that various mono- or polyvalent alcohols interfere with these excitations, while other substances, like sugars, promote them.

It seems probable that dimerizations are involved in these phenomena, as described by Scheibe,[2] Rabinowitch and Epstein,[3] and others. If so, the excitations could be symbolized by the following equations:

$$\begin{aligned} &A + B \rightarrow AB, \\ &h\nu + AB \rightarrow A^{**}B \rightarrow A^{*}B^{*}, \quad \text{or} \\ &h\nu + AB \rightarrow A^{*}B^{*}, \end{aligned}$$

A and B standing for the two dimerizing molecules and the asterisk for their excitation. Why dimerization facilities transition into the triple state has to be decided by further studies.

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*MALE SEGREGATION RATIO ADVANTAGE AS A FACTOR IN MAINTAINING LETHAL ALLELES IN WILD POPULATIONS OF HOUSE MICE**

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It has been observed that certain populations of wild house mice (*Mus musculus*), comprising most of those sampled from different parts of the United States, contain heterozygotes for *t* alleles at locus *T*.[1] Since most of the alleles identified are recessive lethals,[2] the question arises as to what agencies are responsible for the high frequencies of lethals in wild populations.

One such agency has been identified by estimating the relative frequencies of gametes containing + and *t* alleles in the progenies from male heterozygotes (+/*t* and *T*/*t*). The ratio of *t* gametes to all gametes has been estimated from samples of several males each from twelve different populations. These ratios have been found to vary between 0.90 and 0.99; that is, *t* gametes are always transmitted by males to the great majority of offspring.[2] Transmission by female heterozygotes occurs in normal proportions (0.5).

This peculiarity (the cytogenetic mechanism for which is unknown) has been called "segregation ratio" abnormality.[3] Clearly this leads to a tendency for such alleles to establish themselves in populations by what has been termed "segregation ratio advantage." Prout[4] has examined, in a preliminary way, the relations between *m*, the male segregation ratio, lethality of *tt* homozygotes, and the gene frequency of *t* under random mating. He has shown that values of *m* exist sufficient to compensate for lethality and maintain the *t* allele at an equilibrium frequency; the conclusion was that segregation ratio advantage is an evolutionary force that must be evaluated.

Prout[4] obtained his formulas on the assumption that m was the same in both sexes. He then remarked that the same results would hold if the segregation ratio differed in the two sexes, provided that m was taken to be the arithmetic mean of the two values. In a personal communication Prout pointed out that this remark was incorrect and gave our formulas (3) and (5) for the case where only one sex has an anomalous segregation ratio. Since Prout is not publishing his results, these formulas are rederived below. Tables and graphs are presented, discussing this new derivation and its implications, including some properties not previously foreseen.

The Mathematical Model.—In seeking a simple model which relates male segregation ratio and gene frequency at equilibrium, the following assumptions are made:

1. Only two alleles + and t exist at this locus in the model population; + is completely dominant over t.
2. The adaptive values of the genotypes dealt with are $+/+ = 1$; $+/t = 1$; $t/t = 0$.
3. Mutation rates are negligible.
4. Mating is at random in an infinite reproductively isolated population.
5. The female segregation ratio is 0.5.

The terms used in deriving equilibrium values are as follows:

1. Parameters of the nth generation:
   q_n = frequency of t after selection (i.e., among adults),
   $1 - q_n$ = frequency of + after selection (i.e., among adults),
   D_n = frequency of $+/+$ before selection (i.e., before death of lethals),
   H_n = frequency of $+/t$ before selection (i.e., before death of lethals),
   R_n = frequency of t/t before selection (i.e., before death of lethals).
2. Male segregation ratio:
$$m = \frac{\text{Number of gametes transmitting } t}{\text{Total number of functioning gametes from each male heterozygote.}}$$
3. Frequency of $+/t$ heterozygotes after selection, $a = 2q_n$.
   Frequency of $+/+$ homozygotes after selection, $b = 1 - 2q_n$.

It follows that

$$a = 2q_n = \frac{H_n}{D_n + H_n}. \tag{1}$$

It should be noted that in the present paper q_n denotes the gene frequency after selection, whereas in Prout [4] q_n denotes the frequency before selection.

Since the gametic frequencies for a male heterozygote are m (t) to $(1 - m)$ (+), while those for females are one-half (t) to one-half (+), we see by Table 1 that the progeny of a mating of two heterozygotes are in the ratio of $(1 - m)/2$ $(+/+)$ to $(1 - m)/2 + m/2$ $(+/t)$ to $m/2$ (t/t). Outcomes of other matings can be obtained similarly.

TABLE 1

Gametes of Male	Gametes of Female: +	Gametes of Female: t	Total
+	$(1 - m)/2$	$(1 - m)/2$	$1 - m$
t	$m/2$	$m/2$	m
Total	$1/2$	$1/2$	1

With random mating the frequency of the three genotypes in the $(n + 1)$th generation before selection will be as given in Table 2.

TABLE 2

Type of Mating (♀ × ♂)	Frequency of Type of Mating	Frequency of Genotypes in $(n + 1)$th Generation before Selection		
		+/+	+/t	t/t
+/t × +/t	a^2	$a^2(1 - m)/2$	$a^2/2$	$a^2m/2$
+/t × +/+	ab	$ab/2$	$ab/2$	...
+/+ × +/t	ab	$ab(1 - m)$	abm	...
+/+ × +/+	b^2	b^2	...	...

Adding the results from Table 2, we have

$$D_{n+1} = b^2 + \frac{a^2(1 - m)}{2} + \frac{ab(3 - 2m)}{2},$$

$$H_{n+1} = \frac{a^2}{2} + \frac{ab(2m + 1)}{2}, \tag{2}$$

and

$$R_{n+1} = \frac{a^2m}{2}.$$

But from equation (1) we have

$$q_{n+1} = \frac{H_{n+1}}{2(D_{n+1} + H_{n+1})},$$

and since equations (2) give H_{n+1} and D_{n+1} in terms of a and b, which in turn are equal to $2q_n$ and $1 - 2q_n$, respectively, we can express q_{n+1} in terms of q_n and m as

$$q_{n+1} = \frac{q_n(2m - 4mq_n + 1)}{2(1 - 2mq_n^2)}. \tag{3}$$

If we now set $q_{n+1} = q_n$, we arrive at the equilibrium formula:

$$\hat{q} = {}^1/_2 \pm \frac{\sqrt{m(1 - m)}}{2m}. \tag{4}$$

Considering the solution $\hat{q} = {}^1/_2 + \sqrt{m(1 - m)}/2m$, it is clear that such a solution is not consistent with reality, since, no matter what value m takes, $\hat{q}$ is greater than 0.5, and the frequency of $+/t$ heterozygotes after selection, or $2\hat{q}$, is greater than 1.0, which is impossible.

It can be easily demonstrated that the other solution,

$$\hat{q} = {}^1/_2 - \frac{\sqrt{m(1 - m)}}{2m}, \tag{5}$$

holds if and only if m is greater than 0.5, i.e., in order for $\hat{q}$ to be positive, $\sqrt{m(1 - m)}/m$ must be less than 1, and this is true if and only if m is greater than 0.5, since, if

$$\frac{\sqrt{m(1 - m)}}{m} < 1,$$

then

$$\frac{1-m}{m} < 1,$$

and

$$\frac{1}{m} - 1 < 1,$$

or

$$\frac{1}{m} < 2, \qquad m > 0.5.$$

Furthermore, it is clear that any consecutive pair of steps imply each other, so that, if $m > 0.5$, then $\sqrt{m(1-m)}/m < 1$. It is clear that if m is less than 0.5, $\hat{q}$ is 0. It follows from equations (5) and (2) that the genotypic frequencies before selection at equilibrium are

$$\begin{aligned} \hat{D} &= 1 - (1+2m)\hat{q} - 2m\hat{q}^2, \\ \hat{H} &= \hat{q}(1+2m) - 4m\hat{q}^2, \\ \hat{R} &= 2m\hat{q}^2. \end{aligned} \tag{6}$$

If we consider $\hat{q}$, $2\hat{q}$, $1 - 2\hat{q}$ $\hat{D}$, $\hat{H}$, $\hat{R}$, and as functions of m (Fig. 1 and Tables 3 and 4), we note an expected rise in $\hat{q}$ and $2\hat{q}$ from a minimum of 0 to a maximum of

TABLE 3

m	$\hat{q}$	$2\hat{q}$	$1-2\hat{q}$	$\hat{D}$	$\hat{R}$
0.00	0	0	1	1	0
0.10	0	0	1	1	0
0.20	0	0	1	1	0
0.30	0	0	1	1	0
0.40	0	0	1	1	0
0.50	0	0	1	1	0
0.55	0.048	0.095	0.905	0.903	0.003
0.60	.092	0.184	.816	.808	.010
0.65	.133	0.266	.734	.717	.023
0.70	.173	0.345	.655	.637	.042
0.75	.211	0.423	.577	.539	.067
0.80	.250	0.500	.500	.450	.100
0.85	.290	0.580	.420	.360	.143
0.90	.33	0.667	.333	.267	.200
0.95	.385	0.771	.229	.165	.282
1.00	0.500	1.000	0.000	0.000	0.500

TABLE 4

m	$\hat{H}$	m	$\hat{H}$	m	$\hat{H}$	m	$\hat{H}$
0.00	0.000	0.50	0.000	0.82	0.470	0.92	0.544
.10	.000	.55	.095	.84	.488	0.94	.551
.20	.000	.60	.182	.86	.505	0.96	.554
.30	.000	.65	.260	.88	.520	0.98	.547
0.40	0.000	0.70	0.331	0.90	0.533	1.00	0.500
		.75	.394				
		.80	.450				

0.5 and 1.0, respectively, and the corresponding expected decrease of $1 - 2\hat{q}$. We would intuitively expect the corresponding rise in $\hat{R}$, and decrease in $\hat{D}$, but the rise

of $\hat{H}$ to a maximum and its subsequent decline to 0.5 at $m = 1$ are somewhat unexpected.

A vague but intuitive way of viewing this behavior of $\hat{H}$ is to note that $\hat{H}$ depends on the frequency of both t and + and that ratios lower than this would produce too few t alleles and higher ratios would produce too few + alleles for a maximum $\hat{H}$.

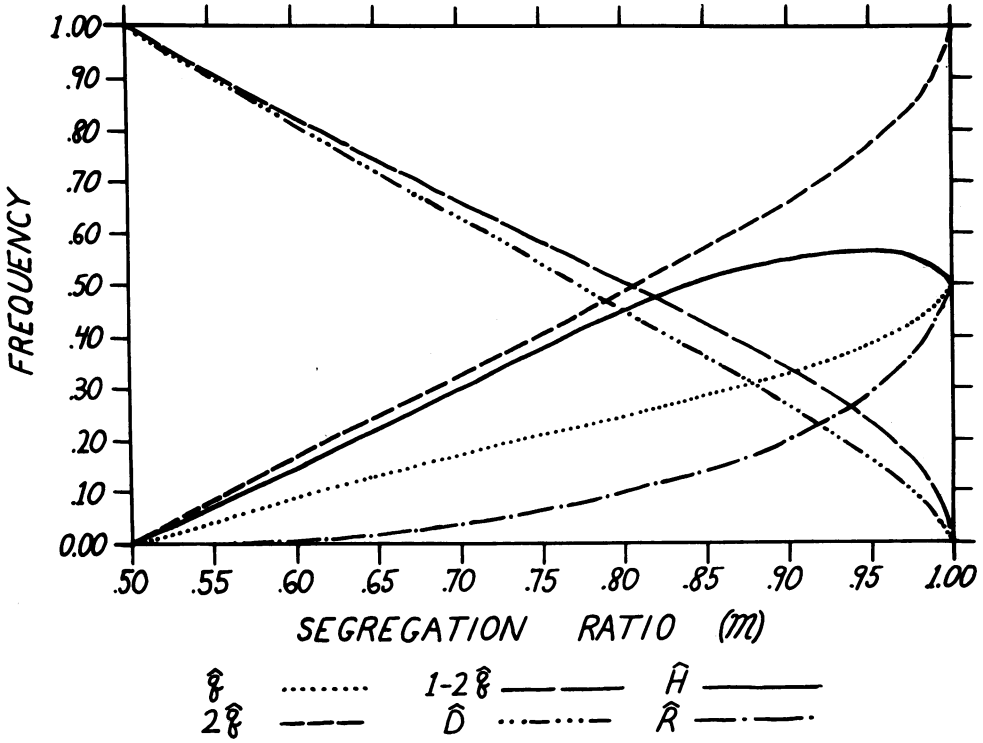

FIG. 1.—The equilibrium values of $\hat{q}$, $2\hat{q}$, $1 - 2\hat{q}$, $\hat{D}$, $\hat{H}$, and $\hat{R}$, are plotted against m, the segregation ratio. Numerical values are given in Tables 3 and 4.

The value of m for which $\hat{H}$ is maximum was obtained by setting

$$\frac{d\hat{H}}{dm} = 1 + \frac{2 - 2m - {}^1/_2 m}{2\sqrt{m(1-m)}} + \frac{\sqrt{m(1-m)}}{2m^2} = 0$$

and solving for m. $\hat{H}$ is found to attain its maximum value, viz., 0.554, when m is 0.959, as shown in Table 4 and Figure 1. It is a curious fact that this value of m is close to the average value of m found experimentally by testing males heterozygous for each of thirteen t-alleles each derived from a different wild ancestor. The average value of the segregation ratios was about 0.96.[5]

It was seen in plotting the frequency of t against generations for $m = 0.5, 0.6, 0.7, 0.8, 0.9$, and 1.0, with an arbitrary set of starting frequencies of +/+ and +/t before selection, that the equilibrium value of t was approached to within 2 per cent by the sixtieth generation. Figure 2 illustrates this, employing $m = 0.9$.

Summary.—Genes such as the t alleles in house mice, which are lethal when homozygous and produce abnormal segregation ratios in male heterozygotes, are

considered from the point of view of their population dynamics. Prout has given formulas which he erroneously stated apply to this situation. In correspondence he has pointed out the error and given the correct formulas, which is rederived in the present paper. These formulas hold for all values of m, the proportion of functional male gametes from $+/t$ males. For $m > 1/2$, t reached an equilibrium frequency at $q = 1/2 - \sqrt{m(1-m)}/2m$ in adults.

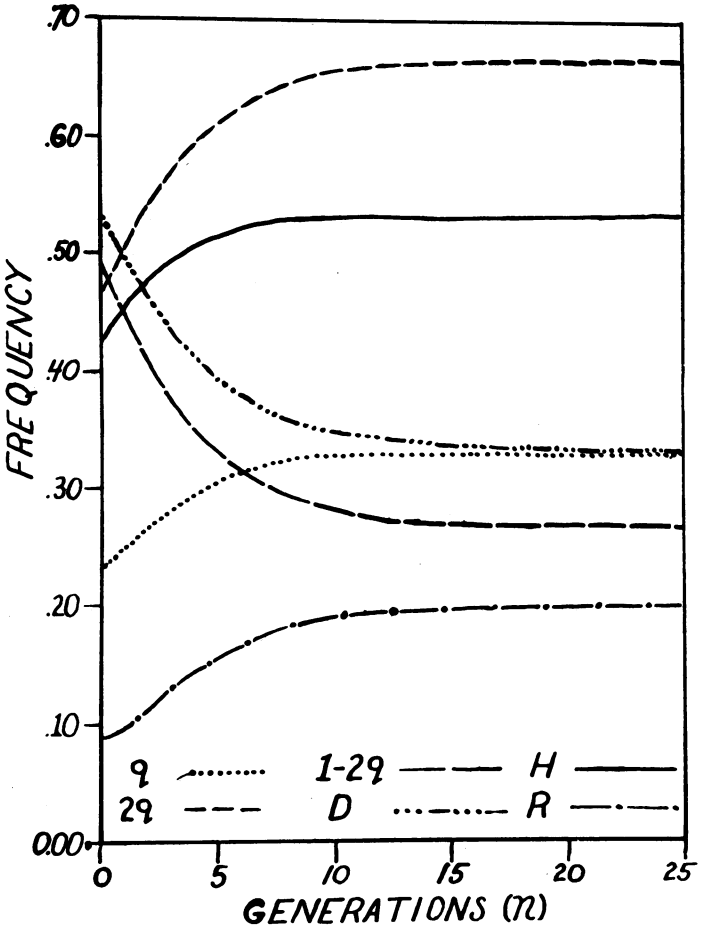

FIG. 2.—Values of q, $2q$, $1 - 2q$, D, H, and R are plotted as they change for each successive generation, starting with the arbitrary set of initial values $D = 0.49$, $H = 0.42$, $R = 0.09$, for $m = 0.9$. The graph illustrates the rapid approach of all variables toward their equilibrium values, even if the starting values differ markedly from the latter.

Tables and graphs of q as a function of time and of the equilibrium values of various gene and genotypic frequencies both before and after selection are given as functions of m, and agreement of these with what one might expect is apparent except in the case of the frequency of heterozygotes $+/t$ before the death of lethal zygotes, which reaches a maximum at $m = 0.959$.

Grateful thanks are due to Dr. Timothy Prout, of the University of California, who introduced me to this problem, to Professor L. C. Dunn, under whose guidance this paper was written, and to Professor Howard Levene, who checked the consistency of the model and made many helpful suggestions.

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*EVIDENCE OF EVOLUTIONARY FORCES LEADING TO THE SPREAD OF LETHAL GENES IN WILD POPULATIONS OF HOUSE MICE**

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A population changes in an evolutionary sense when there is a shift prevailingly in one direction of the proportions of genotypes of which it is composed. It is for this reason that agencies tending to change these proportions, derived primarily from the relative frequencies of gene forms or alleles, are referred to as "evolutionary forces."

Genotypic diversity, the usual condition of all cross-fertilizing populations in nature, tends to remain constant unless the gene frequencies are altered by one or more of these evolutionary forces. For any one pair of alleles, such as A and a, with frequencies q and $1 - q$, the constant or equilibrium frequencies of genotypes under random mating have long been known to be of the form $q^2AA + 2q(1 - q)Aa + (1 - q)^2aa = 1$.

Agencies hitherto recognized as leading to alteration of the equilibrium frequencies are (1) mutation pressure, changes from A to a and a to A at unequal rates; (2) natural selection, that is, unequal fitness or adaptive values of the several genotypes, such as lethality or lesser fertility of AA, Aa, or aa, relative to the others; (3) random fluctuation of gene frequencies in small sections of the population (random genetic drift); (4) differential migration of genotypes into or out of the population.

Equality of the genotypes in all these respects is of course the condition for maintenance of constant proportions.

The main purpose of this report is to present some new facts indicating that a fifth evolutionary force is primarily responsible for the maintenance of high frequencies of certain lethal genes in populations of wild house mice and to examine the effect of this force on equilibrium frequencies of such lethals. This fifth force I refer to as segregation ratio, since it alters the basic Mendelian proportion of functional gametes produced by heterozygotes Aa. In all the above equilibrium com-