

**University of California**

**Ernest O. Lawrence  
Radiation Laboratory**

**TWO-WEEK LOAN COPY**

*This is a Library Circulating Copy  
which may be borrowed for two weeks.  
For a personal retention copy, call  
Tech. Info. Division, Ext. 5545*

**GENE INTERACTION AND INBREEDING DEPRESSION**

**Berkeley, California**

## **DISCLAIMER**

This document was prepared as an account of work sponsored by the United States Government. While this document is believed to contain correct information, neither the United States Government nor any agency thereof, nor the Regents of the University of California, nor any of their employees, makes any warranty, express or implied, or assumes any legal responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by its trade name, trademark, manufacturer, or otherwise, does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof, or the Regents of the University of California. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof or the Regents of the University of California.

UNIVERSITY OF CALIFORNIA

Lawrence Radiation Laboratory  
Berkeley, California

AEC Contract No. W-7405-eng-48

GENE INTERACTION AND INBREEDING DEPRESSION

Jack Lester King

August 9, 1965

## GENE INTERACTION AND INBREEDING DEPRESSION<sup>1</sup>

Jack Lester King

Lawrence Radiation Laboratory and Donner Laboratory  
University of California, Berkeley

August 9, 1965

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 component of variance, and therefore the proportion of transthreshold values (Fig. 1).

---

<sup>1</sup> This investigation was supported in part by a postdoctoral fellowship from the National Institute of Arthritis and Metabolic Diseases and in part by the U. S. Atomic Energy Commission.

## INBREEDING AND QUASI-CONTINUOUS SYSTEMS

The nongenetic and genetic components of variance in the normal parameter are  $\sigma_c^2$  and  $\sigma_{de}^2$ , respectively, and the total variance is  $\sigma_{cde}^2$ . 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 <sup>a</sup>	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) $z = 4\sigma_{cde}$ $\sigma_c^2 = 0$	$3.17 \times 10^{-5}$	$9.15 \times 10^{-5}$	$17.9 \times 10^{-5}$	$54.7 \times 10^{-5}$	$123 \times 10^{-5}$	$232 \times 10^{-5}$
(3) $z = 4\sigma_{cde}$ $\sigma_c^2 = \frac{1}{3}(\sigma_{cde}^2)$	$3.17 \times 10^{-5}$	$5.91 \times 10^{-5}$	$10.78 \times 10^{-5}$	$26.0 \times 10^{-5}$	$54.7 \times 10^{-5}$	$96.8 \times 10^{-5}$
(4) $z = 4\sigma_{cde}$ $\sigma_c^2 = \frac{1}{2}\sigma_{cde}^2$	$3.17 \times 10^{-5}$	$5.22 \times 10^{-5}$	$9.15 \times 10^{-5}$	$17.9 \times 10^{-5}$	$31.4 \times 10^{-5}$	$54.7 \times 10^{-5}$
(5) $z = 5\sigma_{cde}$ $\sigma_c^2 = 0$	$0.0287 \times 10^{-5}$	$0.118 \times 10^{-5}$	$0.41 \times 10^{-5}$	$2.25 \times 10^{-5}$	$7.84 \times 10^{-5}$	$20.8 \times 10^{-5}$

<sup>a</sup> 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].

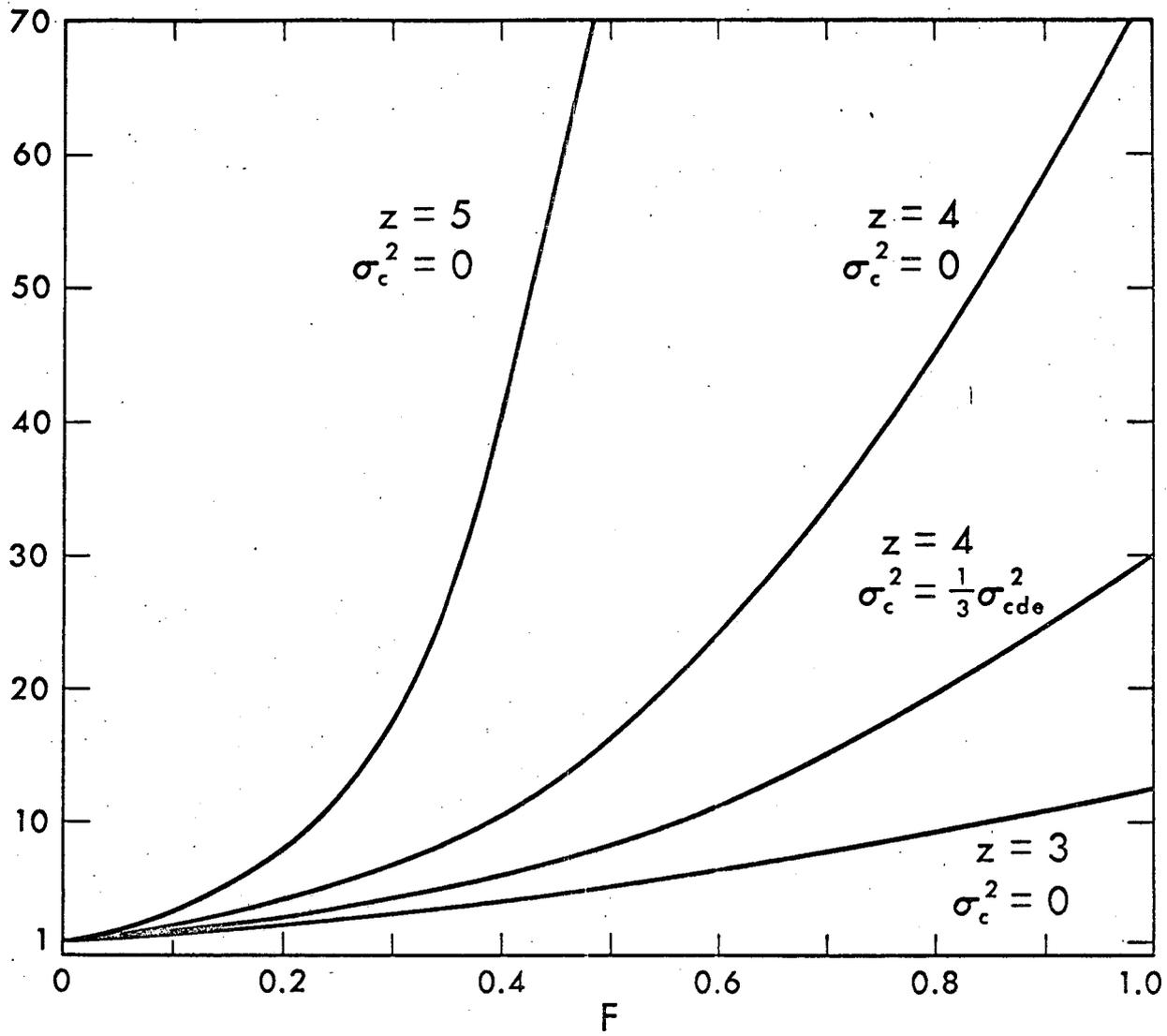


Fig. 1

MUB-7671

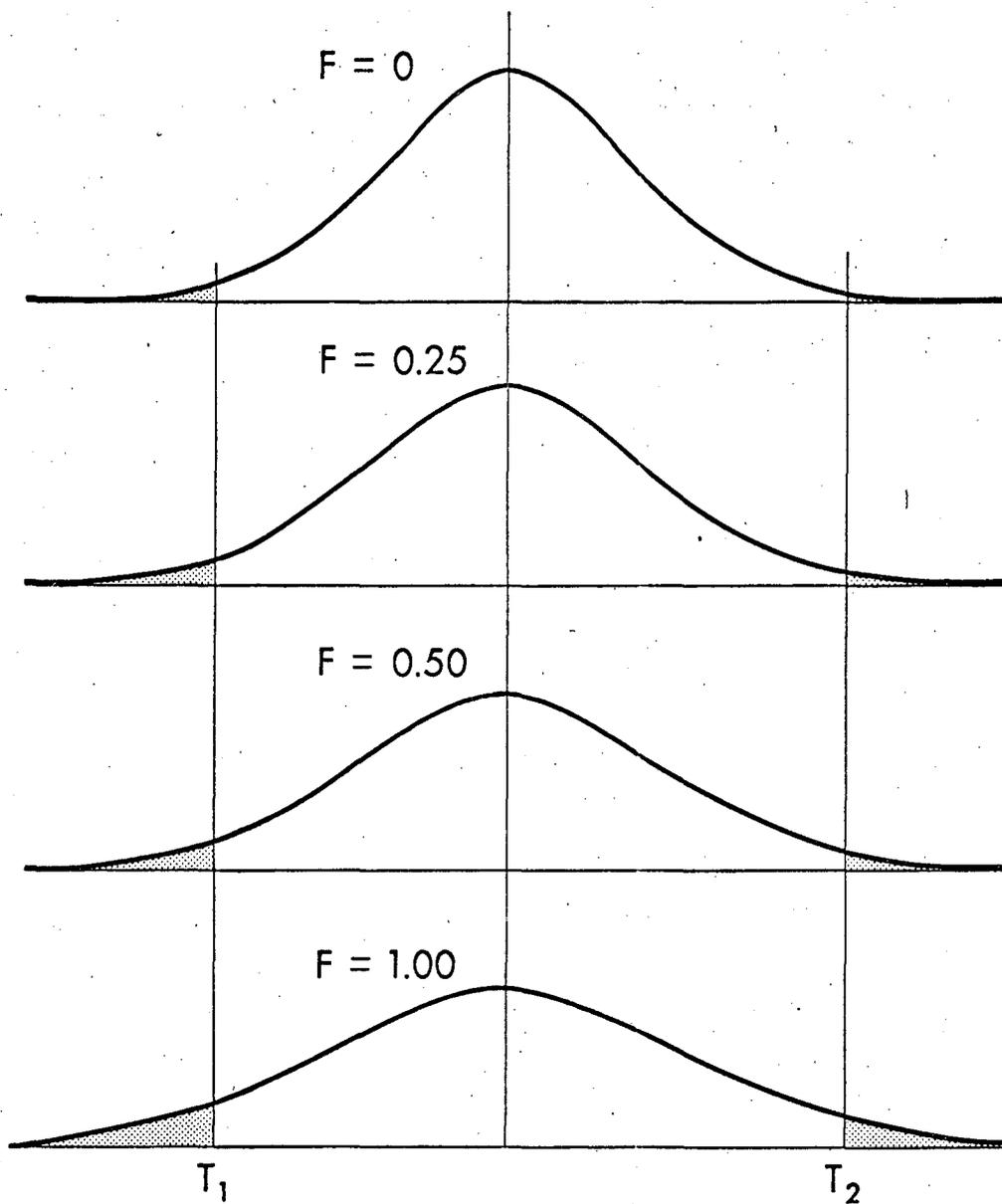


Fig. 2

MUB-7607

This report was prepared as an account of Government sponsored work. Neither the United States, nor the Commission, nor any person acting on behalf of the Commission:

- A. Makes any warranty or representation, expressed or implied, with respect to the accuracy, completeness, or usefulness of the information contained in this report, or that the use of any information, apparatus, method, or process disclosed in this report may not infringe privately owned rights; or
- B. Assumes any liabilities with respect to the use of, or for damages resulting from the use of any information, apparatus, method, or process disclosed in this report.

As used in the above, "person acting on behalf of the Commission" includes any employee or contractor of the Commission, or employee of such contractor, to the extent that such employee or contractor of the Commission, or employee of such contractor prepares, disseminates, or provides access to, any information pursuant to his employment or contract with the Commission, or his employment with such contractor.

