28 yr old man we found eight cells in diakinesis/metaphase I and two cells in metaphase II. Two of the cells in diakinesis/metaphase I contained what we considered to be twenty-two autosomal bivalents; an XX bivalent and a separate Y (Fig. 1), and three cells contained what seemed to be an XY bivalent (Fig. 2). Three cells in diakinesis and both cells in metaphase II were unsuitable for detailed examination.

Table 1. CHROMOSOME COUNT DISTRIBUTION

<43	43	44	45	46*	47	48	Total
1	3	1	4	7	83	1	100

* Karyotypic analysis of cells with forty-six chromosomes

Four cells lack a chromosome in the 21–22 *Y* group
One cell lacks a chromosome in the 6–12 *X* group
One cell lacks a chromosome in the 16–18 group
One cell lacks a chromosome in the 19-20 group

We have some reservations about our interpretation because the quality of the cells was not very high and the cells themselves were too few. The finding of meiotic divisions in one of four patients with typical Klinefelter's syndrome– in whom examination of mitotic metaphases prepared from cells from peripheral blood gave very little evidence of XY, XXY mosaicism (Table 1)—is, however, encouraging and the study will be continued.

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GENERAL

Mean Fitness Increases when Fitnesses are Additive

FISHER'S fundamental theorem of natural selection[1] states that for a random mating population with fitnesses dependent on the genetic constitution at a single locus, the mean fitness of the population increases with time. This is true for an arbitrary number of possible alleles at the locus and for arbitrary fitness values.

Moran[2] has shown that if fitness depends on the genetic constitution at two loci, then the mean fitness of the population can decrease monotonically with time. Two questions arise from this disturbing result: (i) can any restrictions be placed on the fitnesses to secure an analogue of Fisher's theorem; (ii) does any function other than the mean fitness increase monotonically with time? I should like to give an answer to (i) which is applicable in a wide range of important cases by proving the following theorem.

My theorem is that if fitnesses are assumed additive over loci, then the mean fitness of the population increases monotonically in time, irrespective of the number of loci on which fitness depends, of the number of possible alleles at each locus and of the linkage arrangement between the loci. (Fitnesses which are "additive over loci" are those for which, if fitness is supposed to depend on the genotypic constitution at k loci, the fitness of any individual can be expressed as a sum of k terms, the ith term in the sum being characteristic of the individual's genotype at the ith such locus.)

We consider the proof in detail only for the case of two loci A and B, admitting two alleles each: A_1, A_2 and B_1, B_2. Because fitnesses are assumed additive over loci, we can write the fitness matrix in the form

	A_1A_1	A_1A_2	A_2A_2
B_1B_1	u_1+v_1	u_1+v_2	u_1+v_3
B_1B_2	u_2+v_1	u_2+v_2	u_2+v_3
B_2B_2	u_3+v_1	u_3+v_2	u_3+v_3

If the frequencies of the gametes A_1B_1, A_2B_1, A_1B_2 and A_2B_2 which make up the zygotes in generation t are denoted c_1, c_2, c_3, c_4, then the mean fitness W of the population in generation t is given, according to Moran[3], by

$$W = u_1(c_1+c_2)^2 + 2u_2(c_1+c_2)(c_3+c_4) + u_3(c_3+c_4)^2 + v_1(c_1+c_3)^2 + 2v_2(c_1+c_3)(c_2+c_4) + v_3(c_2+c_4)^2 \quad (1)$$

W depends on the frequencies c_1+c_2 and c_1+c_3 only, for we can write $c_3+c_4=1-(c_1+c_2)$, $c_2+c_4=1-(c_1+c_3)$. Note that c_1+c_2 is the frequency of the gene B_1 and c_1+c_3 is the frequency of the gene A_1. The frequencies c'_1, c'_2, c'_3, c'_4 of the gametes which make up the zygotes in generation $t+1$ are found from the recurrence relations (76)–(79) in ref. 3. Given c_1, c_2, c_3 and c_4, the frequencies $c'_1+c'_2$ and $c'_1+c'_3$ are independent of the degree of linkage between A and B loci. Thus the mean fitness W' of the population in generation $t+1$—given by equation (1) with W' replacing W and c'_i replacing c_i, and therefore depending on $c'_1+c'_2$ and $c'_1+c'_3$ only—will itself be independent of the degree of linkage between A and B loci, once the values c_i are given. In particular, it will be equal to the mean fitness in generation $t+1$ for the particular case $R=0$. But it is a classical result that when $R=0$ the population behaves as one where the fitness depends on one locus with four alleles, and Fisher's theorem asserts that for this latter situation, $W' \geqq W$. Thus, because W' is independent of R, $W' \geqq W$ for all values of R.

The key point in this proof is that W depends only on c_1+c_2 and c_1+c_3 (that is, only on gene frequencies). This makes its generalization to an arbitrary number of alleles and an arbitrary number of loci almost immediate, for in all such cases W again depends only on gene frequencies. Given the frequencies of the gametes making the zygotes of generation t, the frequencies of the genes making the zygotes of generation $t+1$ are independent of any linkage arrangement between the loci. It follows immediately that the mean fitness in generation $t+1$ is again identical to that which obtains when all crossing-over frequencies are zero, and, because this latter case can again be viewed as one where fitnesses depend on the (very large number of) alleles at a single locus, we again have $W' \geqq W$ in the completely general case. Kingman's results[4] show further that $W' > W$ unless the population is at an equilibrium point.

This result opens up a range of problems which will be most usefully associated with the forthcoming results of Moran[5] concerning stability points and convergence behaviour in the same model.

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