CHAPTER X

INTERFERENCE

One of the most significant results that a study of crossing over has brought to light is that whole blocks of genes go over together. Thus, if one series be *A B C D E F G H I J K L M N* and its allelomorphic series be *a b c d e f g h i j k l m n* crossing over may give two blocks of genes.

A B C D E f g h i j k l m n
a b c d e F G H I J K L M N

This result can best be demonstrated in cases where a number of loci are followed at once.

The fact that crossing over takes place in blocks is highly significant for the phenomenon of distribution, since it means that pairs of linked genes do not act independently of their neighbors. This fundamental relation was not suspected until quite recently.

The size of the blocks, when only one crossing over occurs between the chromosome pairs, depends on the location in the series of the breaking point. If the crossing over occurs near the middle, the four pieces will be of the same length as shown below:

a b c d e f g H I J K L M N
A B C D E F G h i j k l m n

If it is near the end of the series, two of the resulting pieces will be small, the other two large. Thus:

a b c D E F G H I J K L M N
A B C d e f g h i j k l m n

The two "like" pieces in all cases contain identical series of loci.

The data also show that the series may break at two points, and that when this happens the three blocks of one set always correspond to the three blocks of the other series of genes. Thus interchange at two levels gives:

a b c d E F G H i j k l
A B C D e f g h I J K L

The same relation holds in principle for three or more breaks in the series.

If in such a system the blocks have no commonest length, the break in the series at one level should not bear any relation to the place at which another break takes place. For example, if it is true that when a break occurred between *D* and *E* it had no influence on a break at any other point of the series, the blocks resulting from two breaks would not tend to be more of one length than of any other length. But if the evidence shows that when a break occurs between *D* and *E* the chance of another break occurring in that vicinity is decreased, or increased, the results would be expected to follow some definite law or principle, rather than be simply the result of chance. This is in fact the case. An illustration may make this clear.

Suppose when crossing over takes place within the blocks *A B C D,* and *E F G H,* and *I J K L* it can be recorded. If we know how often, when the break occurs only once in the series, it takes place in the first, in the second, or in the third block, we can then determine in those cases where breaking occurs in the first block, whether it is as likely to take place in the second block as when no break occurs in the first, etc. Such tests have been made (Muller, Sturtevant, Bridges, Weinstein, Gowen) with *Drosophila,* and the same kind of results consistently obtained. It has been found, for example, that when a crossing over takes place between *G* and *H,* a second one is less likely to take place on either side, *i.e.,* between *F* and *G* or between *H* and *I* than when no cross-

ing over takes place between *G* and *H*. Stated in another way, crossing over in one region protects neighboring regions from crossing over. Moreover, this relation follows a perfectly definite law according to the "distances," as determined by linkage relations of genes outside of the region of crossing over. If we take two pairs of factors $\frac{G\ H}{g\ h}$ closely linked together we find that the genes lying immediately to the right and left of $\frac{G\ H}{g\ h}$ never cross over independently of $\frac{G}{g}$ and $\frac{H}{h}$ at the time that a crossover separates $\frac{G}{g}$ and $\frac{H}{h}$. In other words, the genes immediately to the right of *H* always go over with *H*, and those to the left of *G* always go over with *G*, when *G* separates from *H*.

If we consider genes that are less closely linked with *G* and with *H*, we find that while their crossing over is interfered with by the crossing over between *G–H*, it is affected to a limited extent. Genes still less linked with *G* or with *H* are still less interfered with; until finally there is no relation at all between crossing over between *G–H*, and other more loosely linked genes, *i.e.*, crossing over between *G–H* is found to have no relation to crossing over between *L* and *M*. Put in another way, one may say that crossing over at *L* and *M* is no more likely to take place when none occurs between *G–H*, than when it does.

For different pairs of chromosomes the regions that bear this relation to each other have been found to be different. Even within the same chromosome this relation may be different at the ends and in the middle. There are also special factors that affect special chromosomes and special regions of chromosomes. An example will illustrate this relation that is called interference. If in a group of genes *A B C D E F* a break occurs somewhere between *A* and *D* in 6 per cent. of cases, and if between *M* and *T* in the same series (*M N O P Q R S T*), in 10 per cent. of cases, a double break involving both regions simultaneously should, if the breaks occurred independently of

each other, take place in 0.6 per cent. of the cases. But if the regions in question are close together, that is, if the intervening block (*i.e.*, *G F H J K L*) of genes is short, it is found that there are fewer double crossovers than the 0.6 per cent. expected on a purely random basis. This was shown by Sturtevant in his paper on chromosome maps. It means that a break in one region interferes with a break in the other region when the intervening block is short.

The ratio of the number of actual double breaks obtained to the number of double breaks that would occur if one of them did not interfere with the other is termed coincidence. If in the above example only 0.3 per cent. of the cases were double crossovers involving the regions *A B C D E F* and *M N O P Q R S T* the coincidence would be 0.3 per cent. divided by 0.6 per cent., or 0.5.

It has been found that as the distance between two regions increases, crossing over in one of them interferes less and less with crossing over in the other; that is, the number of double crossovers obtained approaches the number expected on a random basis, and coincidence rises gradually to the value of 1. This phenomenon is shown in all the cases where more than one block of genes has been followed. It is especially clear in the work of Muller, who studied a large number of factors in the sex-chromosome of *Drosophila* simultaneously.

When the intervening block becomes sufficiently long so that the coincidence attains the value of 1, interference has entirely disappeared. When, however, the distance is increased still further interference reappears, *i.e.*, coincidence decreases again. There was a suggestion of this in Muller's work; and the work of Weinstein undertaken to get critical evidence on this point indicates clearly that such a decrease exists. For the second chromosome a similar rise and fall with increase of distance is indicated by Bridges' data.

The fact that interference reappears, *i.e.*, that coincidence decreases after reaching a maximum, indicates that the segment of a chromosome between the breaking points tends to be of a particular (modal) length; and that breaks which are closer together or farther apart than this modal length are less frequent. That is, genes not only stick together in blocks, but the blocks tend to be of a definite size, and longer and shorter blocks are less frequent. In the sex-chromosome of *Drosophila*, which is 65 units long, Weinstein's data indicate that the most frequent length of block is about 46. In the second chromosome (which is 107 units long), Bridges' data indicate a modal length of about 15 in the centre of the chromosome and of about 30 on either side of the middle point.

The work on coincidence throws light on the behavior of the chromosomes during crossing over. The cytological evidence has not determined whether when crossing over takes place the chromosomes are twisted loosely or tightly. But Muller has shown that this question may be attacked by certain calculations based on the data of interference. If, as a rule, chromosomes twist in long loops, crossing over at two points close together would be rare, for it would require a shorter twist than usually occurs. The occurrence of long loops would explain the interference of neighboring regions. Moreover the decrease of interference as distance increases would be accounted for, because short loops would be less frequent than longer ones. The reappearance of interference for widely separated regions is explained by supposing that extremely long loops are infrequent as are very short ones. That is, on the supposition of long twists there would be a modal length of loop, and loops of greater or lesser length would be less frequent.

If, however, the chromosomes are tightly twisted into short loops, the interference of neighboring regions might be explained on the supposition that a break at one point allows the chromosomes partly to unravel in the neighbor-

hood of the break, and that this loosens the twisting and prevents another break near by. In regions farther away from the break, the threads would not be so much unravelled, so that the greater the distance from the first point of breaking the more would a second break be likely to occur. That is, interference should grow less at greater distances. But the reappearance of interference at still greater distances seems incompatible with this scheme; thus the actual data favor the first view of crossing over, in which the break occurs during a stage of loose twisting. At any rate, as Weinstein has pointed out, the variation of coincidence with distance must be dependent on other conditions than the mere tension due to the twisting of the chromosomes, and any view which refers the breakage of the threads to the tension of tight twisting must be rejected or supplemented.

Castle has recently suggested that the difference between the values for a long "distance" and summation of short "distances" is due to the loci not lying in a straight line but "out of line." He suggested that when short steps are taken as the basis for map distance they represent the "long way round," as, for instance, in passing from one end of a *V* to the other end, keeping on the line; while when a direct cross is made, giving a shorter "distance," this is a measure of the direct or air-line between the two ends of the *V*. Such a theory is not in harmony with the following facts. The best data (*i.e.*, data sufficient in amount and free from crossover variations) show that Castle's three dimensional figures reduce to a curved line in a plane. In such a curved line the most distant points are nearer to each other in an "air-line" than along the line. Such a graphic representation of the data is possible, but leads to certain inconsistencies.

If Castle's procedure is followed it leads to the placing of the same locus in two or more different places on the basis of adequate and comparable data for both positions. The two cases that Castle says furnish the crucial evi-

dence for his view demonstrate just the opposite, when complications due to crossover variations are excluded, by using only data in which three or more loci are recorded simultaneously. In his attempt to explain the all-important fact of rarity of double crossovers, Castle is obliged to assume that there is a difference in frequency of crossing over in different planes (directions). This assumption can be shown to be inconsistent with the primary assumption that he accepts, *viz.*, that crossing over is proportional to the distance between genes.