STUDIES OF NATURAL POPULATIONS OF *MUS*. II. POLYMORPHISM AT THE *T* LOCUS[1]

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Studies of a number of natural populations of the house mouse, *Mus musculus*, by Dunn and his collaborators (Dunn and Morgan, 1953; Dunn, 1955; Dunn and Suckling, 1956; Dunn, Beasley, and Tinker, 1960; Anderson, 1964) have revealed the existence of a widespread polymorphism at the *T* locus. This polymorphism consists of a series of alleles which are concerned with the development of axial structures in the caudal region of the mouse. These alleles, the *t*-alleles, are divided into two major groups depending on their effect in the homozygous condition. Some of the *t*-alleles, when present in the homozygous condition (t/t) result in prenatal mortality and are described as lethals. Other *t*-alleles in the homozygous condition cause only male sterility, all homozygotes being viable. In view of the selective disadvantage of the *t*-alleles, their ubiquity is unexpected. The major force keeping these alleles in natural populations is an abnormal transmission ratio which favors the *t*-bearing sperm of heterozygous ($+/t$) males (Dunn, 1957).

Since polymorphism at the *T* locus is widespread in natural populations of *Mus musculus*, an examination of the *t*-alleles was included in this study to support conclusions about breeding structure reached from data on other loci (Petras, 1965, 1967). In the process, information was obtained about: (1) the frequency of *t*-alleles in wild populations, (2) the fluctuation in gene frequencies over a four year period, (3) the ratio of lethal and viable *t*-alleles, (4) the number of *t*-alleles in closely associated localities, and (5) additional data on the abnormal transmission ratio in wild heterozygous males. Furthermore, an attempt was made to fit a deterministic population model to the empirical data.

DETECTION AND CHARACTERIZATION OF *t*-ALLELES

Most of the mice used in this study came from farms southwest of Ann Arbor, Michigan. These have been described earlier (Petras, 1967). Six animals from a single dwelling just south of Windsor, Ontario, were also tested.

The wild-caught mice on being brought into the laboratory were bred to animals which were heterozygous for the dominant brachyury allele (T) at the *T* locus. These animals ($T/+$) are characterized by a short, blunt tail. In the homozygous condition the *T* allele is lethal. The offspring of a mating between $+/t$ animals and $T/+$ mice belong to one of three phenotypes: brachy or short blunt-tailed ($T/+$), normal-tailed ($+/+$ or $+/t$), and tailless (T/t).

Frequencies of the four genotypes are dependent on the transmission ratio (m) of the alleles in the gametes. Since most *t*-alleles are transmitted at a significantly higher ratio in the sperm of heterozygous males the usual genotypic ratios of 1:1:1:1 are rarely observed among the offspring. Therefore, if the male parent is $+/t$, since the mean male transmission ratio is 0.935 for viable *t*-alleles and 0.956 for lethal *t*-alleles (Dunn, 1960), then the frequencies

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of $T/+$ and $+/t$ offspring approaches 0.5 in a mating of $+/t$ males and $T/+$ females. However, if the female is $+/t$ and the reciprocal mating is made then the four genotypes expected in the offspring will be in equal frequency.

Since the t-allele transmission ratio in sperm of heterozygous ($+/t$) males has been found to be above 0.5 and usually between 0.8 and 1.0, and since the transmission ratio in ova of $+/t$ females is 0.5, the probability of not detecting a t-allele in a cross between $+/t$ and $T/+$ mice is 0.5 or less per offspring. Therefore, by classifying a minimum of seven T-bearing offspring ($T/+$ or T/t^x), the genotype of a wild mouse of either sex can be determined with a probability of error of less than 0.01.

The tailless offspring obtained from each wild mouse in the mating described above were then used to set up balanced lines by brother-sister matings. In this series of matings both members of a mating pair possessed the same allele (t^x), and produced three genotypes.

Parents: male $T/t^x \times$ female T/t^x

Offspring:	
$0.5(1-m)$	T/T (lethal during development)
0.5	T/t^x (tailless)
$0.5m$	t^x/t^x (normal-tailed if t^x is viable)

If t^x is lethal in the homozygous condition, then no normal-tailed mice (t^x/t^x) should be observed at birth and since T/T animals die in early development only the tailless phenotype is found. However, if tailed mice were found in 5% or more of the survivors then t^x was considered to be viable. Five per cent is an arbitrary value selected because it readily divides the t-alleles studied into two groups on the basis of $T/t^x \times T/t^x$ mating results: those with less than 2% normal-tailed progeny and those having more than 16% normal-tailed offspring. When less than 2% normal-tailed mice appear these are attributed to either the mutation of one t-allele into another and subsequent complementation of old and transformed t-alleles or to the interaction of the genetic background and a usually lethal genotype at the T locus.

The transmission ratio was obtained by dividing the number of tailless offspring by the total of brachy and tailless offspring (i.e., all T-bearing progeny) obtained in crosses between wild and brachy animals. This gives a slight overestimate of the transmission ratio because a small percentage of the brachy animals have tails which appear normal.

Once the various t-allele lines were established, complementation tests were made to (1) determine differences among the various lethal t-alleles isolated, and (2) shed light on possible differences among the viable t-alleles isolated. These tests consisted of mating animals of two t-lines in the following manner:

Parents: $T/t^{x1} \times T/t^{x2}$

Offspring: $T/T, T/t^{x1}, T/t^{x2}, t^{x1}/t^{x2}$

Four genotypes should result. T/T is of course lethal and was not found. T/t^{x1} and T/t^{x2} are both tailless and were always found. If both t^{x1} and t^{x2} are lethal when homozygous, then if more than 5% of the offspring are tailed they were considered to be t^{x1}/t^{x2} where t^{x1} and t^{x2} are not identical, but complement one another. If less than 5% normal-tailed mice are found then t^{x1} and t^{x2} were considered non-complementary. These may prove to be identical, but unfortunately, there is as yet no clear-cut method by which identity of non-complementary t-alleles can be established. A study of the effect of two t-alleles on embryogeny might further resolve the differences between two such alleles. However, no such attempt was made in the present study.

Frequencies of t-alleles in Natural Populations

Frequency estimates of t-alleles (both lethal and viable) in samples collected over a two- to four-year period from various buildings at five localities south of Ann Arbor are presented in Table 1. These estimates are based on the number of

TABLE 1. *Frequency estimates of t-alleles* in the samples obtained from populations of individual buildings over several years. Numbers in parentheses represent animals with at least 7 T-bearing progeny.*

	1959	1960	1961	1962
G. Lindeman:				
Toolshop	.25 (2)	.00 (2)	.17 (3)	.00 (4)
Lean-to	.33 (3)	.00 (3)		
Granary	.17 (3)			.19 (13)
Chicken coop	.50 (2)			
Double garage	.33 (3)		.50 (1)	.00 (1)
Small barn		.00 (5)	.00 (2)	
Chicken house		.06 (9)	.00 (12)	.00 (1)
Corn crib			.00 (1)	.00 (1)
POOLED	.308 (13) ± .119**	.026 (19) ± .026	.053 (19) ± .056	.125 (20) ± .059
Mamarrow:				
Chicken coop	.00 (1)	.50 (2)	.20 (5)	.17 (3)
Hog house	.37 (3)	.00 (2)	.30 (5)	
Barn	.50 (1)	.00 (2)	.25 (2)	.00 (1)
Rabbit house		.33 (6)	.50 (3)	.25 (2)
Corn crib		.50 (2)	.00 (1)	.00 (2)
Granary		.36 (7)		.50 (1)
Old chicken coop		.17 (3)	.00 (1)	
Garage		.00 (1)		
POOLED	.200 (5) ± .152	.280 (25) ± .075	.265 (17) ± .096	.167 (9) ± .103
Guenther:				
Granary		.17 (3)	.17 (3)	.25 (6)
Corn crib		.13 (4)	.00 (1)	.25 (2)
POOLED		.143 (7) ± .107	.125 (4) ± .132	.25 (8) ± .135
O. Lindeman:				
Feed bin		.10 (5)		.00 (1)
Granary		.00 (2)	.50 (2)	.00 (4)
Corn crib		.06 (8)	.17 (3)	.00 (2)
Building not known			.00 (1)	
POOLED		.067 (15) ± .049	.250 (6) ± .156	.00 (7)
Barn on Textile Road			.100 (5) ± .320	.00 (3)
SUMMARY	.278 (18) ± .095	.144 (66) ± .035	.157 (51) ± .042	.128 (47) ± .039

* $f(t) = \frac{1}{2}f(+/t)$, where $f(t)$ is the frequency of the t-alleles and $f(+/t)$ is the frequency of the heterozygote.

** $s = \sqrt{\frac{pq(1+q)^2}{2n}}$, where s is the standard error, p is the frequency of $+$ allele, q is the frequency of the t-allele and n is the sample size (Cotterman, 1954).

heterozygotes in each sample and the assumption that each t-bearing mouse is heterozygous. Only four mice from the Windsor dwelling were completely tested, and these were $+/+$.

The frequency estimates of t-alleles vary considerably from one building to the next. There are, for instance, a number of samples from which t-alleles were absent (small barn, G. Lindeman, 1960; chicken

TABLE 2. *Distribution of lethal and viable* t*-alleles in the Ann Arbor area.*

Farm and Building	1959		1960		1961		1962	
	Viable	Lethal	Viable	Lethal	Viable	Lethal	Viable	Lethal
G. Lindeman (L)								
Toolshop (LTS)	3	0			1	0		
Lean-to (LLT)	1	2						
Granary (LG)	0	1					2	3
Chicken coop (LCC)	5	2						
Double garage (LDG)	0	1			0	1		
Small barn (LSB)								
Chicken house (LCH)			1	0				
Mamarrow (M)								
Chicken coop (MCC)			0	2	1	1	0	1
Hog house (MHH)	0	1			1	3		
Rabbit house (MRH)			3	0	2	2		
Corn crib (MKK)			1	0				
Granary (MG)			4	0				
Old chicken coop (MOCC)			0	1	0	1		
Barn (MB)	0	1						
Guenther (G)								
Granary (GG)					0	1	0	2
Corn crib (GKK)			0	1	1	0	0	1
O. Lindeman (O)								
Feed bin (OFB)			0	1	0	1		
Corn crib (OKK)			0	1	0	1		
Barn on Textile Road (B)					1	0		
POOLED	9	8	9	6	7	11	2	7

Percentage of *t*-bearing mice having lethal *t*-alleles in the pooled samples = 54.3.

house, G. Lindeman, 1961; granary, O. Lindeman, 1962), as well as samples in which all mice tested proved to be heterozygous (rabbit house, Mamarrow, 1961; chicken coop, G. Lindeman, 1959, in which five out of five mice tested, not all having 7 *T*-bearing progeny, were *t*-bearers). Of course, numerous samples had *t*-allele frequencies which fell between these two extremes. The overall frequency for the Ann Arbor data was found to be 0.156 ± .009.

Another interesting feature of the data is the fluctuation in the frequency estimates of the *t*-alleles from one year to the next in mice from a single locality and also in the pooled annual collections. The frequency of these alleles dropped from 0.308 ± .119 in the 1959 G. Lindeman collection, to 0.026 ± .026 in 1960, and then climbed to 0.125 ± .059 in 1962. On the Mamarrow farm the trend was reverse: 0.200 ± .152 in 1959, 0.280 ± .075 in 1960, 0.265 ± .096 in 1961 and 0.167 ± .103 in 1962.

The variations in *t*-allele frequencies observed between samples from single buildings and the frequency fluctuations observed from year to year in samples from a single building support the suggestion of Lewontin and Dunn (1960) that the low empirical *t*-allele frequency is due to the extinction of this allele in some isolates (populations from single buildings) and a gradual trend towards extinction in others. In only a few isolates does the *t*-allele reach or surpass Bruck's (1957) equilibrium frequency.

LETHAL AND VIABLE *t*-ALLELES

From the lines established to maintain the *t*-alleles isolated from the natural populations, information was obtained which

TABLE 3. *Transmission ratios found in wild mice bearing lethal* t*-alleles and the ratio of tailless to normal-tailed offspring in balanced lines.*

Sex	Number	Building and year	Tailless offspring	*t*-bearing mice	Transmission ratio	Balanced lethal mating results	
						Tailless	Normal
Male	129	MHH* – 59	4	11	.364	274	2
	155	MB – 59	2	6	.333	287	0
	424	MCC – 60	29	29	1.000	416	1
	509	MCC – 60	17	17	1.000	122	0
	512	MOCC – 60	18	20	.900	114	0
	1046	MHH – 61	23	28	.821	80	0
	1093	MHH – 61	34	38	.895	147	0
	1091	MRH – 61	26	27	.963	113	0
	1120	MRH – 61	28	31	.871	98	0
	960	MCC – 61	39	47	.830	80	0
	1021	MHH – 61	20	20	1.000	305	1
	1232	MCC – 62	23	24	.958	124	0
	4	LDG – 59	1	8	.125	242	0
	68	LG – 59	8	8	1.000	248	0
	948	LDG – 61	41	42	.976	377	2
	1249	LG – 62	11	12	.917	124	0
	1279	LG – 62	16	19	.842	62	0
	534	GKK – 60	19	19	1.000	82	1
	1045	GG – 61	12	12	1.000	126	0
	1252	GG – 62	13	13	1.000	119	0
	1270	GKK – 62	15	16	.938	156	0
	421	OKK – 60	24	28	.857	112	0
	455	OFB – 60	17	18	.944	384	8
	1026	OG – 61	17	20	.850	159	0
	1029	OKK – 61	9	9	1.000	81	0
	POOLED		466	522	.893		
Female	1053	MOCC – 61	3	6	.500	168	0
	1233	LG – 62	2	7	.280	137	0
	59	LLT – 59	10	23	.435	172	0
	61	LLT – 59	1	2	.500	120	0
	34	LCC – 59	5	5	1.000	472	0
	41	LCC – 59	3	3	1.000	104	0
	1185	GG – 62	5	10	.500	111	0
	POOLED		29	56	.518		

* See Table 3 for key to buildings.

made it possible to group the *t*-alleles into two categories: viable and lethal. A *t*-allele was classified as lethal if no more than 5% of the offspring in the balanced lethal lines had normal tails. No attempt was made to divided the viable *t*-alleles into subcategories. Table 2 summarizes the distribution of the two types of *t*-alleles in the areas sampled.

The occurrence of lethal and viable alleles was clustered, as would be expected if in some areas, especially the smaller buildings, several members of single family groups were collected. One interesting observation was the presence of both viable and lethal *t*-alleles in mice collected from a single building. This occurred seven times. Although, the presence of a single animal with a *t*-allele which differs from the rest can be readily attributed to a migrant, the presence of two mice bearing a *t*-allele which differs from the rest strongly suggests the coexistence of two different *t*-alleles, if not in the same deme

TABLE 4. *Transmission ratios found in wild mice bearing viable* t*-alleles and the ratio of tailless to normal-tailed offspring in balanced lines.*

Sex	Number	Building and year	Tailless offspring	*t*-bearing mice	Transmission ratio	Balanced mating results	
						Tailless	Normal
Male	503	MG* – 60	65	73	.890	193	102
	507	MG – 60	57	59	.966	87	53
	399	MCC – 60	13	31	.419	46	16
	1092	MRH – 61	25	25	1.000	55	11
	1002	GKK – 61	5	10	.500	28	40
	1048	LTS – 61	19	33	.576	42	16
	POOLED		184	231	.797		
Female	464	MG – 60	11	21	.524	89	57
	520	MG – 60	5	11	.455	248	128
	401	MRH – 60	5	10	.500	39	23
	403	MRH – 60	5	12	.417	61	42
	406	MRH – 60	5	10	.500	21	13
	435	MKK – 60	14	22	.636	242	141
	1057	MHH – 61	6	10	.600	50	18
	1037	MRH – 61	2	4	.500	46	31
	1115	MCC – 61	9	21	.429	40	32
	415	LCH – 60	12	21	.571	61	43
	1308	LG – 62	6	27	.222	48	32
	1294	LG – 62	2	15	.133	32	54
	67	LLT – 59	26	26	1.000**	177	52
	9	LTS – 59	2	4	.500	158	114
	31	LTS – 59	3	8	.375	107	46
	36	LTS – 59	2	4	.500	18	29
	11	LGG – 59	3	5	.600	24	12
	28	LCC – 59	7	8	.875	98	38
	37	LCC – 59	2	4	.500	171	52
	38	LCC – 59	7	7	1.000**	196	142
	43	LCC – 59	4	4	1.000	133	35
	1097	B – 61	11	29	.375	69	55
	POOLED		151	288	.524		
			118	255	.463***		

* See Table 3 for key to buildings.
** Probably homozygous.
*** If Female 38 and Female 67 are considered homozygous.

then at least in adjacent demes. The latter situation occurred in the rabbit house, Mamarrow, 1961, and granary, G. Lindeman, 1962. To justify this conclusion information would have to be available on the home range of the mice concerned.

The transmission ratios of lethal and viable *t*-alleles isolated are given in Tables 3 and 4. The male transmission ratio for the lethal *t*-alleles is somewhat lower, 0.893, than the 0.952 recorded by Dunn (1960). The female transmission ratio is not significantly different from the normal 0.5. The viable *t*-alleles are transmitted with a frequency of 0.797 in males, which is significantly different from the lethal, and the female transmission ratio is again normal.

Tables 3 and 4 also give the basis for the classification of *t*-alleles.

The breeding results of the mice bearing viable *t*-alleles (Table 4) indicate that at least some of these animals are homozygous for a viable *t*-allele. Two or perhaps three of 22 females may be homozygous. The latter would change the overall *t*-allele frequency from 0.156 to 0.162.

TABLE 5. *Summary of complementation test matings among balanced lethal lines.**

Mice	4	34	59	61	68	129	155	421	424	455	512	534	948	960	1021	1026	1029	1045	1046	1093	1253
4	242/0	38/0	17/0	43/12	38/0	29/0	21/0	20/0	12/0	2/1	14/0	21/0	23/0	25/0	58/0	47/0		14/0	14/0	30/0	
34		472/0	39/0	48/29	45/0	11/0	42/0	72/0	65/0	52/27	47/0	39/1	23/0	43/1	20/0	57/0	20/0	18/0	30/0	24/0	17/0
59			172/0	24/11	17/0	27/0	19/0	14/0	14/0	14/0	15/0	33/0	15/0	11/0	32/0	21/0	23/0	26/1	19/0	20/0	12/0
61				120/1	24/6	20/8	20/11	6/3	37/11	19/17	31/17	22/11	4/3	19/11	47/24	24/5	16/7	23/9	52/22	24/13	24/7
68					248/0	29/0	19/0	28/0	49/0	40/4	32/0	15/0	29/0	17/0	18/0	12/0	19/0	25/0	23/0		
129						274/2	36/0	16/0	12/0	31/0	17/0	35/0	12/0	46/0	31/0	27/0	30/0	21/0	22/0	17/0	19/0
155							287/0	27/0	30/0	35/0	29/0	27/0	24/0	18/0	15/0	25/2	13/0	12/0	14/0		11/0
421								112/0	30/0	46/4	15/0	42/0	29/1	33/1	22/0	24/0	17/0			14/0	12/0
424									416/1	52/0	36/0	26/0	19/0	21/0	29/0	20/0	19/1	14/0		17/0	
455										384/8	29/0	44/0	18/0	23/0	14/0	34/1		11/0	21/0		15/0
512											114/0	21/0	29/0		36/0	17/0		23/1			14/0
534												82/1	69/0	27/1		14/0	17/0	16/0	23/0	15/0	23/0
948													377/2	7/0	9/0			16/0		21/0	10/0
960														80/0	11/0	14/0	29/0	12/0	23/0		
1021															305/1	12/0	14/2	19/0	14/0		
1026																159/0	16/0	10/0	19/0	4/0	7/0
1029																	81/0	19/0	16/0	27/0	
1045																		126/0	7/0	17/0	14/0
1046																			80/0	11/0	6/0
1093																				147/0	17/0
1253																					168/0

* Number of tailless offspring over number of normal-tailed mice.

COMPLEMENTATION STUDIES

Complementation testing involved combining a variety of *t*-alleles isolated from the wild-caught mice. Although primary concern was with the lethal *t*-alleles since (1) time and space were limited and (2) information about *t*-alleles was more readily obtained when such lethal alleles were involved, nevertheless, a few viable alleles were included in the testing. With the lethal alleles complementation is evidenced by the presence of normal-tailed animals among the offspring of two tailless lines. Unfortunately, such complementation results cannot be recognized in the viable *t*-allele strains because the homozygote *t/t* is viable and has a normal tail. Some insight can, however, be gained into the differences between viable alleles because of their interactions with lethal *t*-alleles.

The results of the complementation matings involving various lethal *t*-alleles are summarized in Table 5. Unfortunately, not all matings produced progeny. These findings suggest the presence of two different lethals and at least one viable *t*-allele in the 1959 population of the G. Lindeman lean-to. The *t*-allele isolated from female 61 complements lethal *t*-alleles isolated from the remaining mice. This was, however, the only *t*-allele which differed from all of the rest. Since it was found in only one offspring of one animal, it is highly probable that this was an allele that had either: (1) arisen in the natural environment and had no time to spread, (2) arisen in the laboratory after female 61 was captured, or (3) come from a population outside the sampling area.

With the exception of the interaction between *t*-alleles from mice 34 and 455, combinations involving the rest of the lethal *t*-alleles resulted in no complementation. Thus, these alleles behave like identical alleles, at least according to the criterion of non-complementary interaction. The complementation of *t*-alleles from mice 34 and 455 is presently inexplicable.

A similar examination of some of the viable *t*-alleles in combination with other viable *t*-alleles and with some of the lethal *t*-alleles, has revealed unexpected complementation results (Table 6). For example, the viable *t*-allele isolated from No. 9 has a varying complementation effect. When combined with the lethal *t*-allele of No. 424 no complementation was observed, limited complementation was seen with the lethal *t*-allele from No. 421, whereas almost complete complementation was seen with the lethal *t*-allele of No. 534. Similarly, the viable *t*-allele isolated from mouse No. 399 complemented one lethal (No. 424), and did not complement another (No. 455). Viable *t*-alleles may, therefore, be useful in further increasing the resolving power of complementation testing.

Table 6 also reveals that the viable *t*-alleles differ. For instance, viable *t*-alleles from No. 399 and No. 415 interact differently with the lethal *t*-allele from No. 155. Such differences in interaction between alleles may be additionally useful in recognizing different viable *t*-alleles.

EMPIRICAL FREQUENCY OF *t*-ALLELES AND POPULATION MODELS

The effect of the aberrant male transmission ratio favoring the *t*-alleles, on the frequencies of these alleles, was first studied by Prout (1953) and later by Bruck (1957). The deterministic model developed by the latter showed that the unusually high transmission frequency of the *t*-alleles in sperm was sufficient to explain not only the ubiquity of these alleles but also to indicate that some other factor or factors were acting against the transmission advantage, because the equilibrium frequency predicted by Bruck's model (0.38) was considerably higher than the average empirical frequency (0.16).

In an attempt to resolve the above discrepancy, Bruck's model has been modified by the introduction of a coefficient of inbreeding. The coefficient of inbreeding in this case is considered to be a measure of the Wahlund effect, that is, a numerical

deficiency of heterozygotes because of population subdivision. Therefore,

$$F = \sigma_q^2/q(1-q)$$

where σ_q^2 is the variance of the gene frequencies in the subdivisions and q is the overall frequency of one of the alleles (Li, 1955).

In developing the present model, all except one of Bruck's assumptions are followed. These include: (1) only two alleles + and t exist at this locus in the model population and + (wildtype allele) is completely dominant over t; (2) adaptive values of the genotypes dealt with are $+/+ = 1$, $+/t = 1$, and $t/t = 0$; (3) mutation rates are negligible; and (4) female transmission ratio is 0.5.

The exception, as pointed out above, is that mating does not occur at random in an infinitely large population.

The terms used in deriving the relationship between the coefficient of inbreeding (F), transmission ratio (m) and frequency of the t-allele (q) are also identical with Bruck's. They are:

q_n = frequency of t after selection and inbreeding;

$1-q_n$ = frequency of + after selection and inbreeding;

D_n = frequency of $+/+$ before selection (i.e., death of lethal);

H_n = frequency of $+/t$ before selection;

R_n = frequency of t/t before selection;

m = number of gametes transmitting t/ total number of functional gametes from each heterozygous male;

a = frequency of $+/t$ heterozygotes after selection and inbreeding ($a = 2q_n$);

b = frequency of $+/+$ homozygotes after selection and inbreeding ($b = 1-2q_n$);

F = inbreeding coefficient.

From the above $a = 2q_n = \dfrac{H_n}{D_n + H_n}$. (1)

The frequency of the three genotypes in generation $n+1$ before selection and with random mating (Bruck, 1956) is:

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

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

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

With inbreeding these become:

$$D'_{n+1} = D_{n+1} + \tfrac{1}{2}FH_{n+1}$$

$$= b^2 + \frac{a^2(1-m)}{2} + \frac{ab(3-2m)}{2} + \tfrac{1}{2}F\left[\frac{a^2}{2} + \frac{ab(2m+1)}{2}\right],$$

$$H'_{n+1} = H_{n+1}(1-F)$$

$$= \left[\frac{a^2}{2} + \frac{ab(2m+1)}{2}\right][1-F],$$

$$R'_{n+1} = R_{n+1} + \tfrac{1}{2}FH_{n+1}$$

$$= \frac{a^2 m}{2} + \tfrac{1}{2}F\left[\frac{a^2}{2} + \frac{ab(2m+1)}{2}\right].$$

From equation (1):

$$q_{n+1} = \frac{H'_{n+1}}{2(D'_{n+1} + H'_{n+1})} = \frac{H'_{n+1}}{2(1-R'_{n+1})}. \quad (2)$$

Since at equilibrium $q_{n+1} = q_n$ and also since $a = 2q_n$ and $b = 1-2q_n$ then:

$$F = \frac{1 - 2m + 4mq_n - 4mq_n^2}{q_n + 6mq_n - 4mq_n^2 - 2m - 1}; \quad (3)$$

conversely:

$$m = \frac{1 - Fq + F}{2(1 - q_n + 2q_n^2 - F + 3Fq_n - 2Fq_n^2)}; \quad (4)$$

and also:

$$q_n = \frac{(4m - F - 6Fm) \pm \sqrt{4Fm(F - 8 + Fm + 10m) + 16m(1-m) + F^2}}{8m(1-F)}. \quad (5)$$

TABLE 6. *Complementation tests involving viable and lethal* t-*alleles and interactions between viable and different lethal* t-*alleles.*

Mice bearing a viable *t*-allele	Mice bearing a lethal *t*-allele									
	4	34	43	61	68	155	421	424	455	534
9	8/4*	8/15	3/2	1/0	18/6	5/9	10/1	32/0	8/9	28/21
399						25/25		4/3	29/0	
415	10/12	10/12	10/8			32/0				9/6

* Number of tailless/number of normal-tailed mice.

The numerical relationship between F and q for a given m are given in Figure 1.

From the *Es-2* data, the coefficient of inbreeding for the pooled Ann Arbor samples was found to be $0.18 \pm .063$ (Petras, 1967). Wild-caught $+/t$ males from the Ann Arbor area revealed that lethal *t*-alleles had a pooled transmission ratio of about 0.89. With these values an equilibrium *t*-allele frequency, based on a deterministic model with inbreeding, was calculated and found to be in the neighborhood of 0.15. The empirical frequency of the *t*-allele based on four years of sampling from a number of localities in the immediate vicinity of Ann Arbor was found to be 0.162 when adjusted for possible viable *t*-allele homozygotes. This surprisingly close correspondence between the observed and expected *t*-allele frequencies not only suggests a possible mechanism for reducing the *t*-allele frequencies in natural populations but also provides evidence consistent with the independent calculation of the inbreeding coefficient.

It must be pointed out that the frequencies obtained from the deterministic population model are not exactly comparable to the empirical *t*-allele data since in the former only lethal *t*-alleles were considered, whereas natural populations at least in the localities sampled are composed of mice having both lethal and viable *t*-alleles. However, since a comparison of the frequencies of these two types of alleles showed an almost equal distribution of the two among the *t*-bearing animals (54.3% of the *t*-alleles isolated are lethal in the populations sampled), the decrease in fertility of the mice homozygous for viable *t*-alleles must have, either in itself, or together with some other factor or factors, a deleterious effect equivalent to that of the lethal *t*-alleles.

In samples collected from other parts of the country, Dunn found the frequency of *t*-alleles to be 0.174 in those populations exhibiting such alleles (see Dunn, Beasley, and Tinker, 1960) and the mean transmission ratio to be 0.952 for the 16 lethal *t*-alleles isolated from these populations (see Lewontin and Dunn, 1961). Anderson (1964) in a more intensive but more localized study around Calgary, Alberta, found the *t*-allele frequency to be 0.238 and the transmission ratio to be 0.95.

If these estimates are valid, then the inbreeding coefficient (F) which would decrease the equilibrium *t*-allele frequency of the deterministic model to the empirical value can be calculated. Such an F value falls between 0.12 and 0.23 depending on the values of the observed *t*-allele frequency and transmission ratio.

The modified deterministic model is also in agreement with the hypothesis which Lewontin and Dunn (1960) developed with the aid of a computer analogue population. These authors concluded that the empirical *t*-allele frequency is the mean of the frequencies observed in small random-mating units or demes in which random loss of the *t*-allele occurs and reestablishment of these alleles, after extinction, by migration or mutation is rare.

However, Lewontin and Dunn's basic

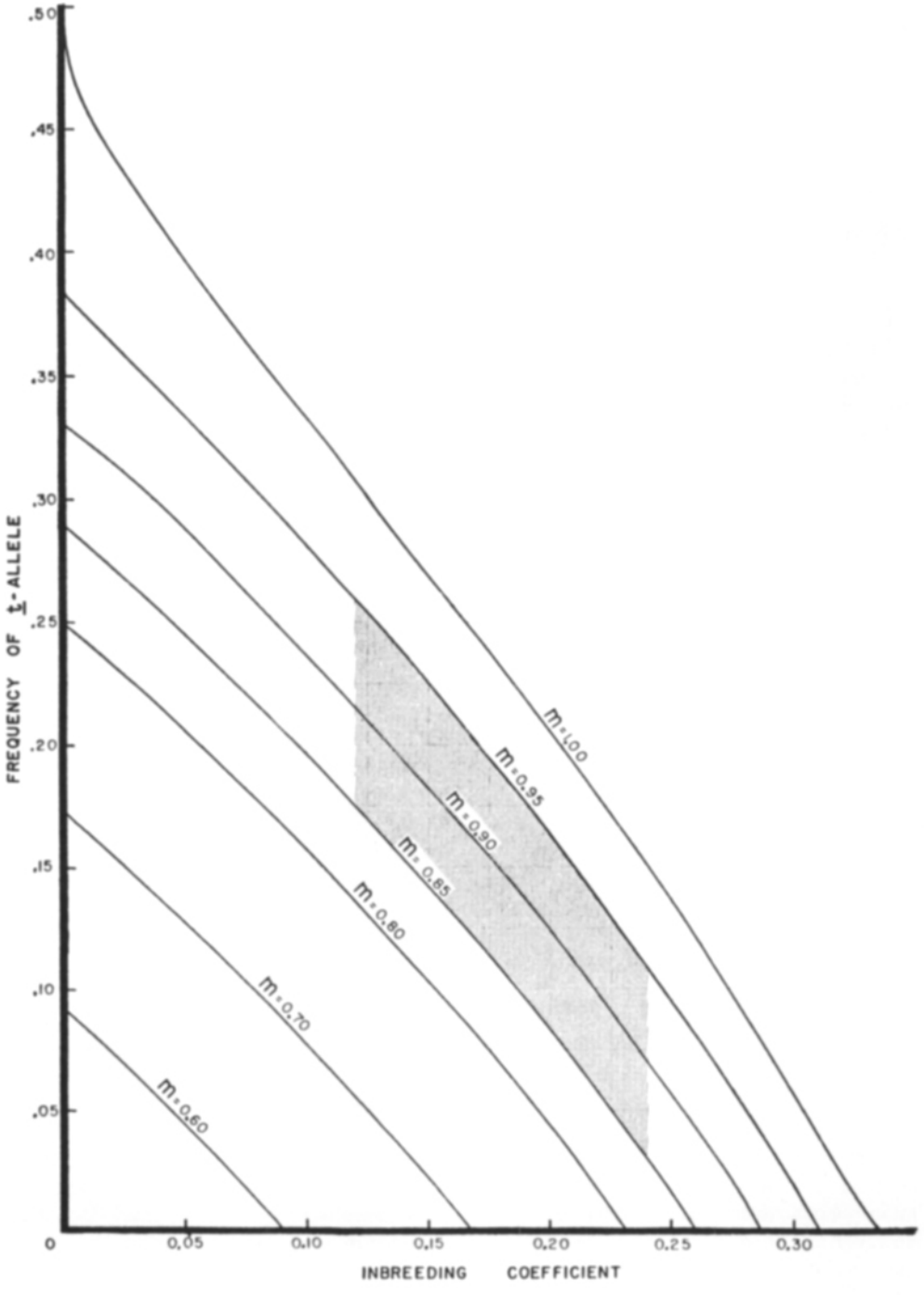

FIG. 1. The relationship between the deterministic equilibrium frequency of a t-allele in a population, the transmission ratio of the t-allele, and the inbreeding coefficient of the population.

model was recently extended by Levin, Petras and Rasmussen (1964) to permit migration among five demes, each composed of six animals. Even with what Levin et al. considered to be a relatively low migration rate (one per cent), the frequency of the *t*-allele in the five demes approached that of Bruck's deterministic model (0.38). The exact cause of the discrepancy between the Levin model and the modified deterministic model is not clear.

Summary

1) An examination of mice collected over a four-year period from several localities in the vicinity of Ann Arbor, Michigan, revealed the existence of a polymorphism at the *T* locus. The overall adjusted frequency of the *t*-alleles at this locus was $0.162 \pm .009$.

2) The frequency estimates of the *t*-alleles varied considerably from one building to the next, ranging from 0 to 0.50. Also, the frequency estimates were found to fluctuate considerably from year to year in a single locality.

3) Complementation tests revealed the presence of at least three groups of alleles: two lethal and one viable. All but one of the lethals isolated were non-complementary and, therefore, considered identical. No attempt was made to further classify either the complementary lethals or the viable *t*-alleles.

4) Both lethal and viable *t*-alleles were frequently detected in mice from a single building. Approximately one-half of the *t*-alleles detected were viable.

5) The pooled male transmission ratios of the lethal and viable *t*-alleles were found to be 0.89 and 0.80 respectively. Female transmission ratios were normal.

6) These transmission ratios and an inbreeding coefficient determined from data at the *Es-2* locus were incorporated into a deterministic population model with the result that the *t*-allele frequencies expected on the basis of this model were consistent with empirical frequencies.

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