so as to be self-explanatory, and each illustrates the behavior of a different kind of sex ratio gene. A sex ratio gene is always designated by the letter a either capitalized or lower case depending on dominance. A normal gene is designated by +.

The initial frequencies of the genotypes for all examples are selected so as to be quite different from the apparent limiting values. The gene's behavior over a wide range of frequencies can thus be observed. Many of the graphs show violent fluctuations for the first few generations. This is due to the arbitrary initial frequencies.

Figures 1, 2, 3, and 4 are concerned with autosomal genes. In these very simple cases all values of w are 1, and the sex ratio gene is in competition only with a normal allele. The sex ratio gene is progressively reduced in frequency and the more rapidly so when it is dominant.

Figure 5 is for two alleles with opposite effects on the sex ratio. An equilibrium is reached with the sex ratio of the population at one-half.

Figures 6 and 7 show an autosomal dominant which has effects other than on the sex ratio. The way in which fitness is altered is the same in both of these except that in Figure 7 the reduction of fitness is in the female and in Figure 6 in the male. The results are quite different. In Figure 7 it is not clear from the graph whether or not an equilibrium will eventually be established with both alleles remaining in the population. In Figure 6 this has actually occurred after 11 generations.

In Figure 7 equilibrium is not established at an intermediate value. The frequencies all go to zero or one. This can be shown as follows. The $A/+$ females can come only from the cross $+/+$ ♂ by $A/+$ ♀, but half the female zygotes from that cross will be $+/+$. The frequency of $A/+$ females will thus decline leaving, eventually, only $+/+$ females. This leads immediately to the consequence that

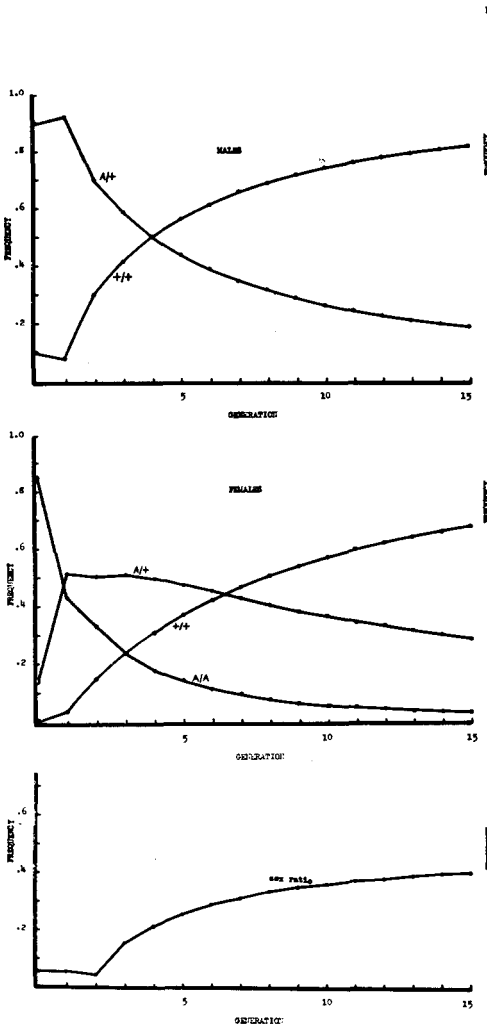


FIGURE 1.—An autosomal dominant causing males to produce only daughters.

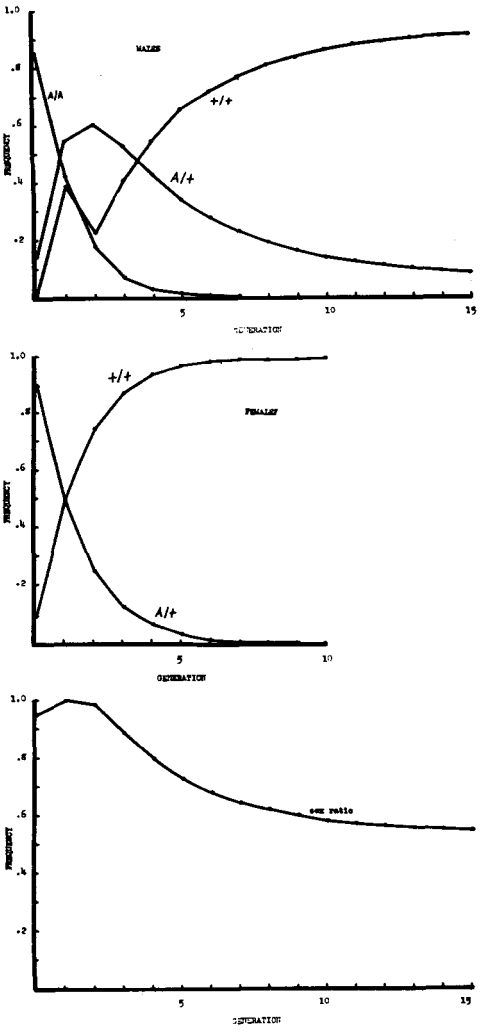
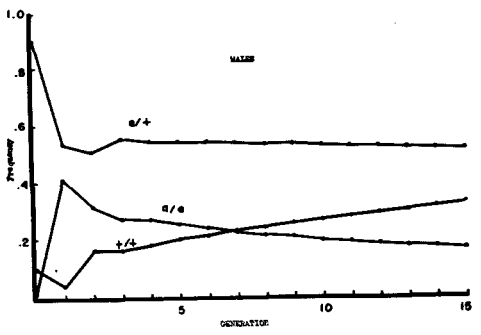
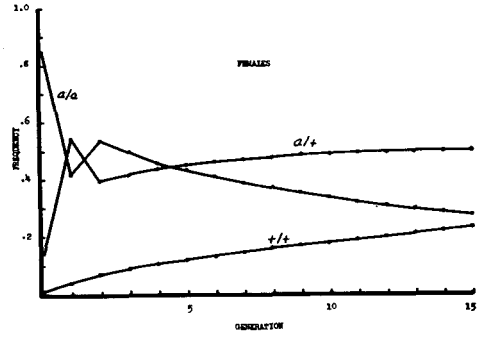


FIGURE 2.—An autosomal dominant causing males to produce only sons.

no A/A males can appear. There now remain in the population only one kind of female but two kinds of male: $A/+$ and $+/+$. The $A/+$ males will also be gradually eliminated due to their property of producing half $+/+$ sons.

The importance of Figures 6 and 7 is this. The effect on the sex ratio tends to reduce the frequency of the gene while the effect on fitness is such as to increase it. It might be expected that such circumstances would lead to an equilibrium with a gene frequency somewhere between zero and one. WALLACE supposed the existence of such a stable equilibrium for the sex-linked sex ratio gene in *Drosophila pseudoobscura*, and his experiments support this supposition. Nevertheless, as a





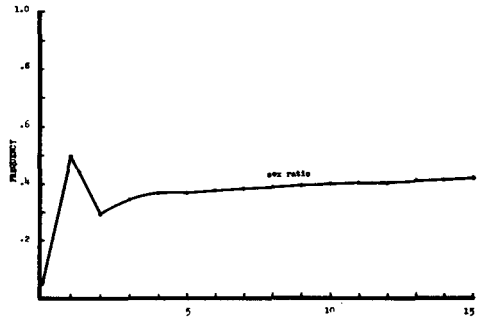
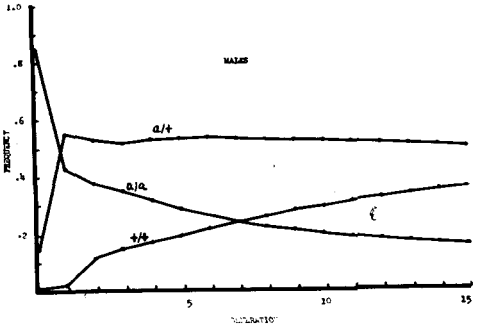
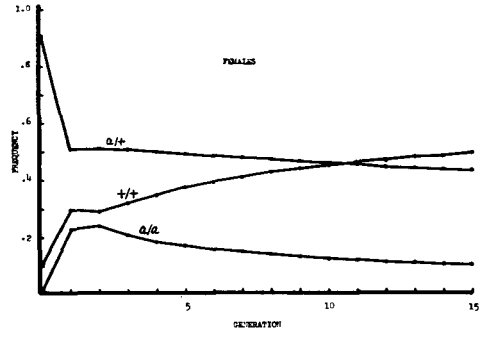


FIGURE 3.—An autosomal recessive causing males to produce only daughters.





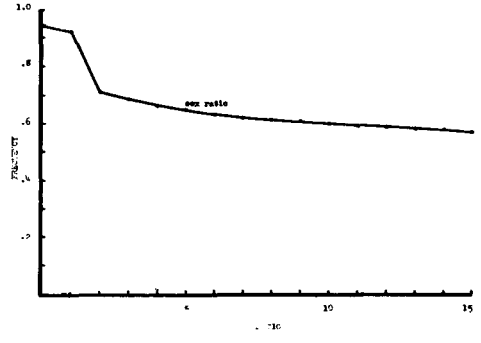


FIGURE 4.—An autosomal recessive causing males to produce only sons.

general principle, the presence of two opposing forces is not necessarily sufficient to establish a stable equilibrium at an intermediate gene frequency. Figures 6 and 7 show that such an equilibrium for sex ratio genes is possible but not invariable.

Figure 8 shows a type II sex ratio gene. Its effect is such that a zygote receiving this gene is certain to develop into a male, while one not receiving it has a probability of one half of so doing. The outcome is that the strong male determining gene is eliminated and the sex ratio of the population approaches one half.

Figure 9 is an example of two alleles, each producing an abnormal sex ratio.

They have opposite effects and both alleles remain in the population which is stabilized with the attainment of an over-all sex ratio of one half.

Many animals which are said to have environmental sex determination may really have a sex determination which is partly genetic. Besides the effect of the environment there may be genes affecting the lability of change toward one sex or the other. This possibility is supported by the contention of COE (1948) respecting the protandrous gastropod, *Crepidula plana*. In this species young individuals living near females develop into males and retain that condition for some time, subsequently becoming females. Those which are not near females undergo only a brief male phase or none. There are, however, exceptions. Some individuals associated with females retain the male phase throughout their lifetimes. Others, although isolated, develop a full male phase. COE suggests that these individuals are genetically different from the other members of the species. Although the case of Crepidula is complicated by alternating sexuality, the facts are

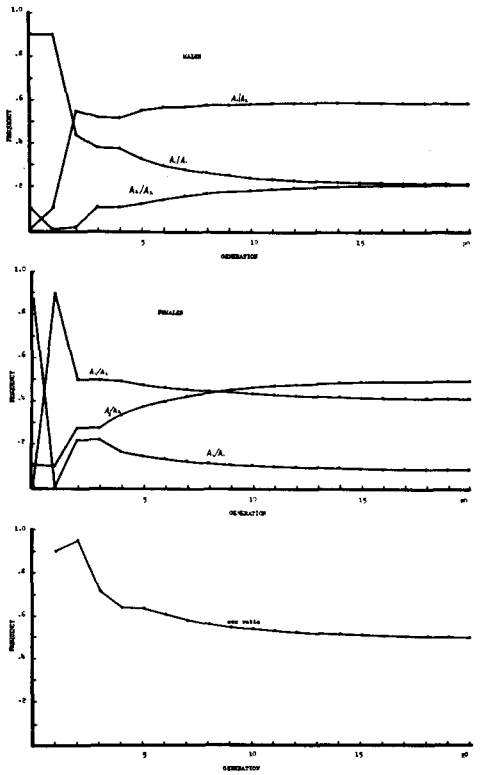


FIGURE 5.—Two alleles with opposite effects on the sex ratio. A_1/A_1 fathers produce only sons; A_1/A_2 fathers produce half sons, half daughters; A_2/A_2 fathers produce only daughters.

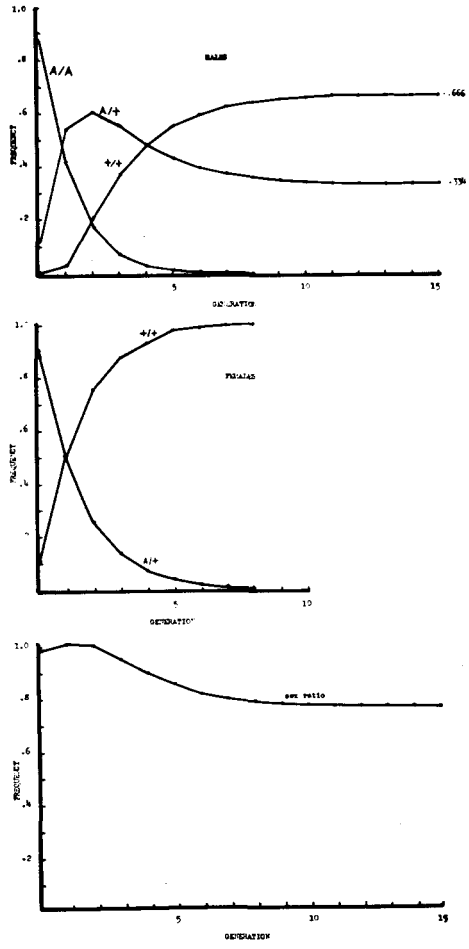


FIGURE 6.—An autosomal dominant causing males to produce only sons. Fitness values for A/A, $A/+$, and $+/+$ males are respectively 1, 1, ½. In the females all three genotypes are equally fit.

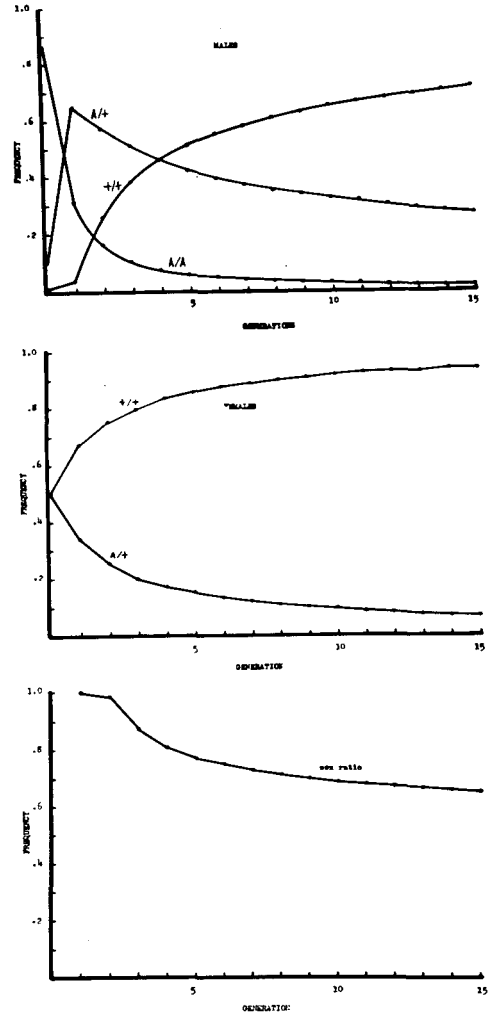


FIGURE 7.—An autosomal dominant causing males to produce only sons. Fitness values for A/A, $A/+$, and $+/+$ females are respectively 1, 1, ½. In the males all genotypes are equally fit.

conducive to the belief that genes modifying environmental sex determination do exist.

If the interpretation of DE LATTIN is correct, his isopods have a kind of sex determination in which there are no sex chromosomes, but also no effect of environment. Instead of being determined partly by environmental and partly by genetic factors, sex is fully determined by a set of genes. These genes, of course, are all autosomal. Genes of this kind are very similar to those in Figures 8 and 9.

Both genes modifying environmental sex determination and those of the sort suggested by DE LATTIN are type II sex ratio genes and therefore similar to those of Figures 8 and 9. The examples suggest that a population with type II sex ratio genes will have an equilibrium sex ratio of one half. (If temporal fluctuations in environment are important, the sex ratio might, of course, fluctuate around this value.) Whether this holds as a general principle can be investigated using an approach similar to that of FISHER.

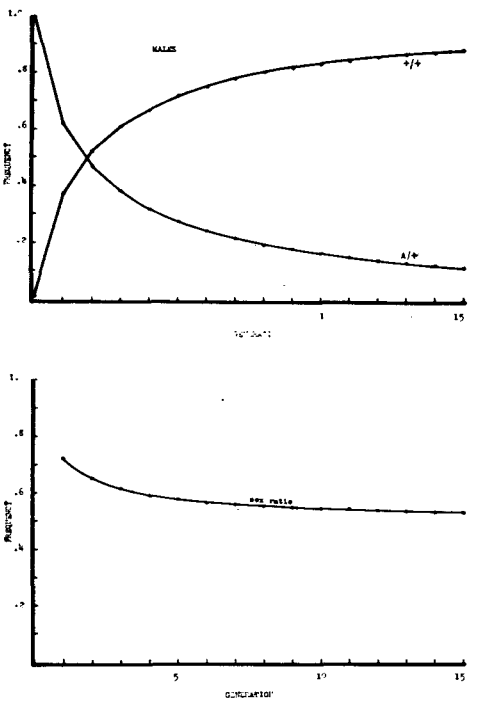


FIGURE 8.—An autosomal dominant type II sex ratio gene. The probability that a zygote becomes a male is 1 if it has an A gene, ½ if it has only $+$.

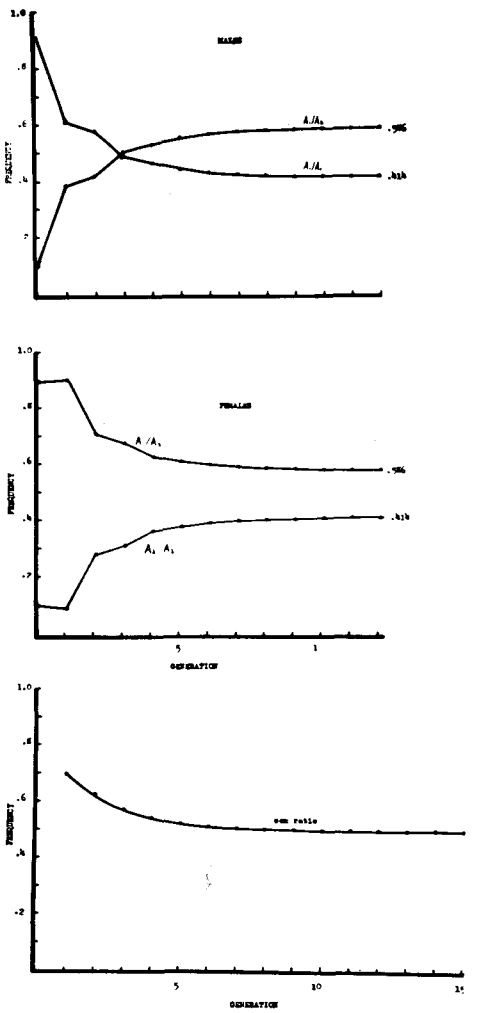


FIGURE 9.—An autosomal type II sex ratio gene. The probability that a zygote becomes a male is 1, ½, or 0 depending on whether its genotype is respectively A_1/A_1, A_1/A_2, or A_2/A_2.

Suppose that the sex ratio is under genic control and that none of the genes are sex-linked—in fact the organism considered has no sex chromosomes. If there are N zygotes in a generation and NM of them are males, then one male zygote is expected to contribute $\frac{1}{2} \cdot 1/NM$ or $1/2NM$ of the genes going to the next generation. Likewise a female zygote is expected to contribute $1/2NF$. These "contributions" may be said to be the genetic value of a male and of a female zygote respectively. Equilibrium must occur when the value of a male zygote is equal to that of a female. This is so because if the values were not equal, parents with genotypes leading to the production of mainly the more valuable sex would be favored over the others. Selection would thus proceed. Equal zygotic values of the sexes means that

$$\frac{1}{2NM} = \frac{1}{2NF} .$$

From this, M must equal F showing that equilibrium is attained at a sex ratio of one half.

Provided this requirement is met, a population may remain heterogeneous for type II sex ratio genes. This is just what has been claimed by DE LATTIN whose populations of isopods were of two color patterns. Strains of these two raised in the laboratory had sex ratios of .68 and .32. Equilibrium would be expected where

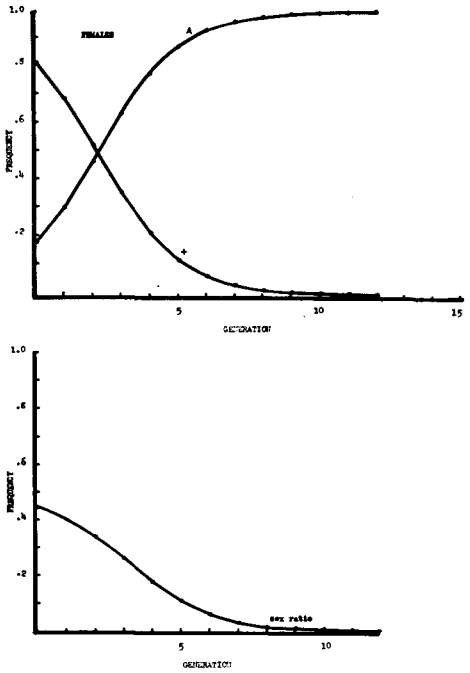


FIGURE 10.—A Y-linked gene causing females to produce only daughters. The female is the heterogametic sex.

the sex ratio of the whole population is one half. This would occur with the two types in equal numbers. Although there were differences from one population to another, DE LATTIN did indeed find the two types in very nearly equal frequencies in natural populations.

A completely Y-linked gene is considered in Figure 10. The female is heterogametic, and the sex ratio gene causes females carrying it to produce all daughters. Here the sex ratio gene increases to fixation. It is not difficult to see what happens. Females carrying the gene give a Y chromosome to every offspring while the normals give a Y to only half. The favored allele at a Y-linked locus is the one that leads to the production of the greatest proportion of the heteroga-

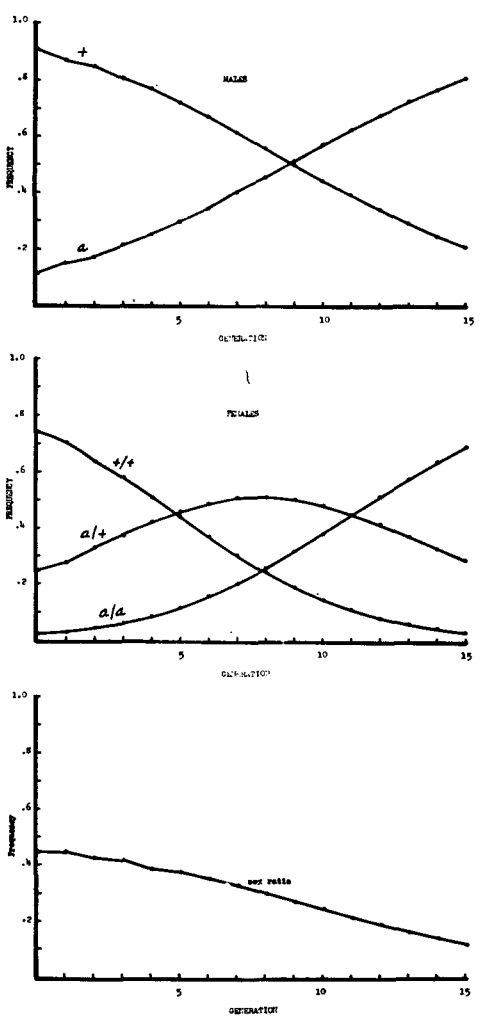


FIGURE 11.—An X-linked recessive causing males to produce only daughters.

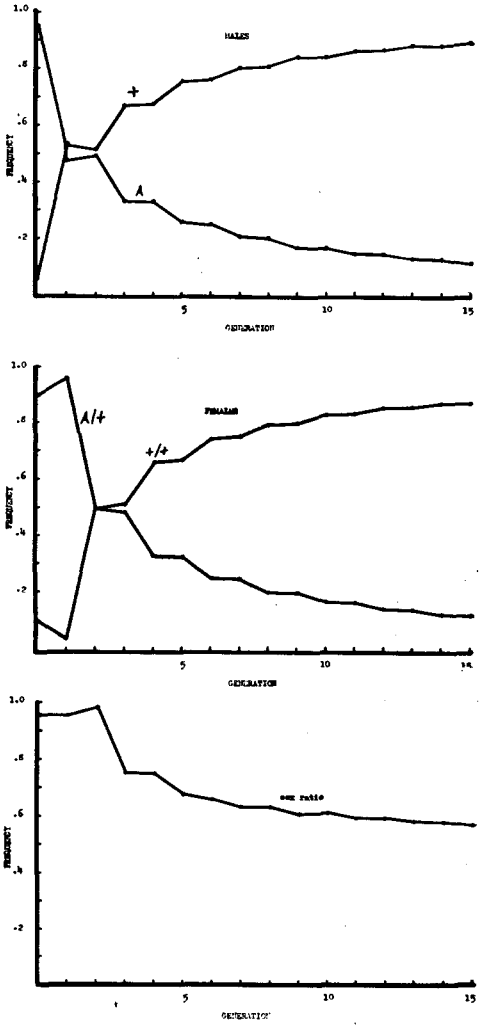


FIGURE 12.—An X-linked dominant causing females to produce only sons.

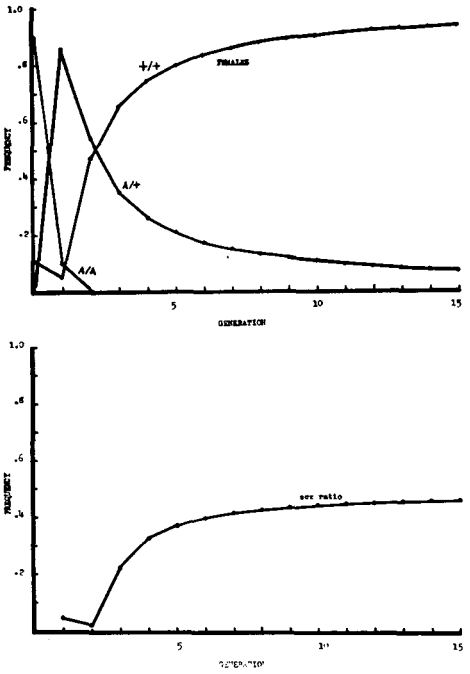


FIGURE 13.—An X-linked dominant causing females to produce only daughters. The frequency of *A* goes to zero in the first generation in the males.

metic sex. Clearly a population cannot remain heterogeneous for Y-linked sex ratio genes unless it is maintained so by fitness differences which counteract the type of selection just described.

HOWARD (1942) describes three kinds of females in the land isopod *Armadillium vulgare*: females which produce nearly all daughters, females which produce nearly all sons, and females which produce sons and daughters in equal numbers. He suggests that this condition is probably due to cytoplasmic factors, but perhaps to genes on the Y chromosome. (The female is presumably heterogametic.) The hypothesis of genes on the Y chromosome can certainly be eliminated. A gene for the production of nearly all daughters would rapidly approach fixation. The gene for mostly sons would very rapidly disappear. If it led to the production of exclusively sons, it would disappear entirely in one generation. The resulting picture is similar to that of Figure 10. The fitness differences necessary to maintain an equilibrium would be extremely high.

Figures 11, 12, and 13 are of sex-linked genes.

Figure 11 is of the kind of gene known in various species of Drosophila. As indicated by GERSHENSON, it tends to increase in the population.

Figures 12 and 13 are of sex-linked genes acting in the female. In both of these examples the gene tends to be eliminated.

A peculiarity of sex ratio genes can be seen in the examples which have been calculated. The zygotic gene frequency as well as the frequencies of the genotypes may be different in the two sexes. X-linked genes under selection can have different zygotic frequencies in the two sexes even when there is no effect on the sex ratio; autosomal genes, except those subject to non random disjunction, cannot.

SUMMARY

A method is given for calculating the genotype frequencies in successive generations in a population with genetic variability of the sex ratio. By computing specific examples the population behavior of genes affecting the sex ratio is investigated.

ACKNOWLEDGEMENT

I wish to thank PROF. CURT STERN, under whose direction the work was done, for having encouraged me to pursue this problem.

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