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Hybrid Dysgenesis in *Drosophila melanogaster*

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Drosophila geneticists have recognized the occasional occurrence of dysgenic traits such as mutation, chromosomal aberration, distorted segregation, and sterility (*1*, *2*). These traits were usually found in experiments with flies newly caught in the wild. Male recombination has also been found under similar conditions (*3*), generally associated with other dysgenic traits, particularly with mutator activity (*2*). These results had been attributed to mutator genes apparently widespread in natural populations, but this interpretation led to an enigma. It was difficult to understand how such genes could be maintained in natural populations since their effects would be expected to result in a drastic reduction of population fitness (*4*).

The first contribution to clarification was that of Kidwell (*5*) who, on the basis of several crosses, suggested that high frequencies of dysgenic events do not occur under natural conditions but are the result of genetic interactions between strains newly derived from wild flies and long-established laboratory stocks. This idea was developed further, and the term "hybrid dysgenesis" has been proposed to designate a "syndrome of correlated genetic traits that is spontaneously induced in hybrids between certain mutually interacting strains, usually in one direction only" (*6*, *7*).

Kidwell, Kidwell, and Sved (*8*) showed that the stocks they used fell into two categories called P and M. It soon appeared that strains established from newly caught wild flies were of the P type, whereas long-established laboratory strains were of the M type (*8–10*).

We have been investigating a specific kind of female sterility (called SF sterility) which occurs in F_1 females obtained from crosses between two types of mutually interacting strains called inducer and reactive; the reactive strains exist only in laboratories. The sterility test permits analysis of the genetic factors involved in this phenomenon. The reactive condition may be viewed as a particular cytoplasmic state of the oocytes, which is mainly maternally inherited. However, this state is ultimately controlled by a chromosomal polygenic system. The inducer condition is determined by a chromosomal factor that is probably a transposable element. Transpositions may occur with high frequency but require a reactive cytoplasm.

The inducer-reactive interaction leads, in addition, to other dysgenic traits, notably to nondisjunction and mutation (*11*). Therefore, this system appears to fall within the domain of hybrid dysgenesis. It is now established that *Drosophila melanogaster* exhibits at least two causally independent systems of interacting strains: I-R and P-M (*10*). Most, if not all, laboratory stocks or wild populations belong to one category of both systems and a dual designation is now possible for all of them (*10*, *11*). A review of the I-R system may clarify the understanding of hybrid dysgenesis and may be of particular interest because (i) the data obtained on I-R interaction could stimulate and facilitate comparative studies with other similar systems already (or still to be) described, and (ii) the various impli-

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cations of this system may be of interest in both general genetic mechanisms and population genetics.

Physiological Characteristics of SF Sterility

The discovery of a specific kind of reduced fertility in F_1 females from crosses between two categories of strains (*12*) provides a useful test for investigating the genetics of this interaction. Since most of our results have been obtained on the basis of this criterion, it is necessary to describe its main physiological characteristics. Sterility occurs in the progeny of crosses made in one direction only, that is, when the mother is of the reactive type and the father is of the inducer type. It is independent of the mates of the F_1 females and exhibits the following features (*13*).

1) Sterile F_1 females (SF females) lay normal quantities of eggs but a certain percentage of these do not hatch. These unhatched eggs are fertilized and initiate mitosis, but their development is stopped between the fifth and eighth cleavage. No other female sterility known in *D. melanogaster* exhibits such a uniform timing of embryo death at late cleavage.

2) The hatching percentage increases regularly as SF females age and can eventually reach control values. This unusual aging effect provides an easy test for identifying SF sterility.

3) Short-term thermic treatment (30°C) of egg-laying SF females leads to a temporary increase in fertility. However, heat treatments have opposite effects depending on the period when they are applied (*14*). During nearly all stages of the development, including early oogenesis, they reinforce SF female sterility, late oogenesis being apparently the only period when they have a curative effect.

The biological causes of embryo death are still not known. It is unlikely that death occurs by chromosome breakage, as suggested by Thompson and Woodruff (*2*), because of the precise timing of the lethal stage and the lack of visible chromosomal aberrations during the first cleavage divisions. The most likely hypothesis is that embryo death is the result of some specific biochemical deficiency in the oocyte resulting in a threshold effect.

These unusual characteristics indicate that it is easy to distinguish SF sterility from any other kind of female sterility occurring in the same species, allowing unambiguous reading of the experimental results. This situation is different from that existing in studies where mutator activity is investigated by scoring mutations or male recombination. In these latter cases, one cannot easily distinguish between events produced by different biological agents, such as genes, viruses, or bacteria. Therefore, it is necessary to demonstrate that male recombination obtained by injection (*15*) is due to the same causal agent as that observed in genetic crosses. This uncertainty may be one possible explanation for the conflicting results obtained in injection experiments (*2, 15, 16*).

Summary. Several dysgenic traits may occur within the *Drosophila melanogaster* species as a result of crosses between different strains. Crossing two mutually interacting categories, named inducer and reactive, may lead, among other abnormalities, to a specific kind of female sterility that has proved useful for investigating the genetic factors involved in the interaction. The reactive state appears to result from a cytoplasmic state ultimately controlled by a chromosomal polygenic system. The inducer character is determined by a chromosomal factor that exhibits all characteristics of a transposable element. Overall, the data contribute to clarification of mutator activities in *D. melanogaster* and open new opportunities to investigate unusual genetic mechanisms.

Distribution of Inducer and Reactive Strains

So far more than 200 strains of various geographical origins have been tested and classified on the basis of SF sterility tests. In addition to the two classes of interacting strains, inducer and reactive, a third class, called neutral, also exists but it consists of only a few strains.

In F_1 females, reduced fertility appears only from a cross between reactive females and inducer males. The reciprocal cross produces normal fertile daughters (RSF females), as do crosses involving a neutral strain or crosses within one class (*12*). Hybrids from all I × I and R × R crosses were fertile.

The inducer and reactive conditions show wide variation. On the basis of the hatching percentage of young SF females, we can distinguish strong and weak stocks in both categories, giving, respectively, low and high hatchabilities when crossed with a standard stock of the interacting category. The ordering of strength obtained in each category is independent of the choice of the standard strain of the other category (*17*). Several lines of evidence indicate that neutral strains represent one extreme limit of variation of the reactive condition, their reactivity being too weak to produce any detectable reduction in fertility (*18*).

The distribution of these categories can be summarized quite simply (*19*). All stocks established from flies recently caught in the wild have been found to be of the inducer type, whatever their geographical origin (Table 1), and they are generally strong inducers. Long-established laboratory stocks are distributed among all three classes.

With the reservation that this environmental distribution must be confirmed by further study, we can conclude that, under natural conditions, dysgenic traits cannot be produced by the I-R interaction. Therefore this system does not agree with the hypothesis proposed by Thompson and Woodruff (*2*), according to which explosive mutational events would occur after hybridization between wild populations.

Reactivity: A Complex Genetic Condition

The wide variation existing in the reactive class has been used to unravel the rules of inheritance of this character. The hatching percentage of eggs of young SF females provides a measure of the reactive strength (or level of reactivity) of their mothers when crossed with males from a standard inducer stock. In reactive stocks in which no selection has been made, there may be a wide variation in the level of reactivity among individual flies; but, by a selective procedure (*12*), homogeneous strong or weak strains that remain stable over several years may be obtained.

Using crosses between genetically marked strong and weak reactive strains, we have studied the hereditary transmission of reactivity, without any interfering action of inducer factor. The most important results may be summarized as follows. Reactivity is an extrachromosomal state that is transmitted mainly by maternal inheritance from one generation to the next, but a minor chromosomal influence is regularly observed. In fact, the reactive state is dependent ultimately on the genotype, as may be demonstrated by replacing the chromosomal genotype of a strong strain

by that of a weak one. The lines thus obtained originate maternally from a strong strain and have a genotype of weak origin. They may be maintained by inbreeding (*20*). Initially these lines show a strong mean level of reactivity with a wide variation, but this level regularly decreases over generations and finally reaches the low level of reactivity corresponding to their genotype. More than ten generations may be necessary to reach this new equilibrium. The three major chromosomes are involved in this genotypic control, and they have additive effects. Therefore, the reactive cytoplasmic state appears to be a quantitative character determined by a polygenic system with a delayed effect.

Additional investigations have been performed with crosses between reactive and inducer strains. The reactive state may be brought by paternal gametes into oocytes of an inducer strain (*18, 21, 22*). The most demonstrative result in this area has been provided from lines that bear chromosomes of a strong reactive strain but which originate maternally from an inducer stock. Initially the level of reactivity of these lines is low but increases in the course of generations and may reach a high level (*23*). Such lines are rather difficult to obtain because all the reactive chromosomes contaminated by the inducer factor must be eliminated (see below).

The effects of aging and thermic treatments are other features of this cytoplasmic state. The reactivity of females decreases regularly with their age (Fig. 1); this decrease is partly inheritable, and a cumulative effect may be obtained over several generations (*24*). Thus, it is possible to shift a reactive stock from strong toward weak reactivity by producing each generation from old egg-laying females. However, this change is always reversible; if young reproductive flies are used again, reactivity progressively returns to the strong level.

The effects of thermic treatments are more complex. When they are applied during late oogenesis, treated oocytes give rise to less reactive females (*24*). But when thermic treatments are applied during any other stage of development, including early oogenesis, they result in an increased reactivity (*14*). As in the case of aging, these effects are partially inherited and always reversible.

Two hypotheses may account for all the available data on reactivity.

1) The direct genetic determinants of reactivity may be an intracellular population of extrachromosomal genetic elements, symbionts, or organelles. This population would be liable to undergo quantitative or qualitative variations through the action of nuclear genes.

2) The reactivity may involve only chromosomal determinants. In this hypothesis, the main difficulty lies in explaining the delayed effects observed. We are led to assume that the products of the genes exert some kind of complex control on the expression of the genes themselves. This could perhaps be achieved by way of structural inheritance (*25*).

Biochemical investigations may permit a choice between these two hypotheses. Preliminary results do not appear to support the first. Several assays designed to relate the reactive state to the presence of viruses or bacteria (electron microscopic examinations, injections, feeding, action of antibiotics) have led us to negative conclusions (*26*).

There are similarities with other known phenomena. The delayed effect of genotype and temperature changes bears striking analogies to those occurring for the extrachromosomal element delta studied by Minamori (*27*) and others. However, a common basis for the two systems seems excluded by the available data. In other organisms, the most striking similarities are found with some nuclear mutants in *Paramecium* (*28*) and in *Saccharomyces cerevisiae* (*29*) where a delayed effect of genotype on mitochondrial expression has been demonstrated.

The effect of nongenetic factors, particularly thermic treatments, also shows similarities with those observed for many years in various organisms and named "dauermodifications" (*30*). The molecular basis for such phenomena is still unknown.

Table 1. Geographical and environmental distribution of the three classes of strains: inducer (I), reactive (R), and neutral (N). See also the 35 stocks tested by M. G. Kidwell (*10*).

Origin	I	R	N
Laboratory strains			
France	33	30	4
Germany	1	1	0
Spain	0	2	0
Finland	0	1	1
United Kingdom	1	11	2
Italy	0	2	0
Sweden	2	7	0
U.S.S.R.	4	0	0
United States	8	1	2
Total	49	55	9
Wild populations			
France	69	0	0
Yugoslavia	1	0	0
Spain	1	0	0
West Indies	8	0	0
Central Africa	7	0	0
North Africa	2	0	0
Réunion	2	0	0
U.S.S.R.	2	0	0
United States	1	0	0
Total	93	0	0

The Inducer Factor: A Transposable Element?

The genetic determinant of the inducer character (called I factor) is chromosomal but exhibits very unusual features. In inducer stocks, this I factor may be linked to any of the four chromosomes (*31-33*). A single chromosome of a strong inducer strain may be sufficient to induce the maximum sterility possible for the level of reactivity of the females used as mates.

In heterozygous males bearing both inducer and reactive chromosomes, the I factor is transmitted with a Mendelian pattern. This is not true for heterozygous females, where a phenomenon called chromosomal contamination occurs (*31*). In such females, all chromosomes of reactive origin may acquire I factor, with a probability that can reach 100 percent. The presence of a single inducer chromosome is sufficient to allow contamination of heterologous as well as of homologous chromosomes. This transformation is irreversible, and a contaminated chromosome exhibits subsequently all known characters of true inducer originating chromosomes. It seems likely that the contaminating chromosome remains unchanged (*34*).

Concerning the mechanism of this phenomenon, two main hypotheses may be suggested. It may imply either an insertion of genetic elements or a derepression of genes carried by all chromosomes but active only on those which are inducer. Several lines of evidence favor the first hypothesis. One of these was suggested by the contamination of reactive chromosomes from the same origin with the use of inducer chromosomes differing by their efficiency (that is, by their ability to induce a more or less important reduction of fertility). The contaminated chromosomes generally show stronger inducer efficiency when contaminated by strong inducer chromosomes than when contaminated by weak ones (*35*).

In some inducer stocks there may exist a polymorphism for inducer chromosomes (called i^+) and others which show no detectable inducer efficiency (called i^0) (*31*). These i^0 chromosomes are relatively stable in their originating strain; however, they can be contaminated if they are present in SF or RSF females with i^+ chromosomes (*33*). This means that chromosomal contamination does not occur with a detectable frequency in in-

ducer stocks; as is discussed below, it requires reactivity. Some i^0 chromosomes have been found to bear a very weak I factor, which leads to a slight decrease in fertility when brought into SF females through strong reactive oocytes (*36*). Thus, the question of existence of chromosomes really lacking the I factor in inducer stocks remains open. These i^0 chromosomes are of experimental interest because they allow the mapping of the I factor (*37*). Only a single locus has been found on an X chromosome and on a second chromosome (approximate locations 1-33 and 2-16); probably two independent loci exist on a third chromosome. These results show that inducer chromosomes may have only a few I elements. They do not, however, resolve the question of how many possible sites can exist on these chromosomes. Preliminary results indicate that I factor lies at different locations on homologous chromosomes from different inducer strains.

The behavior of the I factor shows some similarities with other known systems, such as the "controlling elements" in maize, the various transposable elements already known in *Drosophila* (*1, 38*), and bacteriophage mu (*39*). The analogies with the latter and with other viruses led us to perform several trials in order to detect any infectious property of the I factor by injection or ovary transplantation, all of which gave negative results (*26*). Matthews *et al.* and Slatko (*40*) have found a chromosomal contamination-like phenomenon with the male recombination factor of the T-007 chromosome. This poses the problem of relatedness between this factor and hybrid dysgenesis systems (*11*).

The Inducer-Reactive Interaction

Before surveying the various phenomena produced by the I-R interaction, we draw attention to the incompatibility between these two genetic conditions. We noted above that a change in genotype induces a corresponding change in the level of reactivity but with a long delay. However, this is true only for reactive or neutral genotypes. An inducer genotype leads to a different result, abruptly removing any detectable reactivity. The same result is obtained when contaminated chromosomes of reactive origin are used instead of inducer originating chromosomes although the change would be less rapid. It is therefore easy to transform any reactive stock into an inducer stock without any change in its genotype, except those involved in the contamination process (*22*). We have no information about how the reverse transformation might occur; perhaps it needs an i^0 genotype as intermediate.

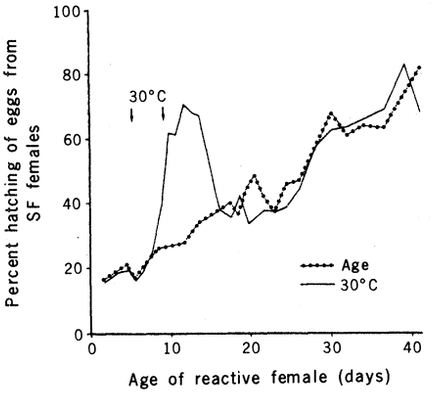

Fig. 1. Changes in reactivity of the female parents of SF female offspring with aging and thermic treatment. The age of reactive mothers is plotted as a function of the hatching percentages of eggs laid by the corresponding young SF females.

Concerning the phenomena produced by the I-R interaction, the most evident is the SF sterility, but chromosomal contamination, too, is the result of the I-R interaction. This appears from the three following lines of evidence.

1) Contamination does not occur within inducer strains (*33*) nor in crosses between stocks of this category.

2) In SF females, contamination frequency increases with the reactive level of the maternal strain (*18*).

3) Contamination occurs at a low level in RSF females (*18*) and it is known that a low level of reactivity is brought by the parental male gamete in these females (*23, 24*).

This dependence of contamination on reactivity suggests that neutral strains may be very weak reactive strains. The Paris stock, which is the only neutral stock that has been extensively studied, gives rise to a low level of chromosomal contamination when crossed with an inducer strain (*18*).

We have shown (*11*) that I-R interaction also produces a high level of X chromosome nondisjunction and mutations in the female germ line. In that the frequency of nondisjunction is strictly correlated with the hatching percentage of eggs from SF females, their production by the I-R interaction is undoubted. Because only the visible ones were scored, a similar quantitative study of mutations was not possible in our study. However, they were found only in crosses where the I-R interaction occurs; and, since all strains used in these experiments were M or neutral in the P-M system, these mutations were undoubtedly related to the I-R system. Some of the mutations were scored in female progeny at specific loci on the X chromosome, others were scored in male progeny at many different loci. Of 15 visible mutations recovered in females, 14 were associated with recessive lethal mutations, an indication that they are not point mutations but rather small deletions. Some of the mutations recovered in male progeny and therefore not associated with recessive lethality appear to be unstable with a reversion frequency ranging from 10^{-3} to 10^{-2}; the revertants, also, are unstable (*36*). This instability bears many common features with those reported by Green (*41*) or by Golubovsky and Erokhina (*42*), which are assumed to be due to insertion elements.

More recently, Prudhommeau and Proust (*43*) have shown that high frequencies of X recessive lethal mutations in the female germ line are also quantitatively correlated with the I-R interaction. The mapping of these mutations shows that they are not randomly distributed and that several of them are associated with short deletions or inversions visible on salivary gland chromosomes.

The above results show striking similarities to those on transposable elements in prokaryotes, such as inserting sequences, transposons, and bacteriophage mu (*39, 44*). Therefore, we may suppose that these mutational events result from insertion of mobile genetic elements, perhaps the I factor itself.

The simplest hypothesis to account for all the data is that I-R interaction has two consequences. The first would be a biochemical deficiency in the oocytes resulting in a halt in development. The second effect would be an amplification of I factor, allowing reinsertions at several places on any chromosome. These insertions might lead either to deletions, inversions, or unstable mutations by mechanisms similar to those proposed for bacterial transposable elements (*44*). Chromosomal contamination would be the direct cause of mutational events and nondisjunctions would be secondary consequences of these rearrangements. If this hypothesis is correct we might expect to find I factor closely linked with loci that had undergone mutation. Preliminary attempts to detect the inducer character at such loci have yielded negative results, but this may only mean that insertion leads in some cases to defective I factors or that the I-R interaction promotes transposition of other genetic elements undetected by our methods.

Another question concerns the possible link existing between the amplification of I factor and a biochemical defi-

ciency in the oocytes. Several hypotheses are possible at present, and the definitive answer can be provided only when we know the biochemical mechanism of I-R interaction; that is, when we understand the molecular basis of reactivity and the biochemical function of I factor. Relevant to this problem is that the I-R interaction does not occur in males. We have already mentioned that no chromosomal contamination has been detected in hybrid males. This is also true for dysgenic traits such as nondisjunction, mutation, and male recombination (*45*). This is evidence that the biochemical events involved in I-R interaction are related to the biochemistry of oogenesis. Further evidence may be found in the strong effect of thermic treatments on late oogenesis in SF and in reactive females.

Comparison Between I-R and P-M Systems

We have mentioned the existence of another system of mutually interacting strains denoted P (paternal) and M (maternal). Here too, a neutral category seems to exist and is denoted Q (*10*). The interaction appears in F_1 progeny from crosses in one direction only (M♀ × P♂). It leads to a specific kind of sterility called gonadal dysgenesis (GD), and to several other dysgenic traits. We must be careful in comparing the two systems because the P-M system has not been studied as extensively as the I-R system, and many uncertainties remain concerning the genetic control and the geographical distribution of strains. For this reason, the following comparison deals with the principal lines only.

The available data on the P-M interaction reveal some similarities as well as differences with the I-R system. One important difference concerns the physiological characteristics of the sterility. The P-M interaction leads to a gonadal atrophy in both F_1 males and females, resulting from an early blockage in development of germ cells. This blockage is effective only at temperatures above 24°C (*46*).

Another important difference is that the P-M system, in contrast to the I-R system, causes several dysgenic traits in males as well as in females. Production of male recombination, for example, is one of the characteristics of P-M interaction (*10, 47*).

Similarities between the two systems may be found in the distribution of strains and in the behavior of the genetic determinants. The first analogy lies in the existence of two main, widespread categories of strains whose interaction leads to several dysgenic traits. The similarity is strengthened by the fact that, in both systems, one category has been found only in the laboratory. However, further study on the distribution of P and M strains is required before it is certain whether or not M populations may exist in the wild. The second analogy lies in the genetic control of the two categories of strains. The P condition, like the inducer condition, is controlled by chromosomal factors that may be linked to any of the three major chromosomes (*48*). Similarly the M condition, like the reactive condition, involves a cytoplasmic state which is ultimately controlled by the chromosomal genotype (*48, 49*).

More data on P and M inheritance are necessary, before further comparison.

The most important gap is the lack of direct evidence for the occurrence of chromosomal contamination in the P-M system. It may only be assumed from an analysis of Engels results (*48*) that if contamination by P does occur, its frequency is lower than contamination by I even when a strong M strain is used. Also the mode of inheritance of M condition has not been ascertained. Data from crosses between P and M strains (*48*) indicate interactions between the M cytoplasm and the P chromosomes. Such an interaction is very complex in the I-R system, involving both the change of reactive chromosomes into inducer chromosomes and an incompatibility between the reactive cytoplasmic state and I factor. If such complex interactions also occur in the P-M system, they could disturb the hereditary transmission of M cytoplasm. Study of this inheritance without the disturbing interference of P factor would require appropriate crosses between strong and weak M strains. Concerning the M condition it would also be interesting to determine whether some kind of nongenetic factors such as aging and thermic treatments have effects similar to those that they have on reactive state.

Engels has produced a very unstable mutation at the singed locus by P-M interaction (*50*). He shows that the instability itself is under the control of P-M interaction: the mutation is unstable in flies where this interaction occurs and stable in flies where it does not occur. In contrast, all attempts to show a correlation between instability and I-R interaction gave negative results (*11*). The three mutations tested, including a singed mutation, were unstable in all conditions, notably in males in which no I-R interaction takes place. In view of the small number of mutations tested in each case, the difference between our results and those of Engels may mean either that both systems produce unstable mutants by two different mechanisms or that each of them produces a special kind of unstable mutant.

The implications of causal independency of the two systems cannot be underestimated, as pointed out by Kidwell (*10*), who found that inducer strains may be either P, M, or Q. Her results together with ours show also that M strains may be either strong or weak inducers, strong or weak reactives, or even neutral in the I-R system. Therefore, it seems impossible that the two systems have the same basis. It seems that the only restriction, preventing a total distributional independency, is that all P strains found so far are also inducer strains. Probably this reflects only that the P condition seems restricted to strains caught more or less recently in the wild while reactive strains are only found among long-established laboratory stocks.

The model proposed by Sved (*7*) to explain hybrid dysgenesis in terms of spatial organization of chromosomes does not fit easily with the existence of two different systems. Moreover, even considering only the I-R system, we do not see how this model might account for all the available data.

I-R System in Relation to Other Mutator Systems in *Drosophila*

Most of the earlier work on indigenous mutator genes under natural conditions consisted of measuring the extent of some dysgenic traits in hybrids from crosses between wild flies and long-established laboratory stocks; therefore, the data obtained do not provide any information on frequencies actually occurring in the wild. We have pointed out that it is no longer possible to neglect the I-R and P-M classifications of strains used in all studies bearing on mutator activity or sterility in *D. melanogaster*. It is necessary to distinguish between results related to the I-R system, to the P-M system, and to other agents. A clear determination of strains is a requisite for investigating one genetic system without any confusing interference. Confusion can be caused by I-R or P-M interactions in studies of independent genetic factors also producing dysgenic traits. This may be the case for the extrachromosomal

element delta (*27, 51*) and perhaps also the segregation distorter system (*52*) although the latter seems to be genetically different from both I-R and P-M systems and is, therefore, less confusing. In any case, the knowledge of the P-M and I-R classifications of the stocks used is essential to exclude the possibility that some experimental results might be produced by several interactions. Kidwell (*10*) has proposed that a dual terminology might be useful for indicating all *Drosophila* stocks: IP; IM; IQ; RM; NM.

I-R System and Natural Populations

The environmental distribution of inducer and reactive strains is not consistent with the hypothesis that this system might be responsible for high frequencies of dysgenic traits in the wild. This of course requires confirmation by a more extensive survey of natural populations. However, with the existence of chromosomal contamination and incompatibility between inducer and reactive conditions, we may reasonably predict that reactive populations can exist in the wild only as isolates. Because of the uncertainties already mentioned, it is not yet possible to be sure that the same conclusion is valid for the M strains of the P-M system.

Although the I-R interaction does not seem to intervene in natural conditions, female sterility and other dysgenic traits eventually lead to complete isolation of the two types of strains from each other. We can reasonably assume, along with Kidwell and Novy (*46*), that in hybrid dysgenesis we are seeing the first steps of a speciation process. Therefore, precise knowledge of the molecular basis of the I-R interaction and the steps of transformation of one category into another might be of interest to population geneticists.

Even though most natural populations apparently carry strong I factors, the adaptative role of these is not known. Studies on the frequency of i^0 chromosomes have been made on stocks bred in the laboratory for several years, but they do not provide any information on their relative fitness under natural conditions. The same is true for the studies of Kearsey *et al.* (*53*) if they also worked on SF sterility. Knowledge of the equilibrium of i^0 level chromosomes in the wild would clarify somewhat the fitness of the inducer condition. However, the problem of the adaptive role of I factor can be resolved only when the biochemical function of this element is determined.

Little is known about the possible occurrence of hybrid dysgenesis systems among other species. *Drosophila melanogaster* exhibits at least two independent systems, and there is no reason why this species should be an exception. We favor the concept that this kind of situation may be of general occurrence, even though there are no supportive results. Other cases of nucleocytoplasmic interactions in the genus *Drosophila* (*54*) or in mosquitoes (*55*) may be distinguished from I-R and P-M systems by several features, notably by the lack of two widespread interacting categories and by the available data on the rules of inheritance. However, the results on the extrachromosomal suppressor of male crossing-over in *D. ananassae* (*56*) show important similarities with hybrid dysgenesis systems. Some interesting analogies may also be pointed out with a recently discovered "mutator system" in maize (*57*).

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