Natural Selection and *Y*-Linked Polymorphism

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ABSTRACT

Several population genetic models allowing natural selection to act on *Y*-linked polymorphism are examined. The first incorporates pleiotropic effects of a *Y*-linked locus, such that viability, segregation distortion, fecundity and sexual selection can all be determined by one locus. It is shown that no set of selection parameters can maintain a stable *Y*-linked polymorphism. Interaction with the *X* chromosome is allowed in the next model, with viabilities determined by both *X*- and *Y*-linked factors. This model allows four fixation equilibria, two equilibria with *X* polymorphism and a unique point with both *X*- and *Y*-linked polymorphism. Stability analysis shows that the complete polymorphism is never stable. When *X*- and *Y*-linked loci influence meiotic drive, it is possible to have all fixation equilibria simultaneously unstable, and yet there is no stable interior equilibrium. Only when viability and meiotic drive are jointly affected by both *X*- and *Y*-linked genes can a *Y*-linked polymorphism be maintained. Unusual dynamics, including stable limit cycles, are generated by this model. Numerical simulations show that only a very small portion of the parameter space admits *Y* polymorphism, a result that is relevant to the interpretation of levels of *Y*-DNA sequence variation in natural populations.

RECENT advances in molecular cloning have enabled investigators to make probes of *Y*-homologous DNA, and in addition to allowing more direct study of the function and regulation of genes on the *Y*-chromosome, these probes have been used to begin to ascertain the levels of sequence variation (CASANOVA *et al.* 1985; DARLING *et al.* 1986; HAREVEN, ZUCKERMAN and LIFSCHYTZ 1986; WILLIAMS *et al.* 1987). These data will yield important insights into the evolution of sex chromosomes, and they raise the challenge of describing the forces that maintain the observed variation. The factors that have classically been invoked by population geneticists, including mutation, migration, drift, and natural selection, are undoubtedly all at work on *Y*-linked genetic variation, but there are some important aspects of the transmission of the *Y* chromosome that make it unique. Because *Y* chromosomes have unisexual transmission, migration may have quite different effects on the population genetic structure of *Y* chromosomes when compared to autosomes. HAMILTON (1967) and HEUCH (1978) suggest that *Y*-linked meiotic drive can be maintained in a population if there is sufficiently infrequent migration due to recurrent extinction and recolonization of local demes. Genetic drift will affect the structure of variation on the *Y* chromosomes, but there will be quantitative differences from autosomes, particularly due to the different effective population size (CHARLESWORTH, COYNE and BARTON, 1987). MULLER's ratchet will apply to the *Y* chromosome (CHARLESWORTH 1978), and it may be an explanation for the preponderance of repetitive heterochromatin on the *Y* chromosome (BRUTLAG 1980; JONES and SINGH 1982).

The theory of natural selection of Y-linked variation is tied inextricably to the theory of sex ratio, and the unusual transmission of the *Y* can result in population dynamics unlike those of any other genetic element. HAMILTON (1967) demonstrated that unbalanced meiotic drive of the *Y* chromosome can lead to very rapid population extinction. Since the *Y* chromosome pairs with an *X*, the segregation properties of the two sex chromosomes must really be considered jointly. There is biological precedent for invoking interactions between the *X* and the *Y*, since COYNE (1985) showed that the fertility of interspecific hybrid males of Drosophila depends on the combination of *X* and *Y* chromosomes. The observation of rare homologous exchanges between the *X* and *Y* chromosome rDNA arrays in *Drosophila melanogaster* (S. W. WILLIAMS, J. A. KENNISON and C. STROBECK, unpublished data), and the obligate crossingover between the sex chromosomes in humans and mice (ROUYER *et al.* 1986) further supports the potential importance of *X*-*Y* interaction in evolution. But the bulk of the *Y* chromosome in most species is genetically isolated by lack of recombination with any other chromosome, giving it clonal transmission properties analogous to haploids and mitochondria.

The objective of this paper is to examine four simple models of natural selection acting on the *Y* chromosome. The models include *Y*-autonomous selection,

X-Y variation in viability, *X-Y* variation in meiotic drive, and a model with pleiotropic effects on the *X* and *Y* chromosome in both meiotic drive and viability. The equilibrium characteristics of these models are solved with the intention of gaining insight into the opportunity of natural selection to maintain *Y*-linked genetic variation.

THE MODELS

Pleiotropic *Y*-autonomous variation: The simplest model for *Y* chromosome variation allows two *Y* chromosomes, denoted *Y* and *y*, and ignores all other genetic variation. In this model and those that follow, the *Y* chromosome refers to the sex chromosome that is found exclusively in the heterogametic sex, and its genetic effects are assumed to reside in chromosomal regions that do not recombine with the *X*. In this scheme, there are two male types, *XY* and *Xy*, and all of the effects of the *Y* chromosome variation will be realized in the phenotypes of these two male types. In particular, the males may differ in any of several components of fitness, including differential mating ability (sexual selection), fecundity, viability and meiotic drive (CHRISTIANSEN and FRYDENBERG 1973). All of these components can be determined by pleiotropic effects of the genes that distinguish *Y* from *y*. When the recursion in *Y* chromosome frequencies is examined, it is readily apparent that there are no conditions on the fitness components that can maintain an internal polymorphism. This implies that in order to maintain polymorphism in *Y* chromosomes by natural selection, there must either be intrinsic frequency dependent fitness, demic heterogeneity in fitnesses (GLIDDON and STROBECK 1975), or there must be an interaction with another genetic element.

***X*- and *Y*-linked viability:** Consider the situation with two *X* chromosomes, denoted *X* and *x*, and two *Y* chromosomes, *Y* and *y*. In this system there are three female genotypes and four male genotypes:

	Females			Males			
Genotype	*XX*	*Xx*	*xx*	*XY*	*Xy*	*xY*	*xy*
Frequency	u	v	w	a	b	c	d
Viability	v_1	v_2	v_3	v_4	v_5	v_6	v_7

In the absence of selection, the recurrence system can be written with the normalization $u + v + w = 1$ and $a + b + c + d = 1$, where the sex ratio remains 1:1. In this case the adult genotype frequencies are obtained from the products of gamete frequencies produced by the two sexes. The genotype frequencies asymptotically converge to HARDY-WEINBERG proportions in females, while the frequencies of the male genotypes at equilibrium are the products of the initial frequencies of the respective gametes. Hence there is no statistical association between the *X* and *Y* chromosomes at equilibrium, and the term *ad-bc* asymptotically decays to zero in a way analogous to linkage disequilibrium. At equilibrium there is no difference in the frequency of the two *X* chromosomes in the two sexes.

Viability can be added to this model by assigning viability parameters v_1 through v_7 to the seven respective genotypes, as shown above. The recursion system is most easily expressed in terms of the frequency of *X* in females (X_f), the frequency of *X* in males (X_m), and the frequency of *Y*(Y). The frequency of *x* in females is $1 - X_f$, and in males it is $1 - X_m$, while the frequency of *y* is $1 - Y$. The population is censused at the gamete stage, and the frequency of *X* in eggs is obtained by weighting the frequencies of female genotypes that can produce *X* eggs by their viabilities and normalizing by the mean viability of females. The complete recursion system for viability selection with *X* and *Y* variation is:

$$X_f' = \frac{v_1X_fX_m + 0.5v_2[X_f(1 - X_m) + X_m(1 - X_f)]}{\bar{w}_f}$$

$$X_m' = \frac{v_4X_fY + v_5X_f(1 - Y)}{\bar{w}_m} \qquad (1)$$

$$Y' = \frac{v_4X_fY + v_6(1 - X_f)Y}{\bar{w}_m}$$

where,

$$\bar{w}_f = X_fX_mv_1 + [X_f(1 - X_m) + X_m(1 - X_f)]v_2 + (1 - X_f)(1 - X_m)v_3$$

$$\bar{w}_m = X_fYv_4 + X_f(1 - Y)v_5 + Y(1 - X_f)v_6 + (1 - X_f)(1 - Y)v_7.$$

This system admits four trivial equilibria, representing fixation for the four possible combinations of sex chromosomes. The stability of these "corner" equilibria are obtained from the Jacobian of the transformation:

$$J = \begin{bmatrix} \partial X_f'/\partial X_f & \partial X_f'/\partial X_m & 0 \\ \dfrac{MN}{[MX_f + N(1 - X_f)]^2} & 0 & \dfrac{X_f(1 - X_f)\cdot(v_4v_7 - v_5v_6)}{[MX_f + N(1 - X_f)]^2} \\ \dfrac{Y(1 - Y)\cdot(v_4v_7 - v_5v_6)}{[mY + n(1 - Y)]^2} & 0 & \dfrac{mn}{[mY + n(1 - Y)]^2} \end{bmatrix} \qquad (2)$$

where

$$M = v_4Y + v_5(1 - Y) \qquad m = v_4X_f + v_6(1 - X_f)$$

$$N = v_6Y + V_7(1 - Y) \qquad n = v_5X_f + v_7(1 - X_f)$$

and

$$\partial X_f'/\partial X_f = \frac{X_m^2(0.5\ v_1v_2 - v_1v_3 + 0.5\ v_2v_3) + X_m(v_1v_3 - v_2v_3) + 0.5\ v_2v_3}{\bar{w}_f^2}$$

$$\partial X_f'/\partial X_m = \frac{X_f^2(0.5\ v_1v_2 + 0.5\ v_2v_3 - v_1v_3) + X_f(v_1v_3 - v_2v_3) + 0.5\ v_2v_3}{\bar{w}_f^2}.$$

When evaluated at the first corner equilibrium ($\hat{X}_m = \hat{X}_f = \hat{Y} = 0$), the Jacobian matrix becomes

$$J = \begin{bmatrix} 0.5\ v_2/v_3 & 0.5\ v_2/v_3 & 0 \\ v_5/v_7 & 0 & 0 \\ 0 & 0 & v_6/v_7 \end{bmatrix}. \tag{3}$$

When the roots of the characteristic equation of this matrix are positive, real and less than one, then the equilibrium is locally stable. In a similar fashion, the stability conditions are obtained for the other three corner equilibria:

Equilibrium	Stability Conditions
$\hat{X}_f = \hat{X}_m = \hat{Y} = 0$	$v_6 < v_7$ and $v_3v_7 > 0.5 \cdot v_2(v_5 + v_7)$
$\hat{X}_f = \hat{X}_m = 0, \hat{Y} = 1$	$v_7 < v_6$ and $v_3v_6 > 0.5 \cdot v_2(v_4 + v_6)$
$\hat{X}_f = \hat{X}_m = 1, \hat{Y} = 0$	$v_4 < v_5$ and $v_1v_5 > 0.5 \cdot v_2(v_5 + v_7)$
$\hat{X}_f = \hat{X}_m = \hat{Y}\hat{} = 1$	$v_5 < v_4$ and $v_1v_4 > 0.5 \cdot v_2(v_4 + v_6)$

(4)

If the leftmost of these stability conditions is violated, then the rare Y chromosome can increase in frequency, and if the rightmost stability condition is violated, the rare X chromosome can increase. The condition of the X chromosomes is simply that the products of the viabilities of the respective male and female genotypes must exceed the product of the viability of the female heterozygote and the average of the viabilities of the two male genotypes that bear the invading X. If there is a sort of heterozygote advantage, then the corner will be unstable.

In addition to the four corner equilibria, there may exist at most two "edge" equilibria that are fixed for one or the other Y chromosome but maintain polymorphism on the X chromosomes. The equilibrium frequencies are:

$$\hat{Y} = 0$$

$$\hat{X}_f = \frac{v_3v_7 - 0.5(v_5 + v_7)v_2}{v_1v_5 + v_3v_7 - (v_5 + v_7)v_2} \tag{5}$$

$$\hat{X}_m = \frac{v_5\hat{X}_f}{v_5\hat{X}_f + v_7(1 - \hat{X}_f)}$$

and, for the other equilibrium:

$$\hat{Y} = 1$$

$$\hat{X}_f = \frac{v_3v_6 - 0.5(v_4 + v_6)v_2}{v_1v_4 + v_3v_6 - (v_4 + v_6)v_2} \tag{6}$$

$$\hat{X}_m = \frac{v_4\hat{X}_f}{v_4\hat{X}_f + v_6(1 - \hat{X}_f)}.$$

The characteristic equation of the Jacobian evaluated at these equilibria can be factored as:

$$(J_{33} - \lambda)[(J_{11} - \lambda)(-\lambda) - J_{12}J_{21}] = 0, \tag{7}$$

because $\partial Y'/\partial X_f$ evaluated at these equilibria is 0. From the characteristic equation, the conditions for the stability of the $\hat{Y} = 0$ equilibrium are:

$$v_1v_5 < 0.5(v_5 + v_7)v_2 > v_3v_7,$$

and

$$\frac{v_4M + v_6N}{v_5M + v_7N} < 1 \tag{8}$$

where $M = v_3v_7 - 0.5(v_5 + v_7)v_2$ and $N = v_1v_5 - 0.5(v_5 + v_7)v_2$. Both conditions must be satisfied for the $\hat{Y} = 0$ equilibrium to be locally stable. The stability conditions for the $\hat{Y} = 1$ equilibrium are:

$$v_1v_4 < 0.5(v_4 + v_6)v_2 > v_3v_6,$$

and

$$\frac{v_5S + v_7T}{v_4S + v_6T} < 1 \tag{9}$$

where $S = v_3v_6 - 0.5(v_4 + v_6)v_2$ and $T = v_1v_4 - 0.5(v_4 + v_6)v_2$. Analysis of the stability conditions reveals that it is not possible to have all four corners and the two edges simultaneously unstable. This implies that we cannot guarantee a protected polymorphism of the Y chromosomes. Since protection is a property of local stabilities, it does not guarantee that an internal equilibrium, if it exists, is unstable.

The recurrence system for viability selection can have an interior equilibrium, and it is found at:

$$\hat{X}_f = \frac{v_7 - v_6}{v_4 - v_5 - v_6 + v_7}$$

$$\hat{X}_m = \frac{\hat{X}_f(-\hat{X}_fv_2 - v_3 + \hat{X}_fv_3 + 0.5\ v_2)}{\hat{X}_f(v_1\hat{X}_f + v_2 - 2\ \hat{X}_fv_2 - v_3 + \hat{X}_fv_3 - v_1 + v_2) - 0.5\ v_2} \tag{10}$$

$$\hat{Y} = \frac{\hat{X}_m\hat{X}_f(v_7 - v_5) - \hat{X}_mv_7 + \hat{X}_fv_5}{\hat{X}_m\hat{X}_f(v_4 - v_5 - v_6 + v_7) + \hat{X}_m(v_6 - v_7) - \hat{X}_f(v_4 - v_5)}$$

When the Jacobian is evaluated at this equilibrium, we find that $\partial Y'/\partial Y = 1$, and the characteristic equation becomes:

$$-\lambda^3 + (1 + J_{11})\lambda^2 + (J_{12}J_{21} - J_{11})\lambda + J_{12}J_{23}J_{31} - J_{12}J_{21} = 0. \tag{11}$$

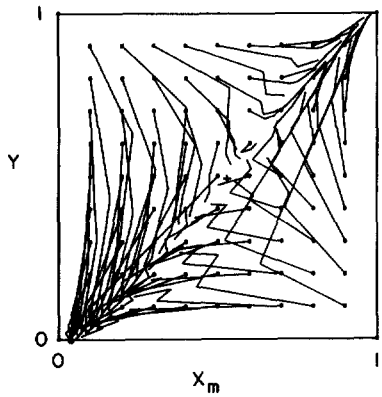

FIGURE 1.—Dynamics of the model with viability determined by the X and Y chromosomes. Trajectories from several different initial starting points are plotted on the same phase plane. For all simulations the viability parameters were: $v_1 = 0.9$, $v_2 = 1.0$, $v_3 = 0.4$, $v_4 = 0.5$, $v_5 = 0.1$, $v_6 = 0.1$, $v_7 = 0.8$. The unstable interior equilibrium occurs at $\hat{X}_f = 0.63636$, $\hat{X}_m = 0.530562$ and $\hat{Y} = 0.488998$ (indicated by "+"). There is a stable $\hat{Y} = 0$ edge equilibrium and the $\hat{X}_f = \hat{X}_m = \hat{Y} = 1$ corner is stable.

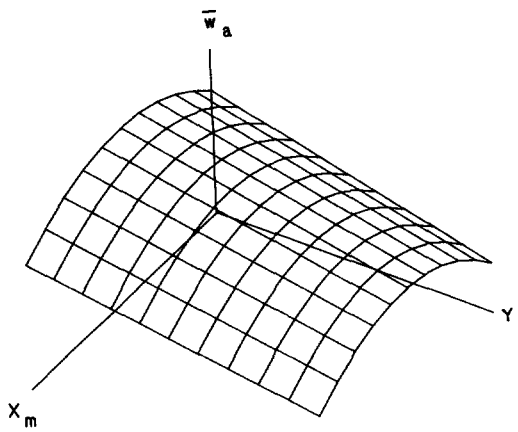

FIGURE 2.—A perspective view of the additive mean fitness $\bar{w}_a$ under the viability model. This is a projection with the constraint $X_f = X_m$. The viabilities were $v_1 = 0.5$, $v_2 = 1.7$, $v_3 = 0.3$, $v_4 = 0.7$, $v_5 = 1.2$, $v_6 = 0.4$ and $v_7 = 1.5$. These parameters result in an unstable interior equilibrium.

This equation has three real roots, and the largest root is always greater than one, so the interior equilibrium is never stable. Because the roots with the largest real part are not complex, the viability model does not show cyclic dynamics (Figure 1).

The mean fitness in this model can be calculated as either the additive mean ($\bar{w}_a = \bar{w}_f + \bar{w}_m$) or as the harmonic mean ($\bar{w}_h = (\bar{w}_f \bar{w}_m)^{0.5}$). Both of these can decrease over time, since differences in the frequency of the X chromosomes in the two sexes results in a damped oscillation in X chromosome frequencies. But in the immediate vicinity of a locally stable equilibrium, the mean fitness measured in both ways does increase. The mean fitness function can be plotted for a constrained projection of the frequency simplex where $X_m = X_f$, and an example appears in Figure 2. A geometric proof that there is no stable interior equilibrium rests on the observation that $\partial w_a/\partial Y$ is independent of Y, so that the surface is composed of straight lines running parallel to the Y axis. Such a surface can have no internal maximum.

This completes the analysis of the viability model. The model can have seven equilibria, with one unique interior equilibrium. Because the interior equilibrium is never stable, we conclude that viability selection cannot maintain Y-linked polymorphism.

***X*- and *Y*-linked meiotic drive:** In this model the only component of selection is the differential production of gametes by heterozygous females or males. This analysis is closely related to the model presented by MAFFI and JAYAKAR (1981). Zygotes are formed by random union of gametes and there is no variation in fecundity. Let Xx females produce a fraction f of X gametes and $(1 - f)$ of x gametes. Males with genotypes XY, Xy, xY and xy produce X (or x) gametes with frequencies m_1, m_2, m_3, and m_4 respectively, and they produce Y (or y) gametes with frequencies $(1 - m_1)$, $(1 - m_2)$, $(1 - m_3)$, and $(1 - m_4)$ respectively. The recursion equations are constructed by considering the frequencies of the gametes produced by females and males:

$$X_f' = X_f X_m + [X_m(1 - X_f) + X_f(1 - X_m)]f$$

$$X_m' = \frac{X_f Y m_1 + X_f(1 - Y)m_2}{X_f Y m_1 + X_f(1 - Y)m_2 + (1 - X_f)Y m_3 + (1 - X_f)(1 - Y)m_4}$$

$$Y' = \frac{X_f Y(1 - m_1) + (1 - X_f)Y(1 - m_3)}{X_f Y(1 - m_1) + X_f(1 - Y)(1 - m_2) + (1 - X_f)Y(1 - m_3) + (1 - x_f)(1 - Y)(1 - m_4)}. \quad (12)$$

The Jacobian matrix for this system of equations evaluated at the trivial equilibrium $\hat{X}_f = \hat{X}_m = \hat{Y} = 0$ is

$$J = \begin{bmatrix} f & f & 0 \\ m_2/m_4 & 0 & 0 \\ 0 & 0 & (1 - m_3)/(1 - m_4) \end{bmatrix}. \quad (13)$$

From the characteristic equation of this matrix we get the following two conditions which must both be satisfied for this equilibrium to be stable:

$$m_3 > m_4, \quad \text{and} \quad f[1 + (m_2/m_4)] < 1. \quad (14)$$

The local stability conditions for the remaining fixation equilibria are:

Equilibrium	Stability Conditions
$\hat{X}_f = \hat{X}_m = 0, \hat{Y} = 1$	$m_4 > m_3$ and $f[1 + (m_1/m_3)] < 1$
$\hat{X}_f = \hat{X}_m = 1, \hat{Y} = 0$	$m_1 > m_2$ and $(1 - f) \cdot [1 + (m_4/m_2)] < 1$
$\hat{X}_f = \hat{X}_m = \hat{Y} = 1$	$m_2 > m_1$ and $(1 - f) \cdot [1 + (m_3/m_1)] < 1$.

(15)

All four corner equilibria can be simultaneously unstable, and when they are there exists an interior equilibrium at

$$\hat{X}_f = \frac{m_4 - m_3}{m_1 - m_2 - m_3 + m_4}$$

$$\hat{X}_m = \frac{(m_4 - m_3)(1 - f)}{(m_4 - m_3)(1 - 2f) + f(m_1 - m_2 - m_3 + m_4)} \tag{16}$$

$$\hat{Y} = \frac{\hat{X}_f m_2 - \hat{X}_m \hat{X}_f (m_2 - m_4) - \hat{X}_m m_4}{\hat{X}_f (m_2 - m_1)}.$$

The Jacobian matrix evaluated at this equilibrium can be simplified somewhat because $\partial Y'/\partial Y = 1$. The characteristic equation is

$$-\lambda^3 + \lambda^2(1 + J_{11}) + \lambda(J_{12}J_{21} - J_{11}) + J_{12}J_{23}J_{31} - J_{12}J_{21} = 0. \tag{17}$$

This equation yields one negative real root and a pair of conjugate complex roots, but the real part of the imaginary roots is always greater in magnitude than one. This means that the interior equilibrium is always unstable, and that the trajectory of chromosome frequencies when perturbed from this equilibrium is an expanding spiral (Figure 3). The meiotic drive model can have the unusual property of all fixation points unstable and a unique unstable interior. The usual condition for "protected polymorphism" is met, and yet no stable polymorphism exists. The actual population trajectory cycles to frequencies arbitrarily close to fixation, so even though the fixations are unstable, the biologically meaningful interpretation of this model is that it cannot maintain a polymorphism.

X- and Y-linked meiotic drive and viability: The final model to be considered allows pleiotropic effects on the X and Y chromosomes such that both meiotic behavior and viability differ among genotypes. The parameterization that will be used is the same as in the previous two models, only now we have both components of selection operating each generation. Recurrence equations can again be expressed in terms of the frequencies of the X and Y chromosomes in male and female gametes. The recurrence equations are:

$$X_f' = \frac{X_f X_m v_1 + [X_m(1 - X_f) + X_f(1 - X_m)]f v_2}{\bar{w}_f}$$

$$X_m' = \frac{X_f Y m_1 v_4 + X_f(1 - Y)m_2 v_5}{\bar{w}_{mx}} \tag{18}$$

$$Y' = \frac{X_f Y(1 - m_1)v_4 + (1 - X_f)Y(1 - m_3)v_6}{\bar{w}_{my}}$$

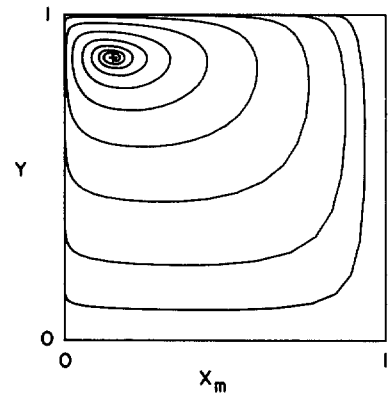

FIGURE 3.—Dynamics of chromosome frequencies under the pure meiotic drive model. For this simulation, $m_1 = 0.15$, $m_2 = 0.81$, $m_3 = 0.13$, $m_4 = 0.07$ and $f = 0.34$. This case has four unstable corner equilibria and an unstable interior equilibrium located at $\hat{X}_m = 0.15$, $\hat{X}_f = 0.083333$, $\hat{Y} = 0.868182$ (indicated by "+").

where

$$\bar{w}_f = X_f X_m v_1 + [X_m(1 - X_f) + X_f(1 - X_m)]v_2 + (1 - X_f)(1 - X_m)v_3$$

$$\bar{w}_{mx} = X_f Y m_1 v_4 + X_f(1 - Y)m_2 v_5 + (1 - X_f)Y m_3 v_6 + (1 - X_f)(1 - Y)m_4 v_7$$

and

$$\bar{w}_{my} = X_f Y v_4(1 - m_1) + X_f(1 - Y)v_5(1 - m_2) + (1 - X_f)Y v_6(1 - m_3) + (1 - X_f)(1 - Y)v_7(1 - m_4).$$

This recurrence system has the same four trivial equilibria as the previous two models. The Jacobian at the first fixation equilibrium ($\hat{X}_f = \hat{X}_m = \hat{Y} = 0$) is

$$J = \begin{bmatrix} \frac{v_2 f}{v_3} & \frac{v_2 f}{v_3} & 0 \\ \frac{m_2 v_5}{m_4 v_7} & 0 & 0 \\ 0 & 0 & \frac{v_6(1 - m_3)}{v_7(1 - m_4)} \end{bmatrix}. \tag{19}$$

The characteristic equation factors, as in (7), to

$$(J_{31} - \lambda)(\lambda^2 - J_{11}\lambda - J_{12}J_{21}) = 0. \tag{20}$$

Local stability is assured when the largest eigenvalue is less than one, and this occurs when the following two conditions are met:

$$\frac{v_6(1 - m_3)}{v_7(1 - m_4)} < 1$$

and, (21)

$$\frac{v_2 f}{v_3}[1 + (m_2 v_5/m_4 v_7)] < 1.$$

The conditions for local stability of the other fixation equilibria are:

Equilibrium	Stability Conditions
$\hat{X}_f = \hat{X}_m = 0,\ \hat{Y} = 1$	$\dfrac{v_7(1-m_4)}{v_6(1-m_3)} < 1,$ $\dfrac{v_2 f}{v_3}\left(1 + \dfrac{m_1 v_4}{m_3 v_6}\right) < 1$
$\hat{X}_f = \hat{X}_m = 1,\ \hat{Y} = 0$	$\dfrac{v_4(1-m_1)}{v_5(1-m_2)} < 1,$ $\dfrac{v_2(1-f)}{v_1}\left(1 + \dfrac{m_4 v_7}{m_2 v_5}\right) < 1$
$\hat{X}_f = \hat{X}_m = \hat{Y} = 1$	$\dfrac{v_5(1-m_2)}{v_4(1-m_1)} < 1,$ $\dfrac{v_2(1-f)}{v_1}\left(1 + \dfrac{m_3 v_6}{m_1 v_4}\right) < 1.$

(22)

All four of the fixations can be simultaneously unstable, but when they are the existence of an interior equilibrium is not guaranteed. There can exist a pair of edge equilibria with $\hat{Y} = 0$ and $\hat{Y} = 1$. Setting $\hat{Y} = 0$ and solving the resulting recursion we get:

$$\hat{X}_f = \frac{m_4 v_3 v_7 - f(m_2 v_5 + m_4 v_7)v_2}{m_2 v_1 v_5 + m_4 v_3 v_7 - (m_2 v_5 + m_4 v_7)v_2}$$
$$\hat{X}_m = \frac{\hat{X}_f m_2 v_5}{\hat{X}_f m_2 v_5 + (1 - \hat{X}_f)m_4 v_7}. \tag{23}$$

The other edge equilibrium is found at:

$$\hat{Y} = 1$$
$$\hat{X}_f = \frac{m_3 v_3 v_6 - f(m_1 v_4 + m_3 v_6)v_2}{m_1 v_1 v_4 + m_3 v_3 v_6 - (m_1 v_4 + m_3 v_6)v_2} \tag{24}$$
$$\hat{X}_m = \frac{\hat{X}_f m_1 v_4}{\hat{X}_f m_1 v_4 + (1 - \hat{X}_f)m_3 v_6}.$$

There are two conditions that must be satisfied for these equilibria to be stable. The first is that both the numerator and denominator of the respective $\hat{X}_f$ must be less than zero. This implies that heterozygotes must have the largest harmonic mean fitness (compounding viability and meiotic drive), where the fitness of "heterozygous" males is the average of the two male types. Note that existence of the equilibria (23) and (24) requires either this kind of "overdominance" or else "underdominance," where in the latter both numerator and denominator of $\hat{X}_f$ are greater than zero. The second condition that must be met to assure the stability of (23) is:

$$\frac{\hat{X}_f v_4(1 - m_1) + (1 - \hat{X}_f)v_6(1 - m_3)}{\hat{X}_f v_5(1 - m_2) + (1 - \hat{X}_f)v_7(1 - m_4)} < 1. \tag{25}$$

For (24) to be stable, the second condition is the same as (25) but with the inequality reversed. Condition (25) precludes the invasion of the rare Y chromosome.

Whenever an interior equilibrium exists, it is unique, but unlike the pure drive model, it is not necessary that all four corners be unstable in order for the interior to exist. By setting the recurrence equation $Y' = Y$, we can solve directly for $\hat{X}_f$, and this can be used to solve the remaining variables at the interior equilibrium:

$$\hat{X}_f = \frac{v_7(1 - m_4) - v_6(1 - m_3)}{v_4(1 - m_1) - v_5(1 - m_2) - v_6(1 - m_3) + v_7(1 - m_4)}$$
$$\hat{X}_m = \frac{\hat{X}_f(1 - \hat{X}_f)(v_2 - v_3) - (1 - f)v_2\hat{X}_f}{\hat{X}_f(1 - \hat{X}_f)(2v_2 - v_1 - v_3) - (1 - 2f)v_2\hat{X}_f - fv_2} \tag{26}$$
$$\hat{Y} = \frac{\hat{X}_m\hat{X}_f(m_4 v_7 - m_2 v_5) - \hat{X}_m m_4 v_7 + \hat{X}_f m_2 v_5}{\hat{X}_m\hat{X}_f(m_1 v_4 - m_2 v_5 - m_3 v_6 + m_4 v_7) + \hat{X}_m(m_3 v_6 - m_4 v_7) - \hat{X}_f(m_1 v_4 - m_2 v_5)}.$$

The Jacobian of the recurrence system evaluated at this point yields a characteristic equation of the same form as the meiotic drive model, since $\partial Y'/\partial Y = 1$. In all cases the characteristic equation will have one negative real root. The other roots may (1) both be real and less than one, giving a stable interior point; (2) both be real and greater than one giving an unstable point; (3) be complex with real part less than one in modulus, giving a stable point with spiral approach; or (4) be complex with real part greater than one, giving an unstable point or a stable limit cycle. Figure 4 illustrates the range of frequency dynamics that are possible under this model.

Numerical simulations: Simulations were performed by choosing parameters and initial frequencies from a uniform distribution, and iterating the appropriate recursions. Although there is no prior biological basis for sampling parameters from any particular distribution, this approach can give a measure of the plausibility of the model's relevance. Since the pure viability and the meiotic drive models never maintain polymorphism, the only purpose in simulating them is to verify the correctness of the algebra. No case of stable Y polymorphism was found for either model, even though the sampling effort was 100,000 trials. For the pleiotropic model with joint effects on viability and meiotic drive, another 100,000 sets of viability and drive parameters were chosen, and populations were simulated until either 20,000 generations or a stable equilibrium had been attained. If 20,000 generations passed with no equilibrium, another test was performed to detect cycling. These simulation results were compared to the dynamics predicted from the conditions for existence and stability of equilibria, and no exceptions to the predicted local stabilities were found. Results of the simulations appear in Table 1.

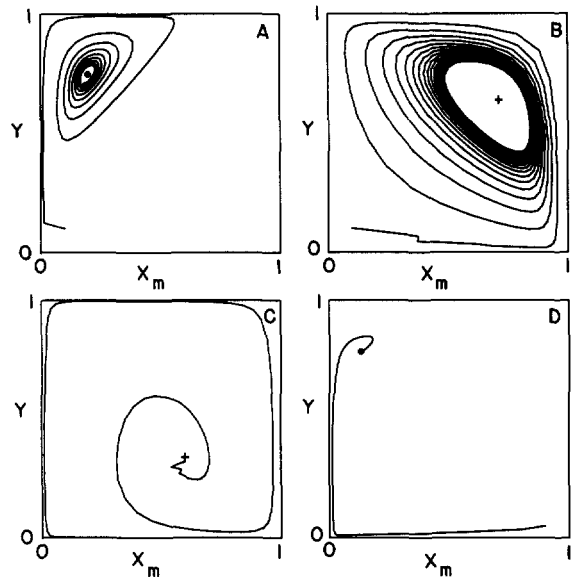

FIGURE 4.—Examples of the dynamical behavior of the model with joint effects of viability and meiotic drive due to both the X and Y chromosomes. The parameter values are:

	v_1	v_2	v_3	v_4	v_5	v_6	v_7	m_1	m_2	m_3	m_4	f
A	0.082	0.448	0.277	0.474	0.636	0.281	0.644	0.850	0.036	0.395	0.895	0.361
B	0.550	0.948	0.933	0.145	0.294	0.334	0.496	0.019	0.996	0.172	0.095	0.484
C	0.790	0.710	0.890	0.320	0.300	0.780	0.370	0.500	0.770	0.850	0.210	0.580
D	0.510	0.950	0.230	0.510	0.880	0.100	0.980	0.380	0.450	0.100	0.930	0.180

Panels A and D have unique stable interior points, B shows a stable cycle, and C has a unique unstable interior point.

TABLE 1

Numerical simulations of models of Y chromosome selection: 100,000 random initial conditions were simulated for each

Result	Meiotic drive only	Viability only	Drive and viability
Fixation[a]	100,000	68,923	68,427
X polymorphism	0	31,077	30,116
$X + Y$ polymorphism	0	0	1,114
Stable cycle	0	0	343

[a] A chromosome frequency exceeds 0.99999.

The conditions for the maintenance of a stable interior point are rather stringent in the sense that not many random combinations of parameters will satisfy the conditions.

DISCUSSION

The four models presented above provide some understanding of the potential for natural selection to maintain polymorphism of the Y chromosome. The results provide a compelling argument concerning the maintenance of Y-linked variation: because it is so "difficult" for selection models to maintain Y polymorphisms, it seems unlikely that such polymorphisms are maintained by balancing selection. A similar argument was also made for the low likelihood of adaptive polymorphism in mtDNA (CLARK 1984). The observation of mtDNA and Y-DNA variation then suggests that if the polymorphisms are maintained by natural selection, it is not through simple constant fitness models. The Y-linked color polymorphisms in poeciliid fish (KALLMAN 1970), which have three sex-determining chromosomes, may involve an implicit frequency dependence (ORZACK *et al.* 1980). The fact that the Y-autonomous model can never maintain a polymorphism suggests that either Y-linked variation is neutral, that it involves frequency dependent fitnesses or geographic structuring, or that it interacts with another chromosome. The potential of interaction with the X chromosome was explicitly explored with the remaining three models.

The second model allowed segregation of two X chromosomes and two Y chromosomes, and each resulting genotype could have a specified viability. Direct solution of the stability of the unique interior equilibrium showed that this model could never maintain a stable polymorphism of the Y chromosomes. Recombination between a sex-determining locus and a locus that confers differences in viabilities can, however, stabilize internal polymorphisms (A. G. CLARK, unpublished data). Along an "edge" of the frequency simplex where the population was fixed for one Y chromosome or the other, the model behaved like the classical X-linked viability model. Heterozygote advantage in females is neither necessary nor sufficient to

maintain an X polymorphism, and at such a polymorphic equilibrium, there need not be an excess of female heterozygotes (BENNETT 1957, HALDANE and JAYAKAR 1964, CANNINGS 1967). The trajectory of mean fitness can show damped oscillations if there is a difference between X_f and X_m, but along the $Y = 0$ and $Y = 1$ edges, the harmonic mean fitness is maximized. This analog to the fundamental theorem of natural selection has been described for the X chromosome (HARTL 1971, 1972).

Regulation of the regular meiotic disjunction of sex chromosomes is particularly important because of the influence on sex ratio. Most of the theoretical interest in meiotic drive of sex chromosomes has focused on X-linked factors that modify segregation. An important result of this work is that modifier alleles that distort segregation can increase in frequency, so that Mendelian segregation of sex chromosomes is unstable with respect to the invasion of such modifier alleles (EDWARDS 1961; THOMSON and FELDMAN 1975). The observation of Y-linked meiotic drive in *Aedes aegypti* (HASTINGS and WOOD 1978) and Y-dependent segregation variation in *Drosophila melanogaster* (CLARK 1987) further motivates the study of Y-linked segregation modifiers. MAFFI and JAYAKAR (1981) analyzed a two-locus model with one locus determining sex and the other determining segregation. When there is no recombination between these two loci, their model is the same as our second model except that we allow meiotic drive in heterozygous females. The dynamics of the two models is qualitatively the same: no polymorphism is possible, but all four fixation equilibria can be simultaneously unstable. When the four corners are unstable, there exists a unique unstable interior equilibrium, and the system shows diverging cyclical dynamics. KARLIN and LESSARD (1986) show that a stable interior equilibrium is possible in a one-locus multiple allele Y-drive model if the frequency of sib-mating is sufficiently high.

The final model allows both viability and meiotic drive to be determined by a pair of alleles at a homologous locus on the X and Y chromosomes. Pleiotropic effects of this type are not unlikely, since many well documented systems of meiotic drive are balanced by deleterious effects on viability. This model can have at most one interior equilibrium, and it is the only model presented that can maintain a stable Y-linked polymorphism. Numerical simulations show however that less than two percent of the parameter space admits such a polymorphism. Experimental data on ribosomal DNA variation on the X and Y chromosomes of *D. melanogaster* (WILLIAMS *et al.* 1987) are broadly consistent with the prediction of the model. There is greater among-continent variation in Y-linked sequences, perhaps due to the more rapid fixation of Y-linked variants, and inability of natural selection to maintain polymorphisms.

Although classical theoretical approaches such as this one are useful in providing a framework for constructing hypotheses about the maintenance of variation, an explanation of Y-linked polymorphism cannot ignore the molecular processes of amplification and gene conversion. There are many additional avenues to explore the theory of Y chromosome evolution. Most of the interest has centered around the mechanism for generating morphologically distinct sex chromosomes, invoking processes of recombination suppression and gene inactivation on the Y chromosome (OHNO 1967; BULL 1983). There is evidence in *Drosophila miranda* (STEINEMANN 1982) and in snakes (JONES and SINGH 1982) that repetitive DNA "invades" the Y chromosome, although the mechanism is not clear. In a recent review PIMPINELLI *et al.* (1986) describe the unusual structure of the *D. melanogaster* Y chromosome. As in most organisms, it is mostly heterochromatic, but there are six segments that are required for male fertility. These fertility factors are unique among eukaryotic genes in that they span up to 100 kb of DNA. There is clearly a mechanism for homogenizing tandem repeat copies of rDNA, since species differences can be profound, yet there is far greater homogeneity among copies within a species (WILLIAMS, DESALLE and STROBECK 1985). The data on sequence organization will have direct impact on the approaches both theoretical and experimental population geneticists take in investigating the evolution of the Y chromosome.

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