The Investigation of the
Genetic Structure
of Populations

"Third-year" Summary Review

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by
Bruce Wallace

- ABSTRACT -

This portion of report COO-3149-5 is a "third year" review of past accomplishments. Among other research items discussed are (1) the possible structure of gene-control regions, (2) intra- and inter-specific competition, (3) laboratory island biogeography, (4) studies on the utilization of various sugars by different geographic strains of Drosophila melanogaster, and (5) a reassessment of the concepts of hard and soft selection.

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Introduction

This is the "third-year" report of activities requested by the Division of Biomedical and Environmental Research. Its format follows the one suggested by the Division.

Main Research Accomplishments

Mid-way through the past three-year period, a new effort was added to the research already undertaken under this contract: It was found that a simple modification of the Britten-Davidson model of gene control is able to account for the long-observed "beneficial" effect of newly-induced mutations carried in heterozygous condition by otherwise homozygous individuals. Time that has been spent in working out the implications of this new model has slowed down progress in other studies but has not caused any of them to be abandoned.

The possible structure of gene-control regions.

Britten and Davidson (1969) suggested that adjacent to the structural genes of many gene loci are sensors which, when activated by appropriate signals, permit the transcription of the structural gene. Thus, the mRNA corresponding to a structural gene may be transcribed only when one or the other of several sensors has been activated. Under a control system of this sort, a gene "acts" only upon request, but it can act in response to a demand made by any one of several different developmental systems.

The Britten-Davidson model has been modified by Wallace and Kass (1974) by postulating the following: loci at which structural genes are under the control of several sensors will operate most efficiently if the

sequences (not types) of sensors in homologous loci differ. Even random differences in homologous sequences (say, AECDB and CBAED) tend to increase both the rapidity with which genes at several loci respond to a common signal and the uniformity in the time of action of these several genes.

In order that sensors might spontaneously exchange positions within the control portion of a gene locus without danger of being lost requires a reverse-repeat (palindromic) pattern of chromosomal DNA. In order that all sensors be able to move freely to any position within a gene's control region requires that the control region be built of a series of overlapping palindromes each of which contains a unique region, the sensor:

$$as_1bb's_2a's_3bb's_4a's_5bb's_6a' \text{ etc.}$$

where $s_1, s_2, \dots$ are sensors. Furthermore, because the sensor rotates with each shift in position, each sensor must itself be built as a palindrome.

In support of the Wallace-Kass model are the observations (1) that the heterogeneous RNA, of which the mRNA is initially a part, is largely double stranded (double stranded RNA can only be transcribed from DNA containing a reverse repeat) and (2) that promoter regions are in fact largely palindromic.

Seemingly, a number of past observations can be related to the Wallace-Kass model. These include the possible structure of the scute locus and the reported co-linearity of missing bristles and chromosomal map position of scute alleles reported by Dubinin (1932) and his colleagues. The model touches as well on the origin of unstable mutations which eventually stabilize in either the normal or mutant form. Many unstable mutations in maize have had their origins in the breakage-fusion-bridge cycle (McClintock 1950); this cycle generates sequences of overlapping palindromes.

The model can also be used in explaining a number of phenomena observed in the past by population geneticists such as (1) the coadaptation of

different gene sequences (inversions) in natural populations, (2) the release of variability through recombination, and (3) the loss and regaining of fitness under artificial selection. It has important bearing as well on the current neutralist-selectionist controversy. Finally, of course, it offers an explanation for the observed beneficial effect of randomly induced mutations which are carried in the heterozygous condition by otherwise homozygous individuals (see Wallace 1959). These points have been discussed in a series of papers (Wallace 1975, 1976; Wallace and Kass 1976).

References:

Britten, R.J. and E.H. Davidson, 1969. Gene regulation for higher cells:
A theory. Science 165: 349-357.

Dubinín, N.P. 1932. Step alleomorphism and the theory of centres of the
gene, schaete-scute. J. Genet. 26: 37-58.

McClintock, B. 1950. The origin and behavior of mutable loci in maize.
Proc. Natl. Acad. Sci. 36: 344-355.

Wallace, B. 1959. The role of heterozygosity in Drosophila populations.
Proc. 10th Int. Cong. Gen. 1: 408-419.

Wallace, B. 1975. Gene control mechanisms and their possible bearing on
the neutralist-selectionist controversy. Evolution 29: 193-202.

Wallace, B. 1976. The structure of gene control regions and its bearing
on diverse aspects of population genetics. (To appear in the
Proceedings of an International Conference on Population Genetics
and Ecology that was held in Israel March 12-23, 1975.)

Wallace, B. and T.L. Kass. 1974. On the structure of gene control regions.
Genetics 77: 541-558.

Wallace, B. and T.L. Kass. 1976. On inverted repeat sequences in chromosomal DNA (to appear in GENETICS, January 1976).

Intra- and inter-specific competition.

A study of competition within eight Drosophila species and between 18 of their paired combinations was completed during this three-year period. "Competition" in this study was measured in terms of adult progeny produced per female in standard (25 mm x 95 mm) culture vials by females of a single species or by females of two competing species.

The most interesting results were the following: If 1, 2, 3, ... females of a single species are regarded as 1 female + 0 competitors, 1 + 1 competitor, 1 + 2 competitors, etc., the average number of progeny per female can be plotted against numbers of competitors. By trial and error it was found that the logarithm of the average number of progeny plotted against the square-root of the number of competitors results in a reasonably straight line over the entire range from 0 to 14 competitor females. In contrast, when the competing females are of a different species (1 melanogaster female + 0, 1, 2, etc. pseudoobscura females, for example), the line breaks sharply after 3-4 competing females and thereafter is roughly horizontal. The contrast between the results of intra- and inter-species competition suggests that different species utilize differently the resources available to them in culture vials; the 5th, 6th, 7th, and additional pseudoobscura females, for example, do not compete with a melanogaster female in the same manner as do the 5th, 6th, 7th, and additional melanogaster females. After a certain

density has been reached, additional heterospecific females and their progeny do not compete with the first species as do the earlier heterospecific females.

This observation has been extended by Mr. T.L. Kass to the semi-species of the D. paulistorum complex. In brief, he finds that "inter-specific" interactions may be as varied and pronounced between closely related semi-species as between, for example, one of D. paulistorum's semi-species and a second species, D. willistoni.

A second aspect of the competition experiments has been studied by Mr. Fidelis Ogah. When females of two different species are placed in culture vials, each vial may yield mixed progeny (as in the case of melanogaster and simulans) or individual vials may yield progeny primarily of one species only (as in the case of pseudoobscura and virilis). In the latter case, the numbers of vials yielding progeny of each species are approximately proportional to the numbers of parental females of the two species in each vial.

Ogah successfully selected strains of pseudoobscura and virilis which when placed together in vials yielded mixed progeny. The contrast between these strains and the unselected ones enabled him to identify the causes for single-species progeny in the unselected strains and the means by which these causes were circumvented in the selected ones. In brief, the patterns of emergence in the case of unselected strains are determined by the liquification of the culture medium by virilis larvae (this results in the drowning of most pseudoobscura pupae) and the inhibition of egg laying by virilis females and the postponement of the development of virilis larvae in the presence of pseudoobscura larvae. The selected virilis strain began egg-laying earlier than the unselected strain and then quickly ceased

before producing enough larvae to liquify the food. These changes in behavior permitted both species to emerge from each vial as mixed progenies.

References:

- Kass, T.L. 1975. Niche overlap and the origin of species: A study of laboratory competition in the Drosophila paulistorum complex. Cornell University Ph.D. thesis. August 1975.
- Ogah, Fidelis, 1974. Studies on competition between Drosophila pseudoobscura and Drosophila virilis in laboratory cultures. Cornell University Ph.D. Thesis. January 1974.
- Wallace, B., 1974. Studies on intra- and inter-specific competition in Drosophila. Ecology 55: 227-244.

Laboratory island biogeography

Much of our effort during the past three years has been spent studying a laboratory model of MacArthur and Wilson's (1967) theory of island biogeography. The laboratory study was conducted in two parts: (1) the accumulation of species on islands under different regimes of immigration (from a constant source) and extinction, and (2) the accumulation under various regimes of immigration and extinction when the immigrants came from the islands, themselves. In the first part, the islands can be visualized as offshore islands that receive immigrants from a nearby continental area; in the second, as islands of an archipelago such as Hawaii or the Galapagos.

The first part of the "island" study has been completed and a manuscript describing the results has been accepted by EVOLUTION. The

number of species on an island is indeed determined by immigration and extinction rates. Although an estimate of the number of species at equilibrium can be made using average rates of immigration and extinction, the true equilibrium number equals the sum of the probability that any of several species will be found on the island. The individual probabilities are determined by the immigration and extinction rates of the individual species: $S_i = \frac{I_i}{I_i + E_i}$ where S_i is the probability that the i^{th} species is present on an island, I_i is the immigration rate for the i^{th} species, and E_i is its extinction rate. The expected total number of species on an island equals the sum of S from $i = 1$ to $i = P$, the number of species in the pool from which migrants are chosen.

A point that might be intuitively obvious to a biologist but not necessarily so, let's say, to a mathematician is the following: extinction rates for various species are not constants; on the contrary, they depend heavily on the composition of the species pool. This point was brought out clearly in our experiments by the inclusion and exclusion of D. melanogaster from the pool of 18 Drosophila species used in the study. The equilibrium number of species on each island was higher when melanogaster was excluded from the pool than when it was present even though its exclusion resulted in a smaller pool (17 rather than 18 species). In effect, melanogaster is a weedy species which when present crowded out other species that might otherwise have reproduced successfully.

The experimental results obtained in the first part of this study suffer from a lack of mystery. Comparable results obtained in field studies would have been extremely exciting because they would suggest additional experiments that would be needed to test various alternative explanations. In the laboratory studies, all information is available

at once: the arrival of each species, the identification of its competitors, and the time of its extinction. Under these circumstances, it is all too clear that the species on an island at any moment are those that have arrived in the past and which have not yet become extinct.

The second part of the "island" study, the archipelago, has been concluded but the data have not been analyzed. In contrast to part one, the archipelago offered each species an opportunity to evolve. Individuals of any species which survived on an island (and, therefore, were migrants during the following cycle of migration) may have done so because they avoided migrating with certain other competitor species or, alternatively, because they migrated with a facilitating species.

The analysis of these data, which must be done with the aid of a computer, will consist of searching for systematic changes in the patterns of association with which the different species entered individual vials. In principle, the calculation is straight forward: Let p_i = the proportion of vials in which species i was found, and p_j = that in which species j was found; then $p_i p_j$ = the expected number of vials containing both. The analysis will consist of searching for systematic changes in the ratio of observed proportion of "joint" entries to the expected proportion.

The data collected from both the archipelago and the earlier island experiments will serve an important second purpose. Most experiments on species competition (such as those described in the preceding section) are limited to species pairs. The "island" data provide information on the outcomes of competition in vials containing two, three, four, and even more species. Again, the analysis of the data must be done by computer. Because 18 species were used in these experiments, there are 9×17 or 153 pairwise combinations and $(18!)/(3! 15!)$ or 816 combinations of

three species. Even with the aid of a computer, some of these combinations must be omitted from the final analysis.

Reference:

MacArthur, R.H. and E.O. Wilson, 1967. The Theory of Island Biogeography.
Princeton University Press.

Studies on the utilization of various sugars by different geographic strains of *D. melanogaster*.

These experiments began in an effort to see whether, within a reasonably short time, strains of *D. melanogaster* that were maintained on a culture medium containing primarily a single sugar as its carbon source would adapt to that sugar, thereby utilizing it more efficiently than unselected strains. For this purpose, a number of strains from three geographic localities were maintained either on a glucose-containing medium or a sucrose-containing one. After two years, these strains and their hybrids were tested on glucose- and sucrose-containing medium as well as on one containing xylose. (The medium in each case was made of 500 ml H₂O, 50 gms sugar, 20 gms dried brewer's yeast, plus propionic acid and chloramphenicol to inhibit yeasts, molds, and bacteria. About 30% of brewer's yeast consists of fructans, glucans, and other carbohydrates; therefore, in addition to the 50 gms of the specified sugar there were about 6 additional grams of polysaccharides.)

The preliminary results showed that although there was considerable variation in respect to the ability of various strains to utilize the three sugars, this variation was traceable to the original strains; it had not arisen during the two year period of isolation and selection.

Consequently, a survey has since been made using more than thirty strains of flies from various geographic regions and nine "sugars" (including none at all). The results of this survey are shown in Table 1. The results are clear: (1) some sugars (glucose, sucrose, and mannose, for example) support larger numbers of developing flies than do others. (2) Sugars which support relatively few flies of one strain may yield large progenies of other geographic strains.

In the case of xylose and strain BV-1 (Blacksburg, Virginia), it is known that xylose acts to inhibit the growth of larvae; they develop faster and in larger numbers on brewer's yeast alone than on brewer's yeast plus xylose. On the other hand, as the Table shows, other strains produced more offspring when xylose was added to brewer's yeast than when it was omitted. Thus, it appears that considerable genetic variation exists within D. melanogaster in respect to either its carbohydrate transport or metabolism.

A reassessment of hard and soft selection.

In 1967 at a symposium on population biology and evolution held at Syracuse University, I used the terms "hard" and "soft" selection for the first time (Wallace, 1968). These terms were not defined; instead, they were illustrated by example.

During the past two years, at the urging of friends who pointed out both the popularity these terms have attained and the confusion their lack of definition is causing, I have attempted to define hard and soft selection in terms of frequency- and density-dependent selection. A re-examination of the original examples shows that hard selection is density- and frequency-independent while soft selection is density and frequency-dependent.

Table 1

Summary of the average number of adult progeny produced per vial on sugar-brewer's yeast media. The "sugar" in each test was as shown or was omitted from the medium ("none"). Propionic acid and chloramphenicol were added to the medium to inhibit the growth of microorganisms.

LOCALITY STRAIN	GLUCOSE	SUCROSE	MANNOSE	MANNITOL	DEXTRIN	XYLOSE	GALACTOSE	LACTOSE	NONE	AVERAGE
BER 1	21	5	14	8	6	0**	48*	2**	29*	15
BOG 3	24	27	75*	18	5	11	14	3**	4**	20
BS 1	5	7	22*	14	8	7	-	0**	9	9
BS 2	52	66*	48	59*	18	15	0**	8	27	33
BV 1	7	20*	6	6	4	1**	4	8	5	7
GA 1	13	26	66*	8	0**	2	3	0**	0**	13
CO 3	12	9	19	19	2	1**	33*	1**	2	11
EV -	63	55	49	42	44	38	-	67*	23	48
KSA 2	49	50	84*	31	137*	24	2**	1**	16	44
KSA 4	-	-	65	-	-	-	-	-	-	65
MO 12	13	35*	17	9	17	1**	30*	0**	1**	14
MNA 3	-	19	29	36*	2	2	29	3	8	16
NO 2	-	12	2	6	6	1	6	4	11	6
PVM -	15	67*	67*	15	5	20	12	-	17	27
PYR 3	57	53	78*	51	70*	10	34	5	24	43
QI 2	6	25	15	41*	24	2	24	0**	1**	15
RVC 2	28	13	27	6	29	25	5	32	3	19
RVC 4	39	34	28	46*	19	8	28	3	8	24
SC 1	2	13	36*	9	0**	6	-	11	0**	10
SC 2	-	-	43	-	-	-	4	-	-	24
VAG 2	17	54*	33	19	4	1**	2	0**	6	15
VAG 3	12	26	33*	13	13	6	25	10	4	16
1 A	47	41	35	29	40	19	2	13	25	28
1 B	3	35*	21	8	2	12	2	3	4	10
2 C	12	46	74*	6	3	1**	3	9	4	17
2 D	49	42	26	43	32	7	44	7	21	30
3 A	-	-	49	25	-	-	72*	0**	-	37
3 C	34	24	21	41	21	4	44	6	28	25
4 B	23	26	37	34	41*	12	6	17	2	22
5 B	1**	14	19	3	40*	7	25	0**	1**	12
8 D	30	46	54	23	36	37	4	27	27	31
9 A	6	52*	101*	17	43	7	21	0**	6	28
10 A	3	13	-	31*	0**	10	8	1**	4	9
10 D	16	12	35	43*	15	1**	6	21	6	17
10 E	10	67*	76*	10	7	10	0**	3	11	21
11 A	31	30	42	39	27	11	24	24	8	26
11 C	24	22	-	-	29	7	56*	11	20	24
AVERAGE	23	32	41	24	22	10	19	9	11	22

* exceptionally high number of progeny

** exceptionally low number of progeny

An examination of Bryan Clarke's effort to combine genetic load theory with ecological models has revealed that all selection occurring in real populations is soft -- that is, both density- and frequency-dependent. Thus, most calculations upon which genetic load theory is based and which are based in turn on hard selection have no bearing on events occurring in real populations.

References

- Clarke, B. 1973. The effect of mutation on population size. *Nature* 242: 196-197.
- Wallace, B. 1968. Polymorphism, population size, and genetic load. In Population Biology and Evolution (R.C. Lewontin, ed.) pp. 87-108.
- Wallace, B. 1975. Hard and soft selection revisited. *Evolution* 29: 265-273.

Plans for Continuation

Scute studies.

As a personal commitment to research on gene control, I have decided to spend some of my time studying recombination at the scute locus. Under the Wallace-Kass model, the mutations of D. melanogaster that are known as scute might represent unstable control regions from which transcription initiation sites (or "sensors") necessary for bristle formation can be lost in certain cells during development. Should the descendants of these cells be called upon later to form bristles, they would be unable to do so.

A detailed account of proposed technical procedures are given in the accompanying renewal request so they will not be repeated here. Suffice

it to say that any scute male may be characterized not only by his own phenotype but also those of his sons which are obtained by mating him with attached-X females (scute is located on the X-chromosome and, hence, in a cross to attached-X females is transmitted from the father to his sons); an example of this type of characterization is shown in Figure 1.

We have over the past months collected a number of scute stocks in which the scute-bearing chromosome has either acquired (through radiation) a Notch mutation (Notch is lethal in males) or a lethal associated with a mutation at the yellow locus. Females heterozygous for these two types of lethal-bearing X-chromosomes can be obtained through the use of a Y-chromosome that carries the normal allele of the Notch locus: sc N/Y-N⁺ males are mated with y-lethal sc/w^aB females.

These heterozygous females, when mated with w^aB males, for example, should produce very few sons. The only males expected to survive are those in which a cross-over has occurred between yellow and Notch (these loci are three cross-over units apart). Because scute lies in this region, a reasonable proportion of these few surviving males are expected to represent cross-overs within the scute locus.

Intra-scute recombinations which produce chromosomes bearing two "scute" sensors are expected under the Wallace-Kass model to give rise to males that are nearly wild type in appearance because of the unlikelihood that both sensors would be lost simultaneously from any one cell during development. Chromosomes bearing no scute sensors should, under the model, show an extreme scute phenotype (such flies may in fact be lethal). At any rate, exceptional males can be mated at once with attached-X females in order to determine whether their exceptional phenotype results from a genetic change at the scute locus (which would be transmitted to sons) or is a

GLYPH

Figure 1

phenotypic accident (sons in this case, would show an expected scute pattern).

Population studies

A. Phyps populations.

In an experiment that has subsequently become a classic, Koopman (1950) showed that reproductive isolation can be enhanced by natural selection. D. pseudoobscura and D. persimilis carrying the genetic markers glass (eye texture) and orange (eye color) respectively were used in his studies so that the progeny of intra- and inter-specific matings could be recognized; the wild type interspecific hybrids were destroyed each generation. Eventually only mutant flies were produced in population cages containing the genetically marked strains of these two species.

Van Valen (1963) later showed that if the wild type hybrids were not destroyed in such an experiment, the debilitating mutant genes were eventually eliminated from the "hybrid" population. The resulting flies, consequently, must have assembled a genotype from fragments of both species: the wild allele at the glass-locus must be of persimilis origin whereas the wild allele at the orange-locus must be from pseudoobscura.

We have set up a number of these pseudoobscura-persimilis populations; they have been named phyps populations, for persimilis-hybrid-pseudoobscura. These will be used for a number of purposes. First, behavior. Persimilis and pseudoobscura flies exhibit a pronounced sexual isolation. Will phyps populations develop their own mating ritual? Do they have at their disposal a potential repertoire so enormous that the flies of each phyps population will hit upon their private mating procedure and, thus, show at least partial sexual isolation from flies from other phyps populations? Or, is

the potential repertoire so limited that all phyps populations are forced to adopt that same mating procedure? In the latter case, is the procedure developed by each phyps population identical to that of pseudoobscura? Persimilis? Or sometimes one, sometimes the other? (Preliminary tests indicate that the mating behavior of flies from population, Phyps-1, corresponds to that of D. persimilis.)

Second, adaptation to unusual conditions. One phyps population (Phyps-2) is being forced to live on very watery medium; many adults drown while laying their eggs and the early larvae are virtually aquatic for the first 24-48 hours of their lives. Another population (Phyps-3) is maintained on formaldehyde-containing food; the present concentration is 0.1%. Formaldehyde is a mutagenic compound; an eventual genetic and cytological comparison of these flies with those of other phyps populations and with pseudoobscura and persimilis will be interesting.

Third, selection for sexual isolation. As the individuals of the Phyps-2 and Phyps-3 populations consolidate their behaviors and adopt to the media on which they are being raised, they will be placed in two-species cages with genetically marked pseudoobscura or persimilis flies in an effort (1) to find conditions under which phyps and the other species will coexist and (2) to see whether reproductive isolation becomes enhanced during the process.

References:

- Koopmann, K.F. 1950. Natural selection for reproductive isolation between Drosophila pseudoobscura and D. persimilis. *Evolution* 4: 135-148.
- Van Valen, L. 1963. Introgression in laboratory populations of Drosophila persimilis and D. pseudoobscura. *Heredity* 18: 204-214.

B. NaCl and CuSO₄ populations.

It was somewhat surprising to learn at the population genetics conference in Israel (March 12-23, 1975) that persons are still interested in the genetic mechanisms of species formation. Because of this interest, an experiment has been started which could have been done at any time during the past twenty years or more but which, in fact, has never been carried out.

Two populations of D. melanogaster have been set up; one is maintained on medium containing ever-increasing concentrations of NaCl, the other on food containing CuSO₄. In both populations, then, selection is establishing genetic resistance to these poisonous salts. Furthermore, the population kept on NaCl is homozygous for the "fast" allele at the Acph-1 locus; that on CuSO₄ is homozygous for the "slow" allele at that locus.

Every four months we plan to begin a (NaCl + CuSO₄) population which will be maintained on both NaCl- and CuSO₄-containing food (each in its own cup, not mixed) using as parents flies drawn from the fast and slow NaCl and CuSO₄ cages. Two of these cages [(NaCl + CuSO₄)-1 and (NaCl + CuSO₄)-2] have already been set up.

At some future time, one can imagine that the flies from the NaCl-1 and CuSO₄-1 cages will be resistant to levels of these salts so high that they (and their hybrids) will be unable to survive on the medium to which the other has become adapted. A (NaCl + CuSO₄) population that is set up at that time should produce fewer and fewer F/S hybrid flies in successive generations as selection for reproductive isolation progresses. When that time eventually arrives, however, we shall have not only the last of the (NaCl + CuSO₄) populations but all preceding ones as well; in effect, we

shall have the entire "fossil" record leading up to what we hope will be, in effect, speciation within the laboratory.

The "sugar" experiments.

The experiments on sugar metabolism will be continued. The survey which has been completed will now be supplemented by a detailed study of what seem to be the more interesting strains. Undergraduates wanting research problems will be used in working out the genetics of the more pronounced differences (work done so far suggest that the inability to use xylose and lactose is recessive but apparently not the result of a single gene in either case). It is hoped that some sugars will prove to be useful as screening substances for eventual mutagenic studies.

Island experiments

The data from the island experiments are to be computer-analyzed.

The temperature gradient.

Mr. James Fogleman, a graduate student, is basing his Ph.D. thesis research on the competition and reproductive behavior of Drosophila species at different temperatures along a temperature gradient.

Fitness and low-level radiation

This research problem, once assigned to a graduate student who then withdrew from Cornell, is not being pursued at the moment. It is an important one, however, that will be re-assigned eventually to an interested

student. (Mr. Milton Timm -- see below -- may be this student.)

Graduate Students:

Graduate students whose research is related to that done under this contract are

Fidelis Ogah: Ph.D. January 1974.

Thomas L. Kass: Ph.D. August 1975.

James Fogleman: Ph.D. candidate working on the temperature preferences of various Drosophila species in relation to competition, selection, and behavior of these flies.

Milton Timm: a Ph.D. candidate in the field of ecology who has recently asked that I be his major professor. In learning standard Drosophila techniques Mr. Timm has studied the mating preferences of D. pseudoobscura, D. persimilis, and D. "phyps" (the introgressive hybrid described earlier). Mr. Timm is interested in studying the effect of radiation on the equilibrium of species-pairs which coexist under competition (D. willistoni and D. pseudoobscura are a pair of this sort).

Alan Hastings: A Ph.D. candidate in Applied Mathematics who is studying the linkage disequilibrium of several linked gene loci in natural populations of D. melanogaster.

There were no post-doctoral fellows associated with this research (the contract does not provide either pre- or post-doctoral fellowship support) during the past three years.

Bibliography:

Theses:

Ogah, Fidelis. Studies on competition between Drosophila pseudoobscura and Drosophila virilis in laboratory cultures. 120 pp. Jan. 1974.

Kass, T.L. Niche overlap and the origin of species: A study of laboratory competition in the Drosophila paulistorum complex. 317 pp. Aug. 1975.

Papers: Research

Wallace, B. 1974. Studies on intra- and inter-specific competition in Drosophila. Ecology 55: 227-244.

Wallace, B. and T.L. Kass, 1974. On the structure of gene-control regions. Genetics 77: 541-558.

Wallace, B. 1975. Gene control mechanisms and their possible bearing on the neutralist-selectionist controversy. Evolution 29: 193-202.

Wallace, B. 1975. The structure of gene control regions and its bearing on diverse aspects of population genetics. Paper delivered at an International Conference on Population Genetics, Israel, March 12-23, 1975; Proceedings of the conference to appear in February 1976.

Wallace, B. 1975. Hard and soft selection revisited. Evolution 29: 265-273.

Wallace, B. and T.L. Kass, 1976. On inverted repeat sequences in chromosomal DNA. To appear in GENETICS, January 1976.

Papers: Other

Wallace, B. 1975. Genetics and the great IQ controversy. Amer. Biol. Teacher 37: 12-18.

Present State of Knowledge

Despite the sustained flurry of excitement created by the discovery of electrophoretic variants among the gene products of many loci, population genetics is essentially marking time while waiting for a new conceptual breakthrough. Nor is the recent spate of work on heat-sensitive enzyme variants likely to change matters; the existence of this type of variation -- and still another -- was reported in one of the first papers on electrophoretic variation (Wright, T.R.F. 1963. The genetics of an esterase in Drosophila melanogaster. Genetics 48: 787-801).

It seems to me that population genetics is in need of two advances: one in genetics proper, the other in ecological theory. Unlike those who are mathematically inclined, I have always felt that population geneticists, and the populations they study, serve as one more (perhaps the ultimate) check on "classical" genetic models. Thus, the discovery of gene-enzyme variation destroyed the myth that each species has an ideal genotype and that every enzyme and every protein found in the individual members of a species have a "normal" composition.

Work carried out at Cold Spring Harbor on the fitness of irradiated populations showed that the expected relationships between mutation rates and average fitnesses of populations did not hold when these expectations were based on classical genetic models.

The observed discrepancies will eventually be resolved, I believe, through an increased understanding of gene action and the control of gene action; they will not be resolved by a superstructure of mathematical calculations. It is for this reason that much of our recent effort has been spent on speculations concerning gene control regions. These controls -- both the construction of individual controls and the interactions between

controls at different loci -- must be important during development and, therefore, in the genetics of populations as well. The detailed knowledge of control structure must come from molecular geneticists; the function of certain micro-structures may be correctly anticipated by others, however. One correspondent expressed matters this way: An understanding of population genetics must await an explanation for the beneficial effects of random genetic change in otherwise homozygous individuals. This claim can be readily extended to development genetics as well.

The second conceptual advance needed for population genetics is in its ecological aspects. This advance must also deal with variation. Even now, many of the calculations encountered in ecological genetics are of the classical, "genetic load" type; these are fundamentally anti-variation calculations. Variation among members of a population is ordinarily looked upon as harmful or, at best, as a pre-adaptation to future environmental changes. I believe there is more to the story. Under the "pre-adaptation" model, variation provides for the lucky genotype that copes with new environmental stress (the role of sex, incidentally, is said to be the generation of this variation). If one views the species (or population) as a player in a "no-win" game as Slobodkin has suggested, variation takes on a different, or at least an additional, function. Variation can act as a collapsible bumper which maximizes the probability that some members of a population will survive what I call "pathological over-crowding." The details of this view of variation have not been worked out. It is interesting to note, however, that the largely heterozygous genotype called for by normal development (under the view being developed here) is also the one that is able to generate considerable variation. But, this variation -- rather than being a "cost" or "load" -- is precisely the feature which a population needs to avoid the collapse which follows the epitome of success, pathological overcrowding.

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