A TEMPORAL SURVEY OF ALLELIC VARIATION IN NATURAL AND LABORATORY POPULATIONS OF *DROSOPHILA MELANOGASTER*[1]

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ELECTROPHORETIC techniques are currently being applied to many basic problems in population genetics and evolutionary biology. Thus far, analyses of protein polymorphisms have focused primarily on describing the amount of allelic variation in natural species and the distribution of this variation among component populations. Relatively little attention has been directed toward the question of how the observed variation behaves within natural or laboratory populations over extended periods of time.

Because of the ubiquitous distribution of *Drosophila melanogaster* and the numerous enzyme polymorphisms already described, temporal studies of this species are particularly favorable. The work to be described centers on three interrelated subjects: the stability of the genetic composition of natural populations during the breeding year, the degree to which neighboring populations resemble each other genetically, and the behavior of allelic variation under laboratory conditions. The third aspect of this study employed recently collected strains from well-established and extensively studied populations. Especially sought were tests that the data derived from laboratory studies are relevant to natural populations as well. In general, the results indicate that gene–enzyme polymorphisms in *Drosophila melanogaster* are stable over space and time, in both laboratory and natural populations.

MATERIALS AND METHODS

Electrophoresis: Proteins were separated on cellulose acetate strips (Gelman Instrument Co., Ann Arbor, Michigan) supported within a Gelman Deluxe horizontal chamber. A continuous well buffer system was used containing 0.1 M Na phosphate, pH 7.0 and 1 mM Na EDTA. Single flies or pairs of flies (when control genotypes were included) were homogenized with a small drop (about 50 microliters) of strip buffer in small Plexiglas blocks into which 1.3 cm deep flat-bottomed holes had been drilled. Strip buffer contained 0.05 M Na phosphate, pH 7.0 and 1 mM Na EDTA. A constant current of 3 milliamperes per strip was maintained for 60 min, within a 4°C incubator. The strips when removed from the chamber were stained at room temperature until a good banding pattern appeared. This time varied from 5 to 20 min, according to the enzyme. Table 1 lists the seven enzymes studied, along with their gene symbol, genetic map location, and heterozygote band pattern. Staining procedures were only slightly modified from the cited authors, and LDH was assayed according to instructions furnished by Gelman Instrument Co.

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TABLE 1

A description of the seven gene-enzyme systems studied

Enzyme	Gene symbol	Map location	Hybrid band in heterozygote	Reference
malate dehydrogenase	*MDH*	2–35	+	O'BRIEN 1969
α-glycerophosphate dehydrogenase	*α-GDH*	2–17.8	+	GRELL 1967
alcohol dehydrogenase	*ADH*	2–50	+	GRELL, JACOBSEN and MURPHY 1965
glucose-6-phosphate dehydrogenase	*Zw*	1–63	—	YOUNG, PORTER and CHILDS 1964
6-phosphogluconate dehydrogenase	*Pgd*	1–0.9	+	YOUNG 1966
acid phosphatase	*Acph*	3–101.4	+	MACINTYRE 1966
lactate dehydrogenase	*LDH*	?	?	this paper

TABLE 2

Collection information on the populations studied

Population symbol	Origin	Collection dates	Average number of lines (or individuals) tested
S.L.	South Lancaster, Mass.	1961	8
East	Syracuse, New York	1966	8
Bkly	Berkeley, California	1967	6
Amh 1	Amherst, Massachusetts	1966	22
Amh 2	Amherst, Massachusetts	1966	19
*Clar	Syracuse, New York	1968	(10)†
Fla.	Collier Park, Florida	1967	6
*Card	Cardiff, New York	1968	(36)†
*Lafa	Lafayette, New York	1968	(30 per week)‡
*Erie	Syracuse, New York	1968–1969	(30 per week)‡

* These populations were collected from nature and analyzed immediately. The remaining populations represent collections of laboratory cultured isofemale lines, all of which were tested during 1968 and 1969.

† The number of individuals sampled for each locus, in a population represented by a single collection.

‡ The average number of individuals tested at each locus, for each of 22 consecutive weekly collections.

Populations: Table 2 provides a list of the ten populations sampled, their origin, and date of collection. Five of these were kindly provided by Dr. ROGER MILKMAN, as unselected strains maintained at 25°C, where each strain had been continued with about 200 adults per transfer.

Sampling: From the six populations maintained in culture as isofemale lines, 15 adults were sampled for each enzyme from each line. Approximate gene frequencies were determined according to the method of HUBBY and LEWONTIN (1966). In the four populations collected during 1968 and 1969 and sampled at once, gene frequencies were calculated directly.

The Lafayette and Erie populations were first sampled in early June of 1968. The Lafayette site, an apple orchard and cider mill, harbored enormous numbers of Drosophila; collections involved one or two sweeps with an insect net over the decaying pomace. The Erie site was a wooded area about 15 miles from Lafayette, and the population density was low; collections involved the use of banana-baited traps. At the onset of collection, Drosophila populations were already estab-

lished, so the week designations under RESULTS are arbitrary. Consecutive weekly collections from both populations continued for 22 weeks each. Adult Drosophila reappeared at the Erie site in mid-May of the following year, but no adults were observed at the Lafayette site by May 30, when collections were terminated. Repeated attempts to uncover viable overwintering Drosophila were unsuccessful, although many larval and adult carcasses as well as nonviable eggs were recovered from material beneath the snow. Two additional populations in the Syracuse area, designated Clarendon and Cardiff, were sampled once during 1968.

Whenever possible, 36 adults were tested weekly for each of five enzymes, in both the Erie and Lafayette populations. For analyses of LDH and Acph, five third-instar larvae from each of ten or more isofemale lines were sampled. At week 20 a large sample of adults was collected from the Lafayette site. Half the animals were routinely analyzed, while the remaining half were placed in a standard population cage. After 16 and 24 weeks in culture, adults were sampled and analyzed. Under these cage conditions a generation interval was found to be about 14 days.

Experimental cages: Cages were made from square one-liter polyethylene refrigerator containers, by boring six 2.5 cm holes in the sides into which 28 g screw-top vials could be snugly inserted. Vials were changed sequentially at 5-day intervals. Thirty-six adults were tested for each enzyme every 28 days. The cages were maintained at 25°C, at which temperature development from egg to adult takes about 14 days.

RESULTS

Variation over time: Seven enzyme loci were analyzed for electrophoretic variation in natural populations. Five loci were found to be polymorphic in the four Syracuse populations, while at two loci, *LDH* and *Acph*, no polymorphism could be detected. Figures 1a and 2 summarize the weekly frequency determinations for each dimorphism during 1968. The two sex-linked dehydrogenases were not studied prior to collection week 12.

Within the Lafayette and Erie populations, allelic frequencies remained relatively constant throughout the collection period. In addition, genotype frequencies were consistently found to be within the limits of Hardy-Weinberg expectations. There was some indication of seasonal variation at the *α-GDH* locus in both populations (Figure 1a). The frequency of the slow allele rose gradually from about 9% in June collections at Lafayette, to about 18% in November samples. A rise from 12% to 25% was recorded at the Erie population during this same period. A least-squares regression analysis was performed on the *α-GDH* data, and is presented in Figure 1b. The calculations identify an increase in the frequency of the slow allele in the Erie and Lafayette populations equal to an average of 0.76 and 0.48 percent units per week, respectively. It is of interest that in earlier studies of two populations collected weekly from Amherst during 1966, the same slow allele was found to be at higher frequency during the fall than in spring and summer. These results are recorded in Figure 3. It is unfortunate that collections from the Amherst 2 site terminated at a time when the rise in frequency of the slow allele was apparent in the Amherst 1 population. The weekly numbering systems in the Amherst and Syracuse collections are roughly equivalent.

Slight but consistent interpopulational differences are recorded at the *α-GDH* locus in Figure 1a, and for *Pgd* in Figure 2. Standard error determinations on estimates from the regression lines (Figure 1b) indeed confirm these interpopu-

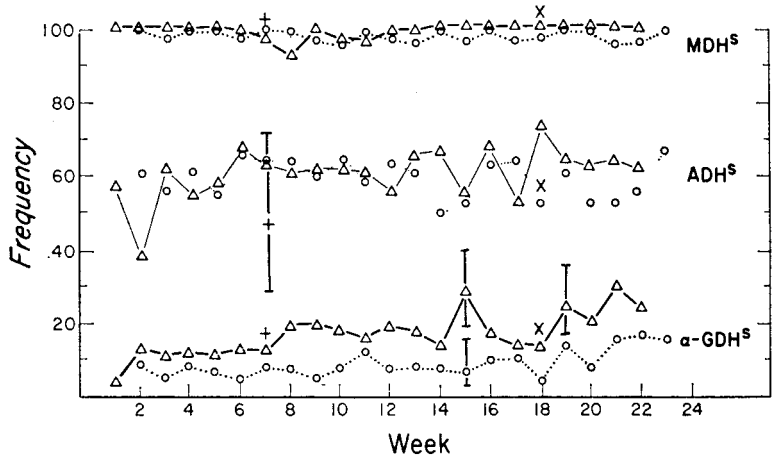

FIGURE 1a.—Weekly frequencies of polymorphic alleles in four natural populations collected in and around Syracuse during 1968. The populations are designated Lafa (O), Erie (△), Clarendon (one collection at week 7), and Cardiff (one collection at week 18). The convention used in numbering weeks is explained under MATERIAL AND METHODS. The frequency of the fast allele is equal to one minus the frequency of the slow allele. In certain representative cases 95% confidence intervals have been included.

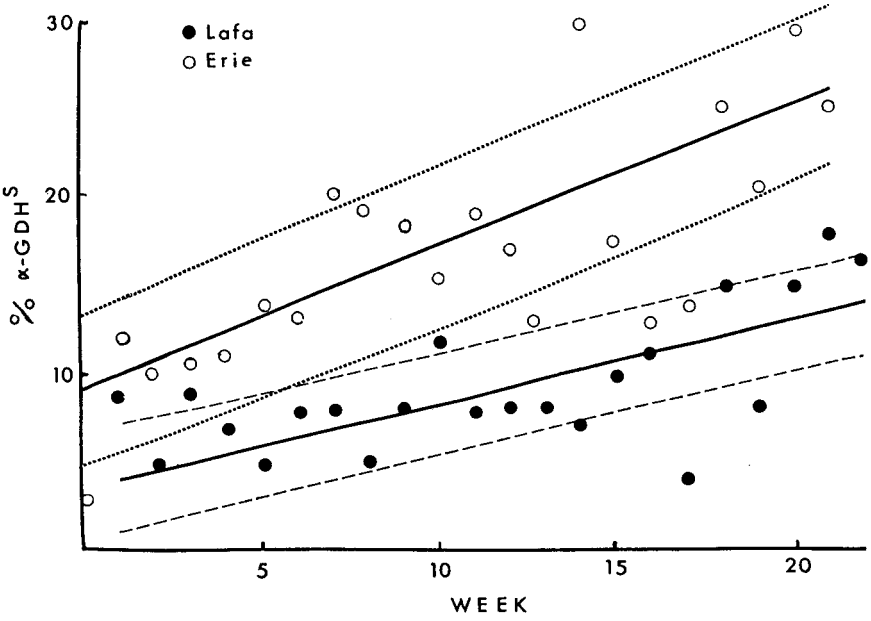

FIGURE 1b.—Regression analyses of the *α-GDH* frequencies in the Lafa and Erie populations. Parallel boundaries along each regression signify the standard errors of the regression estimates.

lational differences for most of the year at the *α-GDH* locus. A similar analysis on the *Pgd* data again revealed significant interpopulational differences, but showed no statistically significant change in the frequencies of alleles over time. Despite the 20 miles separating these populations and the substantial differences in population size, allelic frequencies at the remaining three loci were indistinguishable. Single collections from the Clarendon site at week 7 and from Cardiff

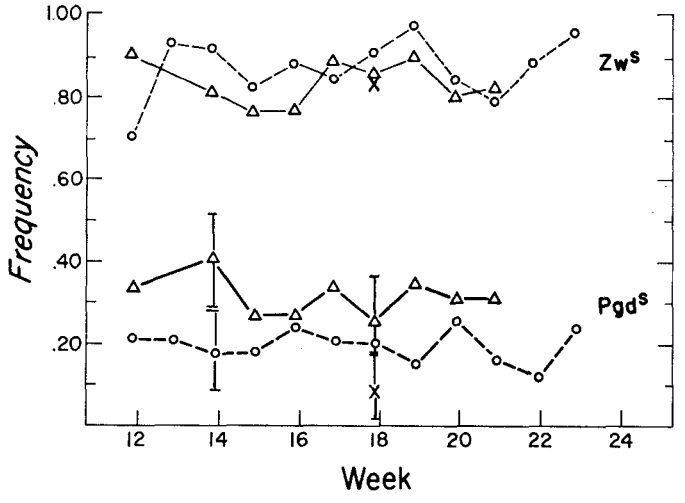

FIGURE 2.—Weekly frequencies of polymorphic alleles in three populations collected in and around Syracuse during 1968. The populations are designated Lafa (O), Erie (△), and Cardiff (×). For certain representative points, 95% confidence intervals have been included.

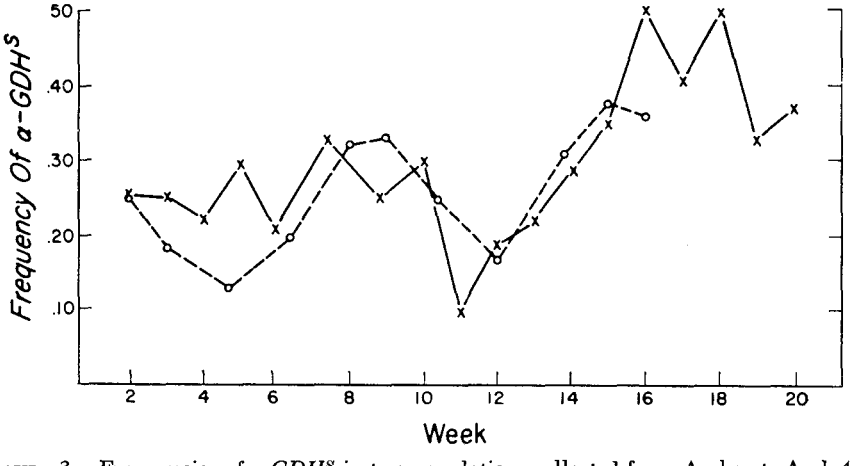

FIGURE 3.—Frequencies of *α-GDH*^{S} in two populations collected from Amherst; Amh 1 (×) and Amh 2 (O). The data are plotted in the form of a consecutive moving average series, in three week averages. A point at week 2, for example, indicates the allele frequency in all the lines collected during weeks 1 to 3 combined. The points from the two populations do not coincide because lines were not available from Amh 1 at week 8, or from Amh 2 for weeks 5, 6, 11, and 13.

TABLE 3

Allelic frequencies from 1968 and 1969 collections, and from the Lafayette week-20 cage

Allele	Population	Collection week during 1968				Cage-weeks in culture			Collection week during 1969	
		20	21	22	23	0	16	24	1	2
α-*GDH*^{S}	Lafa	.08	.15	.18	.17	.08	.10	.13	..	..
	Erie	.20	.30	.25	..	..	..	..	.32	.32
ADH^S	Lafa	.53	.53	.55	.67	.53	.67	.53	..	.
	Erie	.63	.65	.63	..	..	..	..	.87	.57
MDH^S	Lafa	1.0	.96	.97	1.0	1.0	1.0	1.0	..	..
	Erie	1.0	1.0	1.0	..	..	..	..	1.0	1.0
Zw^S	Lafa	.83	.77	.87	.93	.83	.87	.86	..	..
	Erie	.80	.80	..	..	..	..	..	1.0	.90
Pgd^S	Lafa	.22	.15	.12	.21	.21	.05	.04	..	..
	Erie	.25	.25	..	..	..	..	..	.50	.30

at week 18 revealed both a qualitative identity of alleles and a quantitative similarity in allele frequency (Figures 1a and 2), when compared to the Lafayette and Erie populations. It is impossible to compare the environments of these populations quantitatively. Both Cardiff and Lafayette locales are apple orchards and cider mills with huge populations and obvious breeding sites, whereas Erie and Clarendon are more urban with no visible Drosophila breeding sites.

At collection week 20, about 150 adult flies were transferred from the Lafayette site into a standard laboratory cage maintained at 25°C. After 16 and 24 weeks, the cage was sampled. The results are presented in Table 3. Under these conditions one generation takes about two weeks. At three of the five loci polymorphic in the founder population (*αGDH*, *ADH*, and *Zw*), the allelic frequencies after 24 weeks in culture were still within 10% of their original values. At the *MDH* locus, where the natural population maintains the fast allele at about 1%, the cage's apparent monomorphism may well reflect sampling error. A marked decline in the frequency of *Pgd*^{S} from 22% to 5% is apparent during the 24 weeks, although it is impossible to predict whether this allele would eventually have been eliminated.

The return of *Drosophila melanogaster* to the Erie site in the spring of 1969 is recorded in Table 3. For the two weeks studied, allelic frequencies were very similar both to those observed in the previous year and in the Lafayette week-20 cage. Attempts to uncover a population at the Lafayette site were made, but as of May 30 no adult flies were evident. The origin of the spring population is unknown. The failure to detect a diapausing population (see MATERIALS AND METHODS) does not eliminate the possibility of a cryptic, overwintering population. Perhaps either shelters or migration from warmer climates is likely,

although no direct evidence for the mechanism of their recolonization is available.

Variation over space: The similarities of allele frequency in the four natural populations from around Syracuse suggested that an extensive survey of other more geographically remote populations would be of interest. Collections of isofemale lines from Florida, California, Massachusetts, and Syracuse were available. Some of these strains had been in laboratory culture for up to five years, and the effect of this isolation cannot be determined, *a priori*. The results of this survey are presented in Tables 4 and 5, along with information on the four populations previously described. *LDH* and *Acph* were monomorphic in all the populations, and for the same allele. Of five polymorphic enzyme loci, two (*α-GDH* and *Zw*) were polymorphic in all ten populations, two other loci (*ADH* and *Pgd*) were each polymorphic in nine of the ten, while *MDH* was polymorphic in six populations.

The populations not only showed a similarity in the degree of polymorphism, but displayed a striking similarity in the frequencies at which individual alleles were maintained. In eight of the ten populations the frequency of α-GDH^S ranged from 8% to 25%, the frequency of ADH^S ranged from 31% to 67%, and the Zw^F frequency varied between 13% and 38%. In no population was the frequency of MDH^F greater than 12%. The pattern of variation at the *Pgd* locus was the most variable, for while in nine of the ten populations the frequency of

TABLE 4

Approximate allele frequencies for seven gene–enzyme systems in ten natural and laboratory populations of Drosophila melanogaster

Locus	Allele	Population									
		S.L.	Fla.	Bkly	Amh 1	Amh 2	East	Clar	Erie	Card	Lafa
α-GDH	*F*	.75	.83	.92	.68	.75	.50	.85	.84	.82	.90
	S	.25	.17	.08	.32	.25	.50	.15	.16	.18	.10
ADH	F	.31	0	.67	.43	.21	.50	.55	.40	.43	.40
	S	.69	1.0	.33	.57	.79	.50	.45	.60	.57	.60
MDH	*F*	0	.08	.08	.04	.12	0	0	.01	0	.01
	S	1.0	.92	.92	.96	.88	1.0	1.0	.99	1.0	.99
LDH	*A*	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	..	1.0
Acph	*F*	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	..	1.0
	S	0	0	0	0	0	0	0	0	..	0
Zw	*F*	.19	.17	.25	.68	.29	.38	..	.17	.17	.13
	S	.81	.83	.75	.32	.71	.62	..	.83	.83	.87
Pgd	*F*	.50	.50	0	.57	.58	.62	..	.73	.93	.81
	S	.50	.50	1.0	.43	.42	.38	..	.27	.07	.19

TABLE 5

The number of isofemale lines within each laboratory cultured population either fixed or polymorphic for various alleles

Locus	Alleles	Population S.L.	Fla.	Bkly	Amh 1	Amh 2	East
	F	5	4	5	22	22	3
α-GDH	*F+S*	2	2	1	31	22	2
	S	1	0	0	2	1	3
	F	1	0	2	2	0	3
ADH	*F+S*	3	0	4	8	5	2
	S	4	6	0	4	7	3
	F	0	0	0	0	0	0
MDH	*F+S*	0	1	1	1	3	0
	S	8	5	5	13	9	8
	F	1	0	1	7	1	3
Zw	*F+S*	1	2	1	5	6	0
	S	6	4	4	2	5	5
	F	4	3	0	6	5	5
Pgd	*F+S*	0	0	0	4	4	0
	S	4	3	6	4	3	3

Pgd^F ranged between 50% and 93%, in a collection from Florida the slow allele was fixed. It is significant that in no case were two populations fixed for different alleles. As Table 5 points out, the substantial polymorphism recorded in the laboratory strains is maintained to a large degree by heterozygosity within individual lines, and not by the differentiation of lines by allele fixation.

Laboratory cage experiments: It would not be unreasonable to argue that extensive migration between locally adapted populations could result in profound similarities in allele frequency. On the other hand, these similarities could be simply explained as reflections of common underlying selective processes operating on all populations of the species. It seemed possible to distinguish between the two by introducing alleles into population cages and following the course of selection. Strains derived from the Lafayette population were made homozygous for various combinations of the two alleles found at each of the three second chromosome dehydrogenase loci. From these strains a series of replicate cages was established in which either one, two, or all three loci were polymorphic, at an initial frequency of 50%. The genotypes introduced into the cages are diagramed in Table 6. Each cage contained individuals from at least four independently derived strains in order that background genetic variation would be distributed as randomly as possible.

Samples were taken at 28-day intervals, and since each generation requires 14 days, these intervals represent about two generations. At the *α-GDH* locus the average frequency of the slow allele in the eight cages was about 30% after some six generations in culture, as shown in Figure 4. There was essentially no change

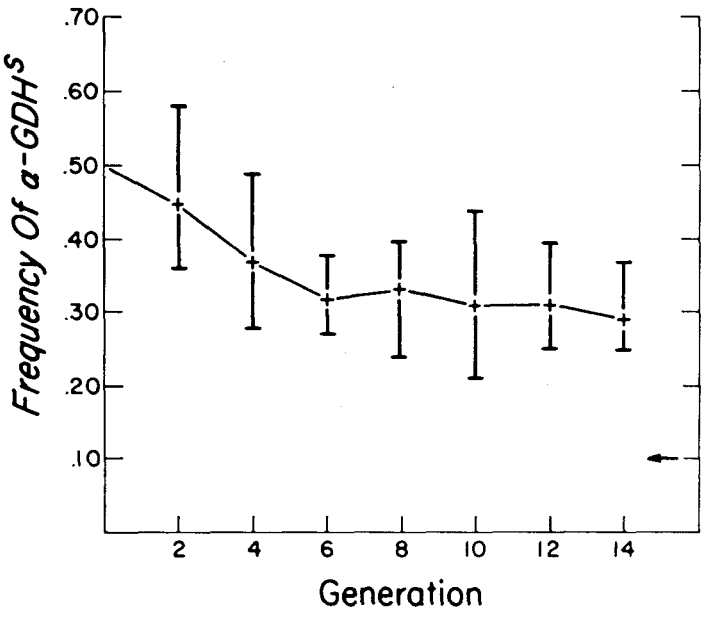

FIGURE 4.—Selection at the *α-GDH* locus in eight laboratory cages. The average frequency and range are presented: the arrow to the right of the figure represents the average frequency of α-GDH^S in the Lafayette population during 1968.

in this average through generation 14, and the reasonably narrow range at generation 6 was maintained throughout. As the arrow to the right of Figure 4 indicates, the average frequency of this allele in the founder population was 10%. After 14 generations of culture, the frequency and range of ADH^F in the four cages were 55% and from 45% to 61%, respectively. These results are shown in Figure 5. In the natural population from which the lines were derived the average frequency of this allele was 60%, as the arrow indicates, with a week-to-week range from 50% to 67%, as shown in Figure 1a. It is clear from these figures that the overall pattern of selection was more uniform at the *α-GDH* locus than at the *ADH* locus. The least consistent pattern of selection was observed at the *MDH* locus, where after 12 generations the frequency of the fast allele in the four cages averaged 17%, with a range from 2% to 30%. These results are diagramed in Figure 6. The average frequency of this same allele in the Lafayette population during 1968 was, as the arrow indicates, 1%.

Although it would be of great interest to quantitatively determine the effects of linkage on the rate and direction of selection, the data in this study are unsuitable for such an analysis. First, exact determinations of chromosome frequencies were not made. Second, even a cursory examination of the results of individual cages (Figure 7) reveals large differences in response, even between replicate cages. This difference is most prominent between cages 4a and 4b. In cage 4a the divergence of α-GDH^S and MDH^S frequencies occurred rapidly in the face of unfavorable linkage conditions (see Table 6); while in the replicate, cage 4b, the

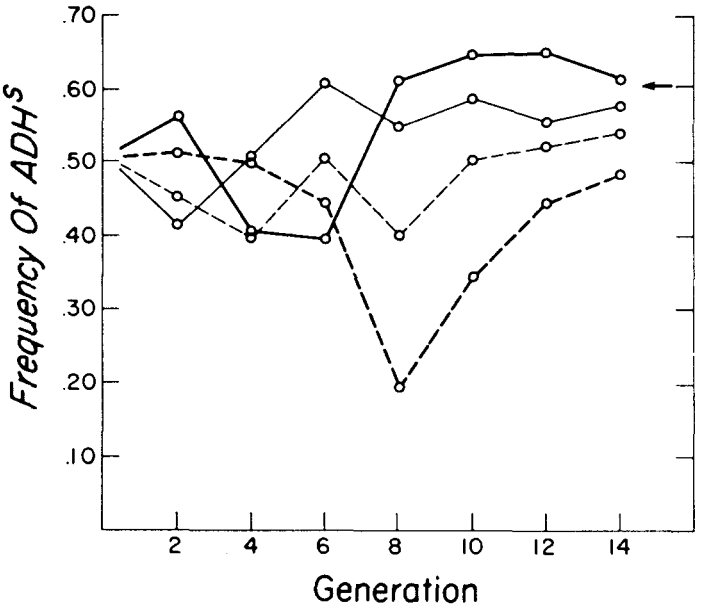

FIGURE 5.—Selection at the *ADH* locus in four laboratory cages. The dashed lines represent cages 2a and 2b, the complete lines 4a and 4b, as described in Table 6. The arrow indicates the average frequency of ADH^S in the Lafayette population during 1968.

effects of linkage appear in the retardation of that divergence for about 8 generations. In cages 3a and 3b this same divergence in allele frequencies was observed; however their rate of divergence was intermediate between the situations in cages 4a and 4b. Such variations are probably based on random events and on interactions between closely linked blocks of genes which differ from cage to cage.

Since the frequency of MDH^F in nature was 1%, one might expect that its elimination in cage populations would occur more regularly than that of α-GDH^S, whose natural frequency hovers around 10%. It did not, and in fact it appears that selection against MDH^F was often retarded by its linkage association with α-GDH^F, which was being selected for. Cages segregating only for *MDH* alleles were not studied, but clearly they would be of interest. If, as in three of the four cages, both maintenance of the α-*GDH* polymorphism and its progress toward equilibrium superseded the elimination of an allele normally maintained at low frequency, then one might begin to suspect no necessary relationship between the equilibrium frequency of these alleles and their respective contribution to fitness.

DISCUSSION

There are essentially two types of explanation for the maintenance of allelic variation in natural populations. The first is nonselective and proposes that the variation in nature may be adaptively neutral, being maintained by mutation

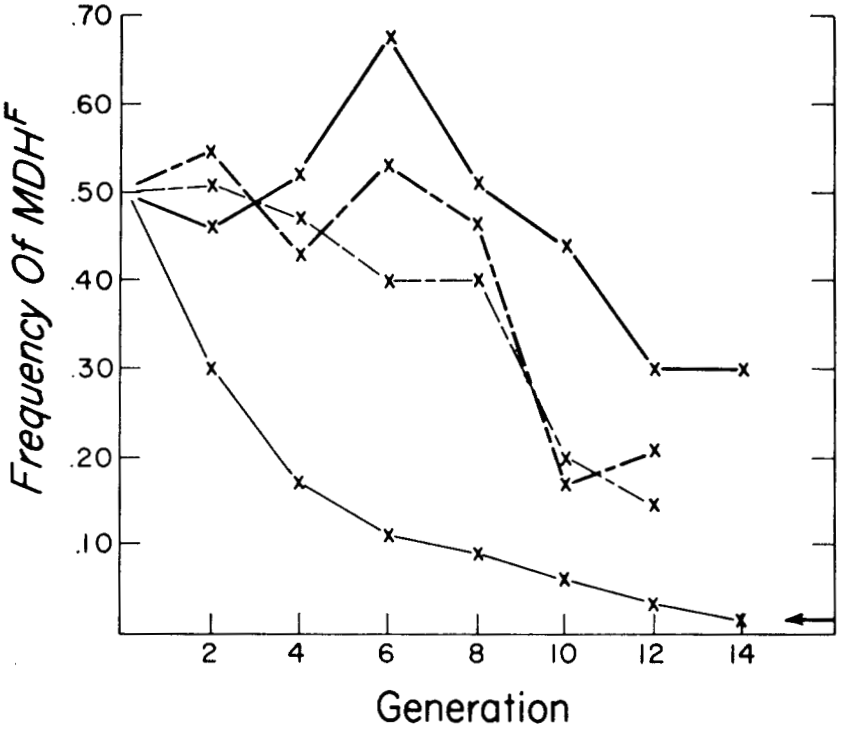

FIGURE 6.—Selection at the *MDH* locus in four laboratory cages. The dashed lines represent cages 3a and 3b, the complete lines 4a and 4b, as described in Table 6. The lighter complete line represents cage 4a. The arrow indicates the average frequency of MDH^F in the Lafayette population during 1968.

and migration which resist the homozygosity promoted by genetic drift (KIMURA 1968). The alternative proposes that allelic variation is adaptive, and is then maintained by one or more form of selection. The evidence presented here for *Drosophila melanogaster* does not correspond to the predictions of a nonselective model.

Throughout all the populations sampled here and elsewhere (O'BRIEN and MACINTYRE 1969; GRELL 1967), we continue to detect only the same few ubiquitous alleles. These include in one case a laboratory population established twenty years ago in Africa (O'BRIEN and MACINTYRE 1969). Moreover, the evidence suggests that these alleles are maintained within a limited frequency range both in natural populations and in laboratory populations in which migration (contamination) is probably quite rare. In recent reports very similar patterns of allele frequency distribution were observed at a number of loci in North American populations of *Drosophila pseudoobscura* (PRAKASH, LEWONTIN and HUBBY 1969), and in Danish populations of Mus (SELANDER, HUNT and YANG 1969).

In addition, the present study finds that allelic frequencies tend to remain quite constant during the breeding year and from one year to the next. The

apparent case of seasonal selection at the *α-GDH* locus, the small but consistent differences between Lafayette and Erie populations in *Pgd* and *α-GDH* allele frequencies, and the frequency cline at the *Pgd* locus in *Drosophila melanogaster* populations of eastern North America (O'BRIEN and MACINTYRE 1969) are not contradictory to the general pattern of constancy and stability. The requirements

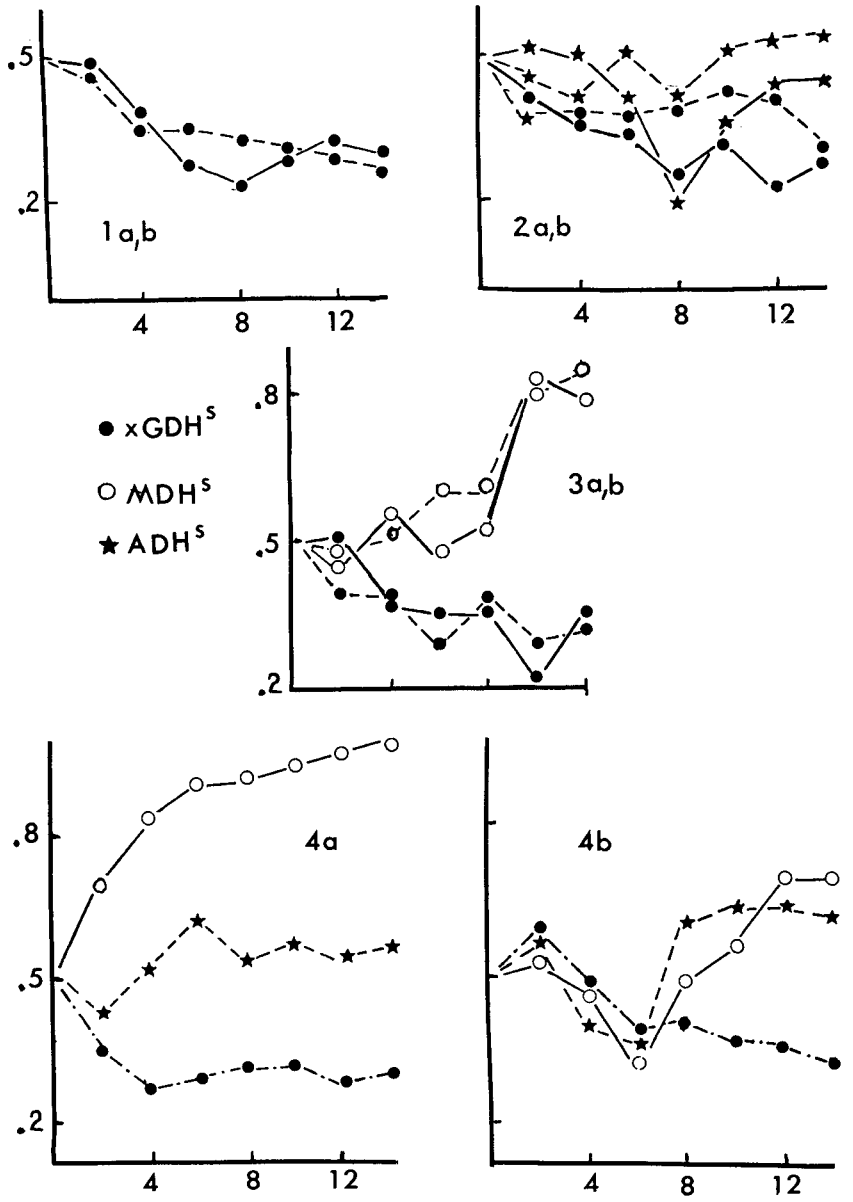

FIGURE 7.—Selection of slow alleles in the eight laboratory cages whose initial genotypes are diagramed in Table 6. The abcissa in all cases indicates the generation number; the ordinate, slow allele frequency.

TABLE 6

The initial genotypes in the population cages

Cage	Locus *α-GDH* (2–17.8)	*MDH* (2–35)	*ADH* (2–50)
1a,b	*F* / *S*	*S* / *S*	*S* / *S*
2a,b	*F* / *S*	*S* / *S*	*F* / *S*
3a,b	*F* / *S*	*F* / *S*	*S* / *S*
4a,b	*F* / *S*	*F* / *S*	*F* / *S*

of species membership may direct the patterns of allelic distribution, but superimposed on these phyletic requirements, to a limited extent, are local environmental pressures (as well as stochastic mechanisms) which operate to modify these frequencies. By species requirement I simply imply, for example, that in a differentiated organism the same enzyme may be required to function within cell types differing in such parameters as pH or ionic strength. Should allozymic variants differ in their pH or ionic optima, then the basis for constant frequency distributions would reside within the organism's development. A similar kind of reasoning is apparently involved in the evolution of isozyme systems like LDH.

It is perhaps of interest that among the more geographically distant populations, Berkeley and Florida, some allele fixation was observed. Whether this fixation simply reflects sampling error, or whether very wide geographic differences magnify small interdeme variations requires further and more extensive sampling of Drosophila populations. *Drosophila melanogaster* is a colonizing species, and its population structure is undoubtedly not representative of all species. So that it further remains to be seen whether other species of varying population structure exhibit these same patterns of allele distribution over space and time.

The clear patterns of selection in the laboratory cages add further confirmation to the general picture of stable, adaptive frequency distributions. When a small founder population colonizes a new area, introducing allele frequencies unlike those of the central population, selective forces can operate to regenerate and maintain those former frequencies. In three of four cages in which both *α-GDH* and *MDH* were polymorphic there was some indication that the size of a frequency deviation from its equilibrium value is not completely correlated with the rate at which equilibrium is reestablished. The preliminary observations, however, await further analysis.

The ubiquitous distribution of the same few polymorphic alleles over space,

the stability of that distribution over time, the similarities of allele frequency in natural and laboratory populations, the maintenance of substantial variation after years in isolated culture, and the consistent pattern of selection in eight laboratory cages in which migration is prohibited are all in substantial disagreement with the predictions of a nonselective model for the maintenance of genetic polymorphism. The evidence suggests instead that strong selective processes are operating, apparently at the level of the species, to regulate the distribution of alleles among the populations. At the level of the deme some degree of local adaptation occurs, but species membership is of prime importance. While the evidence provides no information on the nature of these selective processes, two models appear to fit the data.

Heterosis, selection for heterozygotes, could account for all the observations. In this model the distribution of allelic frequencies within a population would be a function of the relative selective values of each genotype, where the heterozygote, perhaps because of the physiological advantage of having more than one form of a polypeptide in a differentiated organism, would have the greatest adaptive value. If these values were consistent throughout the species, all the populations would be expected to have identical frequencies. Environmental variation might alter selection coefficients temporarily and population bottlenecks could result in temporary fixation. This is especially true in cases like *MDH*, where equilibrium frequencies are maintained around 1%. Substantial allelic variation could be maintained by heterosis, in the absence of mutation or migration, in small as well as large populations, and with a quite tolerable level of genetic death due to selection against homozygosity (MILKMAN 1967; SVED, REED and BODMER 1967). With species membership the predominant selective agent, both natural and laboratory studies of variation should provide essentially similar data. In this study on *Drosophila melanogaster* the patterns of allelic distribution in natural populations and laboratory cages did prove to be quite similar.

In recent years experimental evidence has been presented for frequency dependent selection (EHRMAN 1968; KOJIMA and YARBROUGH 1967; KOJIMA and TOBARI 1969). With such a mechanism substantial polymorphism could be stabilized even within small and isolated populations by selecting toward some particular frequency distribution at every locus. The adaptive values need not remain constant during selection, but rather would increase with the reduction of an allele's frequency below its equilibrium value. If the frequency distribution at any locus were a property of the species then a high degree of similarity would be expected between all populations, natural or not. Similarly, any perturbation from equilibrium would be met with directed selection toward the equilibrium. In general, these expectations were confirmed in this study. The exact physiological mechanism of frequency dependent selection remains obscure. Of course, it is not necessary that a single, or even two, processes are responsible for the maintenance of all polymorphisms in nature. Neither is it essential that all the variation at a single locus be maintained by a single process.

SUMMARY

Electrophoretic techniques were employed to investigate the distribution of allelic variation at seven enzyme loci in ten natural and laboratory populations of *Drosophila melanogaster* separated by space and time. The allelic frequencies at five dimorphic loci showed a general similarity over space and a marked constancy over time. Selection was observed at three second chromosome dehydrogenase loci in a series of experimental population cages derived from one of the natural populations. The direction of selection in all cases was toward the frequencies observed in the original natural population.

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