COMPETITION BETWEEN CHROMOSOMAL ABERRATIONS ASSOCIATED WITH CURLY AND THEIR WILD TYPE HOMOLOGUES IN LABORATORY POPULATIONS OF *DROSOPHILA MELANOGASTER*¹

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INVERSIONS are commonly found in natural populations of animals, but translocations rarely occur. While inversions may affect the viability of an individual, favorably as well as unfavorably in certain cases, relatively complete pairing in meiosis can occur, normal gametes are formed, and the fertility of the organism is seldom affected, even when crossing over occurs within long inverted segments of inversion heterozygotes (STURTEVANT and BEADLE 1936; CARSON 1946). In translocation heterozygotes, however, the rearrangement of the chromosomes into new combinations leads to difficulties in meiosis, since the normal homologues pair with the chromosomes in the translocation (for *Drosophila* and references to other species, see e.g. STURTEVANT and DOBZHANSKY 1930; DOBZHANSKY and STURTEVANT 1931; GLASS 1933, 1935; BROWN 1940; PIPKIN 1940). Segregation in meiosis leads to the formation of some gametes which may be deficient for large segments of genetic material, while other blocks of genes may be duplicated. In most plants and animals, therefore, except those in which segregation is directed, translocations result in low fecundity. In addition to this, most translocations in *Drosophila* also adversely affect the viability of the flies carrying them, especially if they are present in the homozygous condition (MULLER and ALTENBURG 1930; PATTERSON, STONE, BEDICHEK and SUCHE 1934). For these reasons inversions should stand a much better chance of becoming established in natural populations of animals than translocations, and such is found to be the case.

The fact that translocations do occur and in some animal species are evidently maintained in natural populations, although rarely, makes it of interest to examine the adaptive value of translocations in laboratory populations where they compete with their wild type homologues. This report deals with the experimental study of one such translocation, itself marked with the dominant gene *Curly*, which is associated with inversions in the second chromosome.

An account of a portion of the work to be presented has been published earlier in abstract form (ERK 1952).

MATERIALS AND METHODS

The cages used in these experiments (fig. 1) are essentially a modification of the general design originally developed by DA CUNHA (1949). Each cage utilizes a battery of six quart-size square milk bottles. The central chamber is formed by an

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FIGURE 1. View of the population cage, partly disassembled to show the removable end-gates and top port cover, as well as the method of connecting the food bottles.

eleven-inch length of corrugated copper spouting, each end being closed by a removable gate. The gates consist principally of 32-mesh copper gauze, and not only provide for the ventilation of the cage, but also can be easily removed for cleaning the cages between experimental runs. Six lateral ports into the central chamber are provided by short lengths of $1\frac{3}{4}$ in. O.D. brass tubing soldered to the spouting at proper intervals. A similar piece of tubing is attached to the top of the chamber; the latter is covered by a cap made of a turned piece of brass sheeting, allowing for easy removal or addition of flies to the population. The bottles are securely coupled to the central chamber by the proper length of $1\frac{3}{4}$ in. automotive radiator hose.

The translocation used was originally obtained by DR. BENTLEY GLASS in an X-irradiation experiment; a second chromosome containing the dominant marker *Curly* became associated with an unmarked third chromosome in the aberration. The translocation, $T(2;3)^{69}Cy$, which is lethal when homozygous, has been maintained in a balanced condition for more than ten years, each successive generation being started from *Cy* males and non-translocation females from the same culture. The *Curly* chromosome used in the control cages was extracted from a stock where it had been used as a balancer for the second chromosome for many years. *Curly* manifests itself phenotypically by causing the wings to be curled up over the body; it is a dominant associated with inversions in the right and left arms of the second chromosome which strongly suppress crossing over throughout the length of the chromosome, and is lethal when homozygous. The discovery and genetics of *Curly* wing were reported by WARD (1923).

The *Curly* translocation was chosen for two reasons. The intimate association of the translocation with an easily classifiable dominant marker permitted large samples and the immediate determination of the frequency of the aberration in the population. Secondly, even though *Curly* is lethal in the homozygous condition, its pres-

ence as a heterozygote might have a favorable effect on the viability of the fly. The disadvantageous effect of the translocation resulting from lowered viability and partial sterility would be somewhat compensated thereby, and an opportunity would be offered to examine the adaptive value of a translocation when associated with a relatively beneficial gene.

In the control cages identical experiments were conducted, except that Curly in these experiments was not associated with a translocation, but only with the usual inversions in chromosome 2. Hence the parallel experiments serve as a measure of the adaptive value of Curly and its inversions, when competing with its wild type homologue, as well as providing a control for any viability effect that might be due to the inclusion of Curly in the translocation.

Prior to the initiation of the cage experiments, males from the translocation and control stocks, indistinguishable phenotypically in that both showed Curly, were outcrossed to virgin females from the Oregon-R wild type strain. F_1 males were backcrossed to Oregon-R females for a number of generations, so that eventually only the Curly chromosomes of the two stem stocks remained, the rest of the genome being largely replaced by Oregon-R chromosomes. This is not to imply that the genetic backgrounds were isogenic, but only that they were similar with the exception of the chromosomes bearing Curly and the third chromosome which had undergone mutual translocation with the Curly chromosome. The Curly chromosome too goes back to the same origin in both cases, and has kept its identity because of the suppression of crossing over throughout the chromosome.

Because of the recognizability of the heterozygotes, the Curly and wild type flies to make up the initial populations could be collected from the same culture bottles. Curly and wild type males and virgin females were collected from both the translocation and control stocks and maintained in separate containers for a few days before being introduced into the cages. The flies were then etherized, counted, and placed in a single dry vial. When all had recovered, the flies were introduced into the cage through the top port. In all experiments the initial population consisted of 400 individuals, divided equally into Curly (heterozygous) and non-Curly flies, each group being subdivided into equal numbers of both sexes. The initial gametic frequency (p) of the Curly chromosome was therefore 25 percent in both the translocation and control cages.

A single bottle containing standard cornmeal-oatmeal-dextrose-agar medium is attached to the cage at the time the flies are introduced. The initial population invades this bottle, since at this time the other ports are plugged. A fresh food bottle is added weekly, and the population is allowed to expand into the new bottle, since there is free communication in the central chamber between all the attached bottles. With the maximum number of six bottles, the cage will support a population of about 6000 individuals, as determined by actual count. Populations of smaller size could be easily studied by using fewer bottles.

Samples of the adult population were taken at weekly intervals after the population had expanded to its maximum. In the first two or three samples of the experiment, bottles were inverted over the top port and connected by a piece of hose. Those flies that happened to be close would fly or walk into the collecting bottle during the time it was in place, usually a half hour. It was later found that this

method of sampling discriminates against the Curly flies, which are not as adept in regaining a foothold once they have slipped from the sides of the collecting bottle. All later samples were taken at a side port just prior to the introduction of a fresh food bottle there. The collecting bottle was placed in the same position as the food bottles, and the flies were allowed to enter the dry bottle. Two half hour samples were taken in succession for ease of counting, and the results were totaled. The flies from both samples were allowed to recover, and were then introduced into the cage population again through the top port.

The cages were kept in a specially constructed constant-temperature incubator, and the temperature throughout the experiment was maintained at $25^{\circ} \pm 1^{\circ}\text{C}$.

RESULTS

The adaptive value of Curly in successive isolated generations

As the Hardy-Weinberg Law is deduced from the assumption of a random union of gametes, it should hold for chromosomal aberrations in populations as well as for single or linked groups of genes. The genetic equilibrium obtains unless disturbed by one or more of the factors capable of altering the frequency of genes (or gene arrangements) in populations, namely, mutation, migration, random genetic drift, and selection. While all of these may play a role in natural populations, it is probable that the changes in gametic frequencies observed in these studies are due primarily to the forces of selection.

In natural populations as well as in the cage studies, generations may overlap when the generation time is sufficiently short. To simplify the determination of the adaptive value of Curly, a complementary experiment was undertaken in which the successive generations were isolated. In the initial generation approximately 50 males and 50 females, all Curly, were placed in a regular culture container. The initial frequency of Curly was therefore 0.5, since all flies showing the character are necessarily heterozygous. The parents were removed to a fresh bottle after eight days, and allowed to remain there for an additional eight days. The first off-spring would emerge on the ninth or tenth day (later if the competition was severe), thus excluding the overlapping of generations. The F_1 flies were counted daily and placed in a fresh culture bottle. This procedure was repeated for each generation; except for the smaller sizes of the populations, all conditions were the same as for the cage studies.

From the mating of the Curly heterozygotes of the initial generation, three types of offspring are produced: Cy/Cy , $Cy/+$, and $+/+$ in the ratio of 1:2:1. Since Curly homozygotes are lethal, only the heterozygotes and the wild type flies survive to produce the next generation. If we assume that selection acts entirely against the homozygotes, and that the heterozygotes and wild type flies are equivalent in their adaptive values, then the frequency of the Curly chromosomes in the $n + 1$ generation is equal to half the frequency of the heterozygotes ($2pq$) divided by the total number of flies following elimination of the Cy/Cy flies:

$$p_{n+1} = \frac{p_n q_n}{2p_n q_n + q_n^2} = \frac{p_n}{1 + p_n} \quad (1)$$

The curve of expected selection against Curly, as determined from formula (1), is the broken line in figure 2. The solid line represents the actual gene frequencies of Curly in 30 successive isolated generations. It will be seen that, subject to some fluctuation, the actual decrease in the frequency of Curly follows the curve of expectation until the 13th generation. From that point on, if we hold the adaptive value of the wild type flies at 1, the relative reproductive fitness of Curly increases, and the frequency of Curly begins to rise again. The rise continues strikingly through the 30th generation.

If we examine the significance of the frequency of Curly heterozygotes at the 15th generation, it is found that not only does the level differ significantly from

FIGURE 2. The improvement in the adaptive value of Curly heterozygotes in isolated successive generations. The broken line represents the expected frequency, the solid line the actual results obtained.

the low point of the 13th generation ($\chi^2 = 21.09$, d.f. = 1, $P < .01$), but also from the theoretical curve of selection at the 15th generation ($\chi^2 = 19.94$, d.f. = 1, $P < .01$). Since all the values of succeeding generations differ even more than that of the 15th generation from the low point at the 13th generation and from the respective points of comparison on the theoretical curve, the differences must all be highly significant. This emphasizes the real improvement of the adaptive value of Curly heterozygotes, when compared to the wild type; the cause of this reversal in selective value is obscure at present.

The population cage experiments

In the population cage studies, both the experimental and control populations were followed in duplicate experiments conducted simultaneously. The populations were maintained for a period of four months, at which time all the adult flies in the cage were counted and classified except those remaining in the central chamber of the cage; it is estimated that at least 95 percent of the total adult population was counted in each cage at this final census. The latter and the weekly samples are summarized in table 1.

The point in each experiment when collections from the side ports were started is indicated by an asterisk. It will be seen that in cages 1 and 3 the gametic frequency of Curly in the first sample so taken is much greater than in the earlier ones. It must be concluded that the samples taken at the top port earlier did not represent the true gametic frequency of Curly in the population at the time, and all those figures should be considerably higher, thus making the transition from the initial gametic frequency of 25 percent less abrupt. Since quantitative correction of the early values involves assumptions which appear very uncertain, and since the gametic frequencies must have been changing quite rapidly during the period of the early samples, it was decided not to attempt correction but rather to use the later samples as a basis

TABLE 1
Samples from the population cages

Curly Inversion						Curly Translocation					
Cage 1			Cage 3			Cage 2			Cage 4		
Time in days	Number in sample	p	Time in days	Number in sample	p	Time in days	Number in sample	p	Time in days	Number in sample	p
0	400	.2500	0	400	.2500	0	400	.2500	0	400	.2500
32	972	.0206	29	264	.0379	48	961	.0021	44	763	.0066
67	966	.0176	66	213	.0164	67	1386	.0022	65	483	.0031
75	1255	.0080	72	585	.0154	74	706	.0043	71	584	.0069
81	619	.0452*	79	354	.0890*	81	340	.0221*	80	256	.0078*
89	492	.0336	87	309	.0923	89	172	.0087	87	344	.0058
96	739	.0216	95	506	.0603	96	1307	.0023	94	370	.0135
102	323	.0248	102	626	.0765	103	702	.0064	101	404	.0124
110	925	.0146	110	538	.0437	111	1292	.0023	108	703	.0064
117	1614	.0140	117	714	.0525	117	581	.0017	115	897	.0028
123	4709	.0312	125	5709	.0605	124	5888	.0047	124	6769	.0056

* First side port collection.

for determining the probable course of selection against Curly during the earlier part of the experiment.

In determining the expected curve of selection against Curly, if we assume that the Curly homozygote is lethal and that the reproductive fitnesses of $Cy/+$ and $+/+$ flies are equal, the progress of selection against Curly should follow the theoretical curve in figure 2, starting at the 0.25 level.

In calculating the selective disadvantage of the Curly translocation heterozygotes, if we let o represent the orthoploid gametes and a the aneuploid gametes, then six types of gametes will be formed: along one axis of disjunction, o_1 ($T-Cy$)¹, o_2 , a_1 ($T-Cy$) and a_2 , and along the other axis, o_1 ($T-Cy$), o_2 , a_3 ($T-Cy$) and a_4 . The only viable combinations among these gametes are o_1o_2 , o_2o_2 , a_1a_2 , and a_3a_4 . In addition to these individuals in the population, viable offspring will result from the union of the orthoploid gametes of the Curly heterozygotes and the gametes of the $+/+$ flies, as well as from the union of gametes from the normal flies alone.

At the start of a given generation, $T-Cy/+$ and $+/+$ flies are present in frequencies X and Y and, it is assumed, interbreed at random. The parent combinations can be summarized in the expression $X^2 + 2XY + Y^2$, representing all possible zygotic combinations. The class X^2 consists of random union of the six types of gametes produced by the Curly heterozygotes. The Y $+/+$ flies will produce $+$ gametes which will combine randomly with the $T-Cy/+$ gametes, as well as with other $+$ gametes. Since the Cy/Cy and inviable aneuploid combinations are eliminated immediately, the frequency of $T-Cy/+$ flies in the $n + 1$ generation can be summarized:

$$X_{n+1} = \frac{2X_n^2(o_1o_2 + a_1a_2 + a_3a_4) + 2X_nY(o_1)}{X_n^2(o_2^2 + 2o_1o_2 + 2a_1a_2 + 2a_3a_4) + 2X_nY(o_1 + o_2) + Y^2}.$$

Since segregation in a translocation cross-figure is random with respect to a given axis of disjunction (GLASS 1935), we would expect orthoploid and aneuploid gametes to be formed in a ratio of 1:1. If this obtains, then $3X^2/16 + XY/2$ of $X^2/4 + XY + Y^2$ viable flies are Curly translocation heterozygotes. Performing the indicated division and simplifying, the frequency of $T-Cy/+$ flies in the $n + 1$ generation is $(8X - 5X^2)/(16 - 16X + 4X^2)$, or

$$X_{n+1} = \frac{X_n(8 - 5X_n)}{4(X_n - 2)^2}.$$

Since p , the gametic frequency of the Curly translocation gametes, is equal to $X/2$,

$$p_{n+1} = \frac{X_n(8 - 5X_n)}{8(X_n - 2)^2} = \frac{4p_n - 5p_n^2}{8(1 - p_n)^2}. \quad (2)$$

Formulae (1) and (2) can be used to determine the expected curves of selection against Curly and the Curly translocation. After ten generations of selection against the Curly homozygote, Curly should persist at a gametic frequency of 0.0714; 14 percent of the flies in the population would be phenotypically Curly. On the other

¹ ($T-Cy$) represents the Curly translocation, although strictly, the aneuploid gametes possess only a part of the translocation.

hand, after ten generations the translocation is expected to be virtually eliminated, with only four gametes in 10,000 carrying Curly. Hence, even though the initial gametic frequency of a translocation might be quite high, it would not be expected to survive in a population unless the disadvantages of low fecundity and viability were somehow compensated.

DISCUSSION

Theoretical considerations on the progress of selection against Curly have assumed that each generation was separable and distinct. Where generations overlap somewhat, as they do in the population cages or in natural populations where there is more than one brood during the fertile period of the parents, the selective value of a particular genotype is more complex, and it would be expected that there would be some difference between the actual and the theoretical courses of selection. In the experiment where successive generations were isolated, the theoretical and actual results differed little through the 13th generation, indicating that, relative to one another, the adaptive values of the Curly inversion heterozygotes and the wild type flies were approximately equal. In the cages, flies capable of extending their fertile period into the next generation would have a reproductive advantage, and this would enhance the overall adaptive value of their genotypes. Since Curly flies tend to get mired more easily than wild type flies in the cages, Curly flies may be at a selective disadvantage in competition when the time period is extended, as in a continuous population.

FIGURE 3. The expected curves of selection against Curly homozygotes over 8 and 10 generations, as compared with the actual progress of selection against Curly.

Since successive generations are not separable in the cages, it is necessary to estimate the average length of generation that is approximately equivalent to those of separable generations. At 25°C, the first adults eclose in a fresh food bottle about ten days after the bottle has been added to the cage. Females are most productive early in their reproductive life, and usually reach a peak on the second or third day. In the brood of any given female, presumably zygotes from those eggs which were first laid would have an initial advantage in securing food, so that the "average" fly which replaces a given fly in the population would result from a zygote produced during the first few days by the parent. The average generation time is therefore probably between twelve and fifteen days, and during the course of the experiment (about 120 days), between eight and ten generations would have been completed.

Using these estimates representing the probable limits of the number of generations completed during the course of the experiment, the actual data are plotted against the two theoretical curves of selection; this is done for Curly alone in figure 3, and for the Curly translocation in figure 4. As will be noted from the graphs, the gametic frequency of Curly alone apparently fluctuated somewhat from week to week; although of the same magnitude, the frequencies in the two populations differed consistently throughout the course of the experiment. The Curly chromosome was present at frequencies of 3.12 and 6.05 percent when the experiment ended. The populations containing the Curly translocation differed less widely,

FIGURE 4. The expected curves of selection against the Curly translocation over 8 and 10 generations, as compared with the actual progress of selection against the translocation.

and when the experiment was terminated their gametic frequencies were almost identical, 0.47 and 0.56 percent respectively.

The comparison of the data curves with the theoretical ones emphasizes the similarity between the expected and the actual results. The data from cage 1 are at variance with the general picture, of course, and the difference between the final gametic frequencies of Curly in cages 1 and 3 is statistically significant. Such results in a single cage might be obtained if there had been for some reason unusually rigorous selection against the Curly heterozygotes in the initial generation when the total population was small. The successive samples from cage 1 show good consistency, and it seems obvious that the selective elimination of the Curly flies must have occurred prior to the first sample. The curve for the frequency of Curly in cage 1 clearly belongs to the same family of curves as the others, but inasmuch as it differs significantly from that of cage 3, it seems advisable to use chiefly the results of cages 2, 3 and 4 in drawing conclusions.

If the final frequency of Curly in cage 3 is compared with the expected values at the end of 8 and 10 generations, the frequency actually obtained is significantly lower for both cases, with χ^2 values of 39.28 and 10.47 respectively (d.f. = 1); the χ^2 for significance at the 1 percent level is 6.635. Thus, in addition to the component of selection which results from the inviability of the Curly homozygotes, there is selection against the Curly heterozygotes as well.

At the termination of the experiment, the populations in cages 2 and 4 carrying the translocation were similar, as determined by a homogeneity test ($\chi^2 = 1.12$, d.f. = 1, $P = .20 - .30$), and the data may be conveniently lumped. 131 out of 12,657 flies were Curly heterozygotes, giving a gametic frequency of 0.0052. However, the expected frequencies of Curly after 8 and 10 generations are lower, 0.0015 and 0.0004, respectively. Because of the size of the population, this difference is extremely significant; assuming that 8 generations had been completed, the χ^2 value for the difference is 228.31 (d.f. = 1). If as many as 10 generations had been completed, the χ^2 would be greater, viz. 1465.27 (d.f. = 1). Since this difference could scarcely be due to chance, we attribute it to the selective value of the Curly translocation apart from that resulting from the Curly homozygote lethality or the formation of inviable zygotic combinations from aneuploid translocation gametes. However, the difference between the expected and the actual results would be less if the percentage of orthoploid gametes formed were greater than 50%; PIPKIN (1940) studied a translocation that formed 59% orthoploid gametes.

The persistence of the translocation in the population may be due to the association of Curly with the translocation. If the depression of the adaptive value of Curly heterozygotes in the control cages is real, then somehow this effect is not manifested when Curly is associated with the translocation. An alternative explanation would be that the Curly heterozygote had itself undergone an improvement in reproductive fitness like that seen in the later generations of the experiment where successive generations of Curly were isolated. Or again, the translocation itself might be the cause of the better than expected viability if fewer aneuploid gametes than expected were produced.

It seems most likely, however, that Curly undergoes a favorable interaction with

the translocation, resulting in a higher adaptive value for the combination. It is well known that the combination of mutants which are individually deleterious, may result in superior viability under certain conditions, when compared to a standard; this has been demonstrated in *D. funebris* by TIMOFÉEFF-RESSOVSKY (1934), and by a number of workers in *D. melanogaster*.

SUMMARY

Using population cages consisting of a battery of six quart-size square milk bottles interconnected by a common central chamber, populations of *Drosophila melanogaster* of approximately 6000 individuals can be supported.

Studies were made of the adaptive value of Curly, a second chromosome dominant, lethal when homozygous, and associated with inversions in both arms of the chromosome, when Curly is in competition with its wild type homologue. Duplicate populations were maintained for a period of four months, during which time the frequency of the Curly chromosome dropped from an initial 25% to 3.12% in one population and to 6.05% in the other. It was shown that the drop was significantly more than would be expected on the basis of the lethality of the Curly homozygotes, and that selection must in addition act against the Curly heterozygotes to lower further the frequency of the Curly gene.

In an experiment with smaller populations, Curly was allowed to compete with its wild type homologue in successive, isolated generations. The frequency of Curly followed the curve of expectation through 13 generations, at which time it showed an improvement in adaptive value which persisted through the 30th generation; thus under certain conditions the relative adaptive value of Curly heterozygotes may improve when in competition with the wild type.

Population cage experiments of identical design were conducted to examine the adaptive value of Curly when associated with a 2,3 translocation. Again duplicate populations were maintained, and at the end of four months of selection, the gametic frequency of the Curly translocation had dropped from an initial frequency of 25% to 0.47% in one population and to 0.56% in the other. Although great, the drop in the frequency was not as great as would be expected on the basis of an additive effect of the lethality of Curly homozygotes and the inviability of zygotes formed from aneuploid translocation gametes. In fact, the frequency was maintained at a significantly higher level than was to be expected from inviability due to these causes alone, not to consider the lowering of viability that might be due to the Curly heterozygotes. It appears likely that Curly in association with the translocation had a favorable effect on the viability of the translocation heterozygotes.

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