CHAPTER VII

MULTIPLE ALLELOMORPHS

The meaning of the term multiple allelomorphs may be illustrated by the following example:

1. If a white-eyed male of Drosophila is mated to a red-eyed female, the F_2 ratio of 3 reds to 1 white is explained by Mendel's law, on the basis that the factor for red is the allelomorph of the factor for white.

2. If an eosin-eyed male is mated to a red-eyed female, the F_2 ratio of 3 reds to 1 eosin is also explained if eosin and red are allelomorphs.

3. If the same white-eyed male is bred to an eosin-eyed female, the F_2 ratio of 3 eosins to 1 white is again explained by making eosin and white allelomorphs.

There are here three factors, any two of which may meet, and whenever they do, they behave as allelomorphs. They form a system of triple allelomorphs.

On the chromosome hypothesis the explanation of this relation is apparent. A mutant factor is located at a definite point in a particular chromosome; its *normal allelomorph is supposed to occupy* a corresponding position (locus) in the homologous chromosome. If another mutation occurs at the same place, the new factor must act as an allelomorph to the first mutant; as well as to the "parent" normal allelomorph.

Since these factors have the same location they must all give the same linkage values with other factors. This has been shown to be true. For instance, the factor for white eye color of Drosophila is very closely linked to that for yellow body color. The "distance" between them is 1 unit, which means that crossing over takes place about once in a hundred times. Eosin eye color gives the same crossing over frequency with yellow.

White eye color gives with miniature wings about 33 per cent. crossing over. Eosin gives the same value with miniature.

White gives 44 per cent. of crossing over with bar eye. Eosin has the same value. Similar relations hold for all of the characters of the first group; they all have the same linkage values for eosin that they have for white. This example indicates that the conception of allelomorphs should not be limited to two different factors that occupy identical loci in homologous chromosomes, but that there may be three, as above, or even more different factors that stand in such a relation to each other. Since they lie in identical loci they are mutually exclusive, and therefore no more than two can occur in the same animal at the same time. This is both demonstrated by the facts and postulated by the chromosomal mechanism.

On *a priori* grounds also it is reasonable to suppose that a factor could change in more than one way, and thus give rise to multiple allelomorphs, unless it is supposed that the only change possible in a factor is a complete loss of the factor, as postulated in the presence and absence theory.

There is, however, an alternative theory to that of multiple allelomorphism. This alternative is complete linkage. The numerical result can be equally well explained if, instead of occupying identical loci, the factors are so near together that they never (or very rarely) cross over. For reasons that will be given later we are inclined to think that the explanation of multiple allelomorphism is in most cases the more probable one, but the arguments in favor of this view may be deferred until the facts have been described.

There is a general relation that so far holds for all cases in which multiple allelomorphs have been discovered, namely, that the factor-differences produce similar effects. All of the following examples illustrate this relation.

In rabbits (Fig. 50) the Himalayan pattern has been shown to behave as a recessive to self-color and a dominant to albino. Any two of these three types of pigment formation and distribution give a 3:1 ratio in F_2 but no two of them, when crossed, ever produce the third genetic type. In other words the factors behave as though allelomorphic, for only two can be gotten into any one individual. A similar relation has been described by Baur in the columbine, where three types of leaves, green, variegated (green

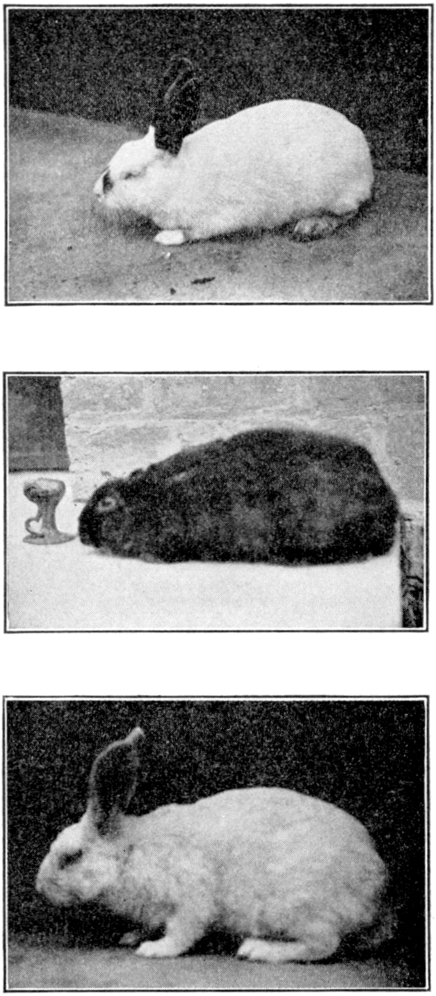

FIG. 50.—Himalayan, black and white rabbits. The factor that stands for each is allelomorphic to the others.

and yellow), and yellow form a triple system. Emerson's case for pod and leaves in beans—green pods, green leaves; yellow pods, yellow leaves; yellow pods, green leaves—also fulfill the conditions of a triple allelomorph system. Shull has reported a case in Lychnis which he interprets as due to triple allelomorphs for sex-determining factors. Two of them give reversible mutations as have white and eosin in Drosophila.

Cases in which more than three allelomorphs have been found may next be considered. The cases seem to show that here also the same character is affected by each of the mutant factors that form the multiple system. In a few instances the characters have been recognized as due to multiple allelomorphs, but in most of them no sufficient interpretation has been offered or else the explanation of complete linkage has been advanced.

Tanaka has reported a case in the silkworm moth which seems best interpreted as one of quadruple allelomorphs. The four larval patterns called striped, moricaud, normal, and plain (Fig. 51), are the characters involved. Besides showing the ordinary behavior of multiple allelomorphs when mated together these characters show linkage to another pair of factors (for yellow and white cocoon color). So far as the data go, the strength of this linkage seems to be the same in all combinations tested.

In mice it has been shown (Cuénot, Morgan, Sturtevant, and Little) that yellow, black, gray with gray belly (wild type), and gray with white belly (second wild type) are allelomorphs. It will be observed here that the factor in the wild type gray mouse is responsible for the appearance in each hair of the three pigments, chocolate, yellow and black. Gray is therefore a mosaic effect, for these colors are stratified in each hair from the base outward in the order above named. The allelomorphic factor for yellow gives rise to only one of these

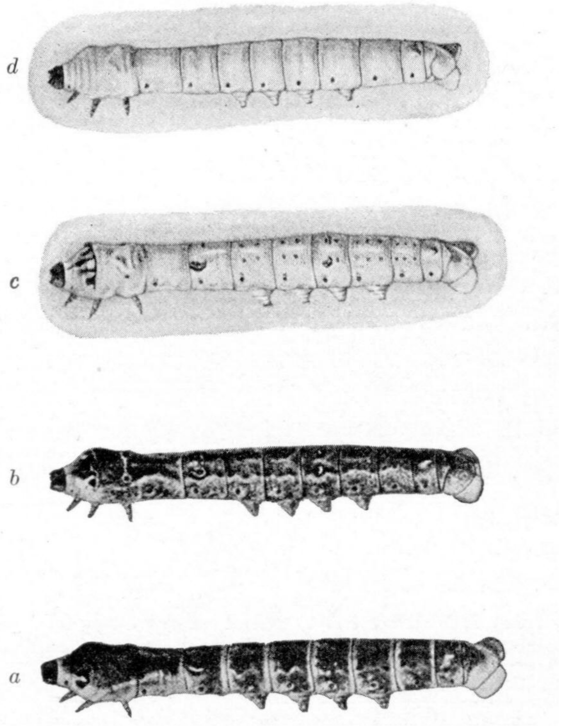

Fig. 51.—Four allelomorphic characters in the silkworm: *a*, Chinese striped yellow; *b*, Chinese moricaud yellow; *c*, Japanese normal yellow; *d*, Chinese plain white.

colors, although the others may to some extent appear, especially in old mice. The third allelomorph produces only black or at least the chocolate pigment, if present, is obscured by the darker color. Finally, the fourth allelomorph produces gray on the back and sides while the belly is pure white (the under hair is black). This series illustrates how allelomorphs of the same locus may not only determine the color, but also act to determine where a color is to develop. The allelomorphs differ therefore in regard to what part of the body they affect, or the time in ontogeny when they act, as in the banded hair of the gray mouse.

This case serves, therefore, as an excellent introduction to the cases that Emerson has described in corn (maize), in which the red color of the grain (pericarp), cob, silk, and husk furnish a wonderful series of character combinations that can be explained on the multiple allelomorph hypothesis. Emerson adopted the hypothesis of complete linkage, but the same arguments as used in other cases lead us to prefer the alternative of multiple allelomorphs. In some varieties of corn the grain, the cob, the silk, and the husk are all red; in others, all white; in others the grain may be red, the cob, silk, and husk white; in others, the grain may be white and the rest red. Practically all possible combinations are known, and so far as tested the combinations that go in through the two parents come out in F_2 according to expectation, *i.e.*, they give no new gametic recombinations. If we assume that there is a system of allelomorphs, such that one affects one combination of parts, another a different combination, the results find a simple and consistent explanation. It may seem strange at first that a factor may make the cob red and not color the grain or husk, while another allelomorph may make the grain and husk red but not affect the cob color, but it is no more strange than that one factor determines one distribution of the pigment over the coat and even in each hair of the gray mouse and another one determines another distribution.

Equally striking is the series of forms of the grouse locust (Paratettix) that Nabours has recently studied. Nine true breeding forms that are found in nature were studied. They differ markedly in color pattern (Fig. 52) but each color pattern behaves as a unit in heredity. The hybrid is in a sense intermediate, the color characters of each parent being superimposed. In fact Nabours finds that simple inspection of the hybrid suffices to show which forms were its parents. In the germ cells of the hybrid the two parental color types segregate as units. The resulting F_2 types are in the 1 :2 :1 ratio. It is obvious, since only two of the color types can exist in the same individual, and since they separate in the germ cells, that the condition of multiple allelomorphism is fulfilled.

All Nabour's crosses relating to color pattern (with some possible exceptions) follow the plan just outlined. The case at first sight appears unique in that the color pattern of each type is complex in the sense that different parts of the body are differently affected and in that in most cases the hybrid shows at the same time the characters of each parent. Both of these peculiarities occur in other cases, however,

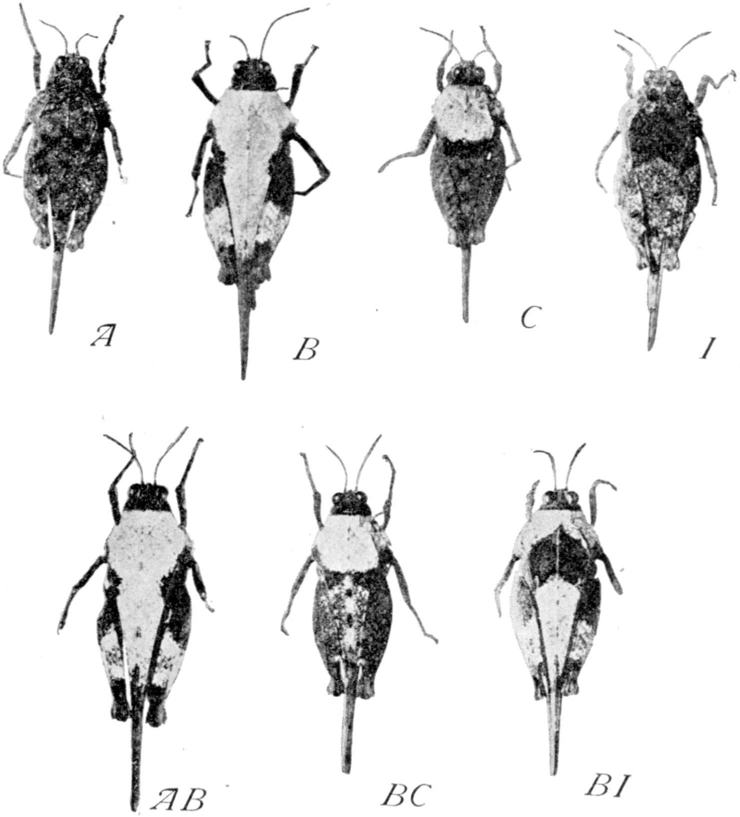

Fig. 52.—Four types, *A*, *B*, *C*, *I*, of Paratettix. Below are hybrids between *A* and *B*, *B* and *C*, and *B* and *I*. (After Nabours.)

as in Emerson's corn for instance, although nowhere perhaps so strikingly as in Paratettix.

In any attempt to decide between the two alternative views of identical loci and of complete linkage the method of origin of the mutant allelomorph is a matter of prime importance. Emerson has described one type ("variegated" corn) in which a mutation (to red) occurs frequently. This mutation is of such a sort, as Emerson points out, that, on the theory of complete linkage, it must involve the mutation of two factors at the same time. On the theory of multiple allelomorphs only one mutation is necessary each time the change occurs. Fortunately we have complete information concerning the origin of the types of Drosophila that fall into this category. One of these may now be given in detail before attempting to decide between the claims of the rival explanations.

In 1911 a few males with white eyes arose in a culture of red eyed flies. From them the stock of white eyed flies was obtained by the usual procedure. In 1912, in a culture of white eyed flies having also miniature wings and black body color, a male appeared that had eosin eyes. He also had miniature wings and black body color, so that there could be no question of his origin from this particular stock. The eosin stock is descended from this male.

In 1913, in a cross between vermilion eyed flies and wild flies several males appeared in F_2 whose eyes were quite different from vermilion. Analysis of the case showed that a mutation had taken place in the stock having vermilion eye color. The new color proved to be a double recessive, for vermilion and for a color called cherry. The new mutation had not occurred at the locus of the vermilion factor, however, but at another locus where there had been a normal factor. Subsequent work with the cherry eye color showed that it was allelomorphic to white and to eosin, the three eye colors and their normal allelomorph forming a quadruple system.

To the preceding history must be added cases of the return mutation from eosin to white. Such a mutation occurred in 1914 in a culture of eosin flies with miniature wings. The parents had been treated with alcohol, but there is no evidence to show that the alcohol had any connection with the event. A single white eyed male appeared among many hundred eosin brothers and sisters. The male had miniature wings. When crossed by ordinary white it produced white through two generations. There can be little doubt that it is the same white as the original white. In a pure bred stock, eosin tan vermilion, a few males were found which had a white eye color instead of the cream color of eosin vermilion. These flies mated to white stock gave white offspring for two generations. Here the case was checked by two control characters, for the new white-eyed males showed tan body color and were proved to carry vermilion. In these controlled cases the mutation took place in the reverse direction from the original one. Three other cases of eosin returning to white which are apparently not explainable by contamination are also recorded.

The appearance of eosin in the white-eyed stock might be interpreted to mean that a mutation in eye color had appeared in the white-eyed stock in a factor located near the factor for white ("completely linked" with it) and that the effect of this new factor, combined with that of the factor for white, which was already there, gave the color that we call eosin. Eosin from this point of view would be due to two consecutive mutations of completely linked, neighboring loci. This interpretation of two consecutive mutations can not be made in the case of cherry, however, for cherry arose from red by one step, just as did white; yet cherry, like eosin, when mated to white, does not give rise to offspring that are red. It would follow on the complete linkage view that cherry and white differ from red by the same factor, but since they are not alike, that one of them must differ from red by still another factor. Since each arose from red immediately, it would follow that one of them must have arisen by a simultaneous mutation in two factors completely linked and affecting the same character. All these assumptions must be made on the theory of complete linkage, but are avoided on the alternative theory of multiple allelomorphs.

Exactly the same argument applies in the case of two other triple allelomorph systems of Drosophila. The recessive mutants pink and peach colored eyes each arose independently from red eyed flies, yet when crossed do not give red, but a color intermediate between pink and peach. Secondly, sooty body color arose in wild stock, although it was found only after the stock had been crossed to ebony, with which it is allelomorphic. Here too the mutant forms though both recessive to normal do not give normal gray color when crossed together, but a color intermediate between sooty and ebony. In both of these cases the complete linkage view would require that one of the mutant types had originated by a mutation in two factors at once. There is still another set of triple allelomorphs known in Drosophila, namely, yellow and spot (Fig. 53) and their normal allelomorph. The above argument does not apply to this case, however, for although spot and yellow are both recessive to gray and give yellow when crossed to each other, spot originated in flies containing already the allelomorph for yellow.

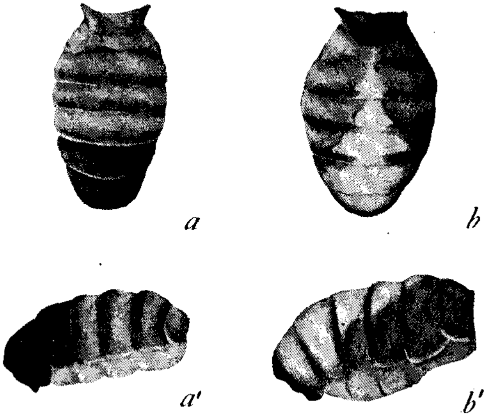

FIG. 53.—The abdomen of normal *a,a'*, and spot, *b,b'*, males. The other allelomorph is yellow (not shown here).

The reasons may now be given that incline us to think that the theory of identical loci is much more probable for the cases known than is that of complete linkage (in the sense defined). No one of the reasons is in itself conclusive, but taken together they weight the scales heavily on one side.

1. When two mutants that depend on "multiple allelomorphs" are crossed they give in F_1 a type that is like one or the other of the two mutants, or an intermediate type. This type is scarcely ever like the original (or wild) type. In this respect they differ from other recessive mutant types which when crossed together give the wild type. We understand why in the latter cases the wild form is recovered. It is because each mutant type contains besides its mutant factor the normal (dominant) allelomorph of the other type. Hence the original type is reconstituted in the cross, as has been already stated. But when two mutant allelomorphs occupying the same locus are brought together neither of them brings in the normal allelomorph of the other; hence the wild type is not reconstituted. If the cases in which these allelomorphic factors arose independently are not cases of identical loci then the explanation involves the occurrence of two mutations at the same time, as explained in the case of cherry.

2. It is a characteristic of "multiple allelomorphs" that the same character is affected. Nearness of factors in the chromosome will not explain this fact unless nearness means the same factorial basis, for in the other mutants that we have obtained, nearness of factors is in no way related to the kind of character

or part of the body that is affected. It seems therefore more probable that this peculiar fact connected with multiple allelomorphs means that the same portion of the chromosome is changed in one or another direction.

3. It is true that a very wide range of linkage values has been obtained, that extends from almost free segregation to less than 1 per cent. of crossovers. However, if we should construct a curve showing the number of cases exhibiting the various possible linkage values, the number showing complete linkage or, as we should say, multiple allelomorphism, would be far in excess of the number of these to be expected from the general shape of the rest of the curve. This indicates that multiple allelomorphs are in a class by themselves, not merely extreme cases of the same type as an ordinary linkage case.

4. There is an *a priori* consideration that may not be out of place in the argument. There is no sufficient reason for supposing that only one sort of mutation can occur in a given locus in the chromosome. If the basis of the chromosome is a chain of chemically complex substances (*e.g.*, proteins), any slight addition or loss or even re-arrangement of the atoms in the molecules of a bead in such a chain might well produce an effect on the organism, and perhaps a more marked effect on that particular character that stands in closest relation to that chemical body. Since we know that mutations and even "reverse" mutations actually occur, it would be indeed strange if only one kind of change were

possible in a given locus. But if more than one kind of change did take place in a locus, a series of multiple allelomorphs would result.

The ability of the theory of multiple allelomorphs (identical loci) to explain the peculiarities of so many cases in such widely separated fields proves the usefulness of the hypothesis. Although the theory of complete linkage also will cover the numerical results in these cases (and some of the simpler cases cited may prove to fall under this head) there is the very strong first-hand evidence that has just been given that makes the theory of multiple allelomorphs more probable than the former theory. It is important to recognize that there is this strong evidence in favor of multiple allelomorphs, quite aside from special cases of complete linkage, for, as will be shown in the next chapter, there are some far-reaching consequences of the theory of multiple allelomorphs.

A word may not be out of place here concerning the relation of the theory of multiple allelomorphs to the question of the variability of factors. The fact that more than one change may take place in the material at a given locus must not be taken to mean that the material is undergoing continuous fluctuating variability, for such mutations occur rarely and the factors later behave as do others. In fact in only one case (*i.e.*, Emerson's variegated corn) do mutations appear frequently at a given locus. But even in such case the change can not properly be said to be fluctuating, but is of a fixed nature, and when it has once occurred the new factor is no more subject to mutation than are other factors, *i.e.*, the factor has lost its unusual instability.

There is no *a priori* answer possible to the question as to whether a mutation having occurred, a further mutation of the mutated factor is more likely to occur, for it is conceivable that while in one case the new factor might be unstable, in another case it might be even more stable than the original one. In regard to the other question, as to whether a particular locus is more liable to mutate, the work on Drosophila shows that certain loci do mutate more often than do others, and this is shown not only in the recurrence of the same mutation, but also in the occurrence of multiple allelomorphs.