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GENE INTERACTION AND INBREEDING DEPRESSION

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Jack Lester King

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Among the hypotheses for the causes of inbreeding depression and hybrid vigor reviewed by CROW (1948), those considered most probable involve the unmasking and masking of harmful recessives. The deleterious recessives might be maintained in the population through mutation pressure or through the selective superiority of heterozygotes over homozygotes. Another possible and potent basis of inbreeding depression and hybrid vigor, which does not postulate recessivity of deleterious alleles, will be presented here.

In an accompanying article I have suggested that quasi-continuous variation may be a major component of the variation in fitness of outbred populations. If this is in fact the case, inbreeding of previously outbred populations can be expected to cause a loss of fitness in the population, as well as an increase in deviant phenotypes of threshold characters.

Quasi-continuous genetic systems can be analyzed in terms of an underlying continuous normal parameter to which a number of genes make additive contributions; the phenotype is invariant over a range of genetic and environmental variability, but is sharply discontinuous beyond thresholds at one or both extremes of the distribution (WRIGHT 1934; GRÜNEBERG 1952; KING 1965). Inbreeding in a previously outbred population increases the genetic componet of variance, and therefore the proportion of transthreshold values (Fig. 1).

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INBREEDING AND QUASI-CONTINUOUS SYSTEMS

The nongenetic and genetic components of variance in the normal parameter are σ_c^2 and σ_{de}^2, respectively, and the total variance is σ_{cde}^2. Individuals for which the value of the parameter is below the threshold at $-z$ standard deviations from the mean are eliminated by natural selection; the rate of such eliminations is the relative area of the tail, $A_{(z)}$. A degree of inbreeding F would increase the genetic component of variance by $1 + F$, and raise the total variance to $\sigma_{cde}^2 + F\sigma_{de}^2$. The threshold would remain at $-z\,\sigma_{cde}$ below the mean; since the standard deviation would have increased with inbreeding, however, the equivalent threshold on the unit normal curve would be at

$$-z\sigma\sqrt{\frac{\sigma_{cde}^2}{\sigma_{cde}^2 + F\sigma_{de}^2}} = -z'\sigma$$

below the mean. The genetic death rate would be increased to $A_{(z')}$. The observed degree of inbreeding depression would be

$$\frac{A_{(z')} - A_{(z)}}{1 - A_{(z)}} .$$

If the nongenetic component of variance were negligible or, more plausibly, if it remained proportional to the genetic variance, then $z' = z/\sqrt{1+F}$.

The proportion of lethal or deviant phenotypes due to quasi-continuous genetic systems increases radically and nonlinearly with F (Table I and Figs. 1 and 2). For instance, for a system in which the threshold is four standard deviations

from (above or below) the mean and the nongenetic variance is proportional to the genetic variance, sib mating (F = 0.25) increases the proportion of transthreshold values more than fivefold; complete homozygosity (F = 1.00) increases the proportion 73-fold. The corresponding increases are greater for systems with thresholds farther from the mean. If there should be recessivity among the deleterious alleles in the system, the increases would be even more marked. The predicted nonlinearity of inbreeding depression with F is an adequate basis for a test of the hypothesis.

INBRED LINES AND HYBRID VIGOR

Continued inbreeding stabilizes genotypes and greatly reduces the genetic variance within lines. Quasi-continuous systems may become stabilized near their optima, so that no further losses occur from them. Some such systems, however, may become genetically fixed near enough to their threshold values that nongenetic variation continues to cause a substantial reduction in average fitness. When the transthreshold phenotype is not lethal, the deviant phenotype itself may become fixed. Such reductions in fitness would not be subject to alleviation by natural selection, unless favorable mutations should occur within previously fixed lines.

Hybrids between separately obtained inbred lines should show none of this reduction in fitness, unless one or more of the same systems should happen to have become fixed in both lines. Since the F_1 hybrids have very little genetic variability, reductions in fitness due to quasi-continuous systems should be minimal.

CANALIZATION

Quasi-continuous systems with both upper and lower thresholds are said to be canalized. Inbreeding increases transthreshold values at both ends of the distribution [Fig. 2].

SUMMARY

Inbreeding in previously outbred populations increases the genetic variance, and thus greatly increases the proportion of transthreshold values of the underlying parameters of quasi-continuous and canalized systems. If quasi-continuous variation is a major component of genetic variation in fitness and vigor, increases in frequency of transthreshold values may be a major factor in inbreeding depression. Unlike previous hypotheses, the presently suggested basis for inbreeding depression and hybrid vigor does not depend on the unmasking of deleterious recessives. The degree of inbreeding depression is predicted to be nonlinear with the degree of inbreeding; on this basis the hypothesis is testable.

LITERATURE CITED

CROW, J. F., 1948 Alternative hypotheses of hybrid vigor. Genetics 33: 477-487.

GRÜNEBERG, H., 1952 Genetical studies on the skeleton of the mouse. IV. Quasi-continuous variation. J. Gen. 51: 95-114.

KING, J. L., 1965 Gene interaction and the relationship between mutation and genetic death. (Accompanying article submitted to Genetics).

WRIGHT, S., 1934 The results of crosses between inbred strains of guinea pigs, differing in number of digits. Genetics 19: 537-551.

TABLE I

The effect of inbreeding (F) on the frequencies of lethal or deviant phenotypes due to quasi-continuous systems

Hypothetical examples[a]	F = 0	F=0.125	F=0.25	F=0.50	F=0.75	F=1.00
(1) $z = 3\sigma_{cde}$, $\sigma_c^2 = 0$	0.00135	0.00233	0.00368	0.00734	0.0117	0.0170
(2) $z = 4\sigma_{cde}$, $\sigma_c^2 = 0$	3.17×10^{-5}	9.15×10^{-5}	17.9×10^{-5}	54.7×10^{-5}	123×10^{-5}	232×10^{-5}
(3) $z = 4\sigma_{cde}$, $\sigma_c^2 = \frac{1}{3}(\sigma_{cde}^2)$	3.17×10^{-5}	5.91×10^{-5}	10.78×10^{-5}	26.0×10^{-5}	54.7×10^{-5}	96.8×10^{-5}
(4) $z = 4\sigma_{cde}$, $\sigma_c^2 = \frac{1}{2}\sigma_{cde}^2$	3.17×10^{-5}	5.22×10^{-5}	9.15×10^{-5}	17.9×10^{-5}	31.4×10^{-5}	54.7×10^{-5}
(5) $z = 5\sigma_{cde}$, $\sigma_c^2 = 0$	0.0287×10^{-5}	0.118×10^{-5}	0.41×10^{-5}	2.25×10^{-5}	7.84×10^{-5}	20.8×10^{-5}

[a] The nongenetic component of variance in each of the first, second, and fifth examples is either negligible or remains proportional to the genetic variance. In the third and fourth examples, the nongenetic components of variance are constants equal to one third and one half the total variance of the outbred population, respectively.

FIGURE CAPTIONS

Fig. 1. Relative increases in genetic death rate with increases in degree of inbreeding [F]. The genetic death rate of each of four hypothetical examples is taken as one with outbreeding. The genetic death rates are nonlinear with F. See Table I.

Fig. 2. Increased genetic variance causes an increase in the proportion of the distribution which falls above and below the two thresholds of a canalized system [not to scale].

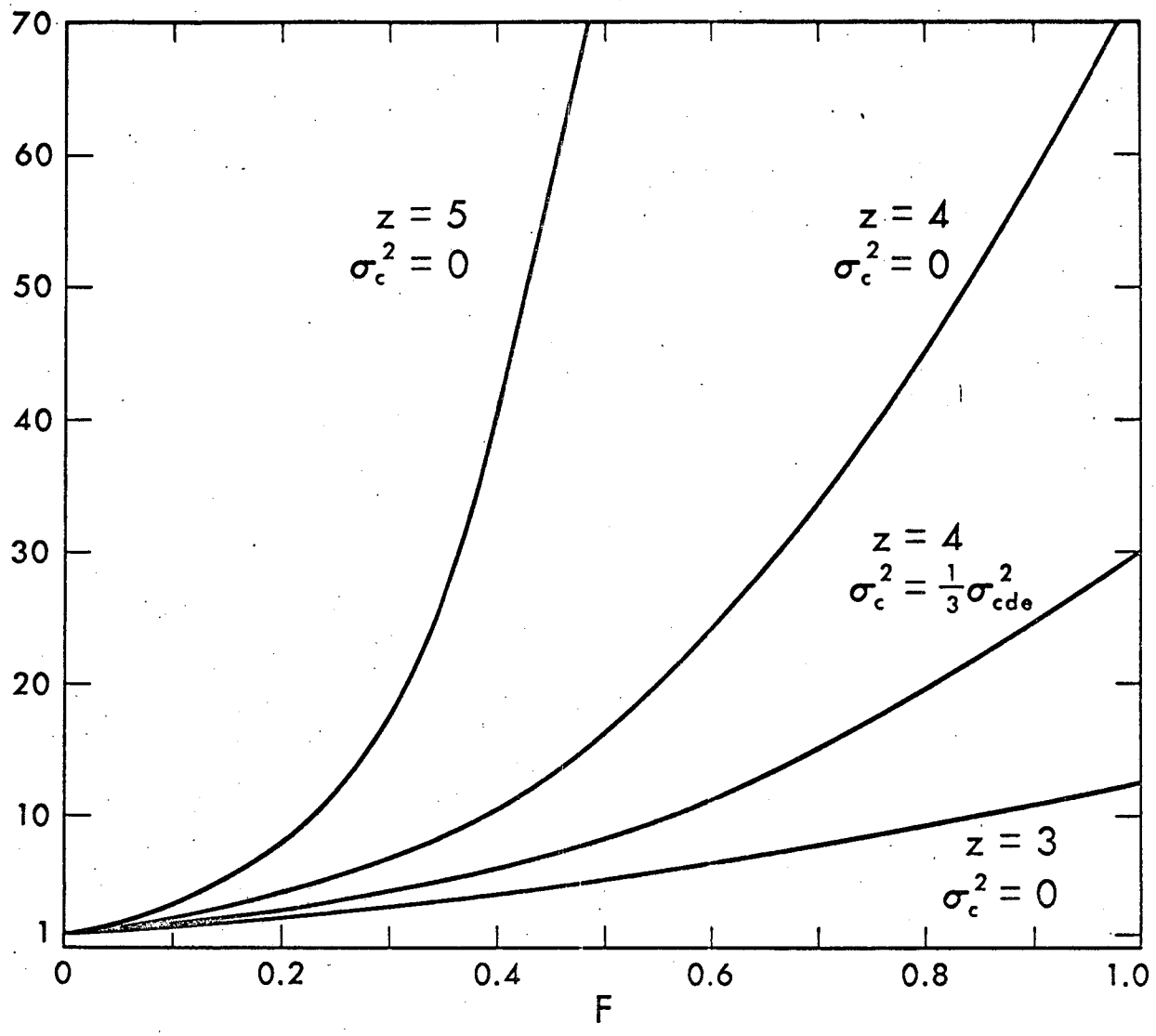

Fig. 1

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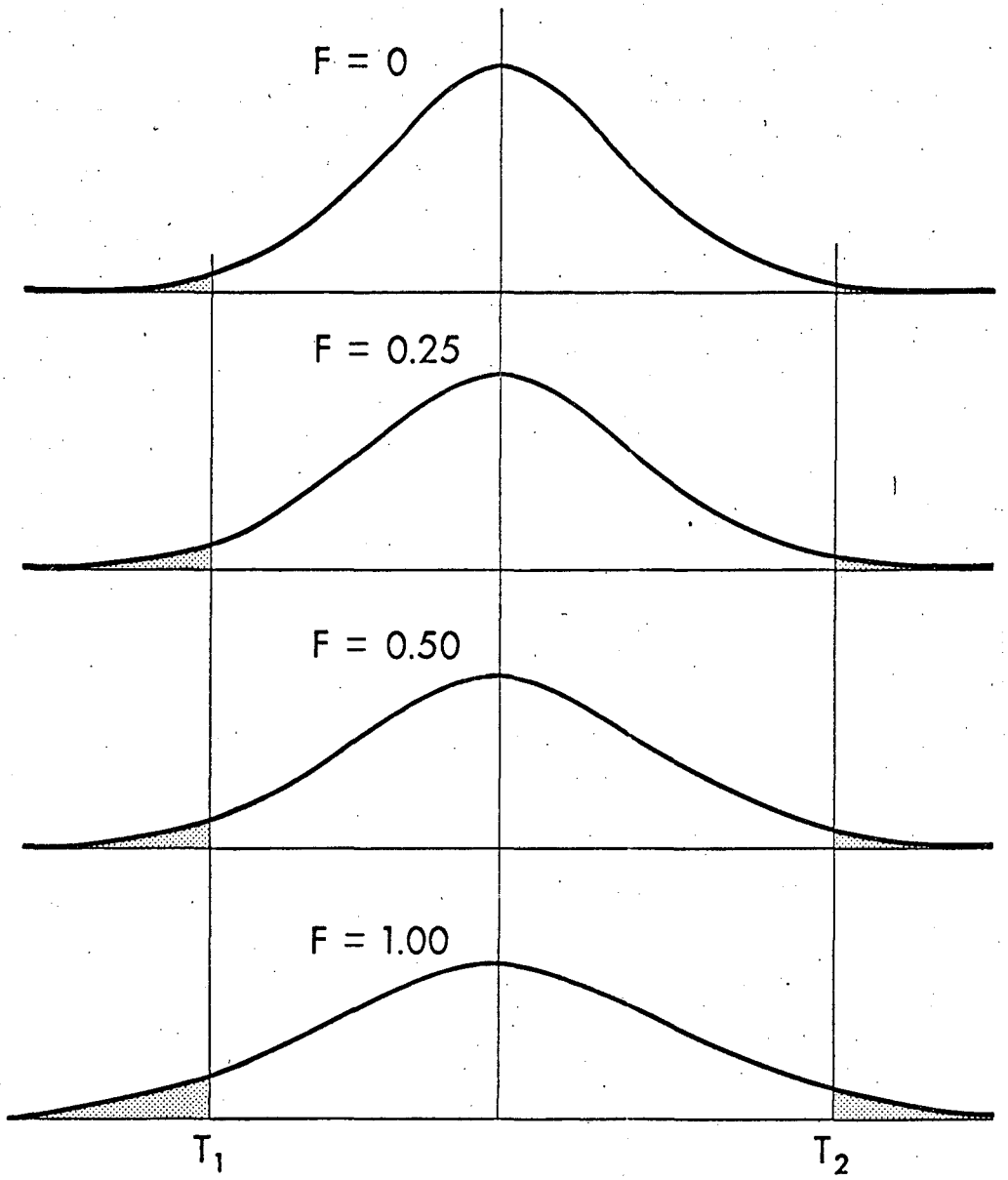

Fig. 2

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