out in a smaller tunnel than the new French one. The 20 ft. tunnel in the United States and the new 24 ft. tunnel at Farnborough were, in fact, built chiefly for such work. The cost of running a full-scale tunnel, and of the preparation of machines for test therein, is necessarily heavy, and there is the limitation that even in such tunnels as those at Chalais-Meudon and Langley Field, only a small aeroplane can be tested. The limit of span, without involving large corrections for the constraint of the limited stream, would probably be about 40 ft.

In spite of such limitations—and every type of tunnel has limitations of some kind—the new equipment should prove of great value to the French in the study of aerodynamics, and it is to be hoped that results obtained by its use will be available to the world at large. It is only by careful analysis and comparison of results obtained in various types of wind tunnel and on machines in flight that the greatest use can be made of the research work of the various institutions in different countries.

Minute Intergenic Rearrangement as a Cause of Apparent 'Gene Mutation'

By H. J. MULLER, A. PROKOFYEVA and D. RAFFEL, Institute of Genetics, Academy of Sciences of the U.S.S.R., Moscow

WHEN it was discovered that chromosome breakage and reattachment usually entail effects resembling those of gene mutations located at or very near the point of breakage, it was suggested, as one alternative interpretation of this phenomenon, that the change in position of genes near the breakage point, with respect to other genes in their immediate vicinity, might in itself be the cause of their altered mode of reaction upon the organism (Muller, 1930). This was an extension of the 'position effect' principle which had previously been proposed for the special case of the bar genes, two of which had been found to have a greater effect when in the same chromosome than when in opposite chromosomes (Sturtevant, 1925). Since 1930, numerous further illustrations have been found, by various investigators, showing the comparative regularity with which effects resembling those of gene mutations in nearby loci accompany breaks, but there has been little or nothing in their evidence that would serve to test the probability of the 'position effect' interpretation as opposed to the alternative conception that the disturbance involved in the process of breakage was of such a nature as to be likely simultaneously to upset and alter (once for all) the inner composition of genes in the vicinity. The senior author has now, however, obtained definitive evidence (see Muller and Prokofyeva, 1934) of the correctness of the 'position effect' interpretation, through the finding that different rearrangements involving the scute locus in *Drosophila* in the great majority of cases result in phenotypically different 'allelomorphs', whereas nearly identical rearrangements (scute 4 and scute *L*8) have given sensibly the same 'allelomorphs'.

The general question thus arises, what proportion of apparent mutations are only intergenic 'position effects' rather than autonomous intragenic changes? Of twenty-seven scute and achaete mutations investigated which have been produced by irradiation, it has so far been possible to demonstrate in eighteen cases that there was a breakage and re-attachment close to the scute or achaete locus. Some or all of the remainder also are probably intergenic rearrangements, for it has been found in this investigation that the rearrangements tend to fall into two categories, gross and minute, the latter being of such a nature that a genetic discrimination between them and true intragenic mutations would be very difficult, or in many cases even impossible.

One example of a minute rearrangement is scute 19, in which only a fraction of a single chromomere (or chromatin 'ring' number 2, as seen in the salivary gland) has, as shown both by genetic and cytological evidence (see Fig. 1), become deleted, by a break on each side of it within the same chromomere, and inserted into another region of the chromatin (within the right arm of chromosome 2). We accept here Koltzoff's explanation of the structure of the salivary gland chromosomes, as bundles of practically uncoiled chromonemata the adjacent chromomeres of which form the 'rings' or 'discs' (see also Carnoy, 1884, and Alverdes, 1912, 1913); our work, however, shows definitely that the genes—usually more than one per chromomere—are contained within these chromomeres. Special genetic and cytological methods explained elsewhere have shown that the displaced section of the chromomere here in question includes only about six (four to eight) genes. This case does not illustrate a method of origination of recognisable 'deficiencies' alone. If such a deficiency included but one or two genes, instead of six, it would in some cases be viable and resemble in its heredity an intragenic mutation, as other work of Muller (in press) has shown. On the other hand, the inserted section, without the deficiency, could be mistaken for a simple genic 'suppressor', especially since, having been weakened in its activity by the effect of its changed

position, it could appear as a recessive (unlike most recessives, however, a duplication of the region in which it lay would not serve to counteract it). These changes might or might not be detectable cytologically, depending on their size. If, finally, instead of having been lost or inserted into another region, the minute section dealt with in the case of scute 19 had only been inverted, while remaining otherwise in its place, the change would not only have behaved genetically like a gene mutation, but also it would have been impossible of recognition as a rearrangement, even by the new cytological method.

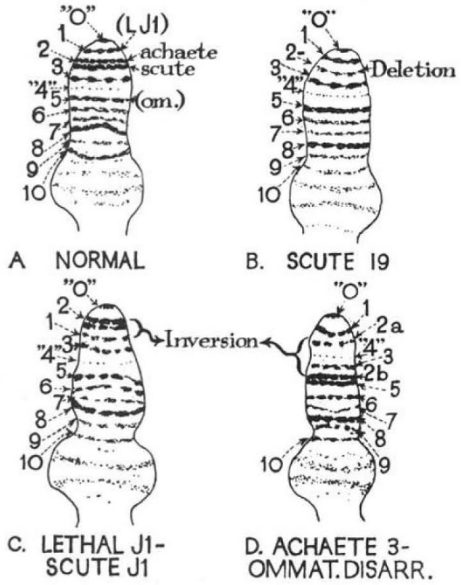

FIG. 1. Appearance of extreme left end of *X*-chromosome of *Drosophila melanogaster* as seen in the salivary gland, in normal material and in the case of three minute rearrangements. The exact or approximate () positions of the gene loci concerned are shown in the figure for the normal. All four drawings are from typical specimens and show only the terminal twentieth (±) of the entire active region of the *X*-chromosome.

The existence of minute inversions of the general type above mentioned was at first only an inference from the above and other cases of insertion, but soon actual proof of them was found. The first case in point was that of scute J1. Here cytological examination (see Fig. 1) proved that an only slightly larger section than the above, involving only two chromomeres or 'rings', 1 and 2, had become inverted (*in situ*). This was precisely the result which the senior author had been led to expect on the basis of this mutation having involved the simultaneous alteration of the effects of two nearby loci: those of lethal J1, normally to the left, as proved by genetic analysis of chromosome fragments broken between the two loci, and of scute, normally to the right. The seeming 'double mutation' here, as probably in most other cases, was simply due to the two different position effects occurring at the two different (but nearby) points of breakage and reattachment.

Another case in which the genetic expectation of a minute inversion, based on 'double mutation', was similarly confirmed by the cytological finding, was that of achaete 3 (= scute 10). Here the mutation other than that at the achaete locus was the ommatidial disarrangement 'om', which was proved to lie slightly to the right of achaete by the same method of analysis of fragments as that used before (analysis by crossing-over being virtually precluded in this as in the other two cases by reason of the small distances involved). In correspondence with this genetic situation, it was found that one point of breakage and reattachment lay within chromomere (= 'ring') 2, near the point in this chromomere where previous cytogenetic analysis by Muller and Prokofyeva (1934) had shown the achaete gene to be, while the other point of breakage and reattachment lay just to the left of or just within chromomere (= 'ring') 5, the region between these two points of breakage being exactly inverted (see Fig. 1).

Since double breaks and reattachments are not all thus accompanied by a *discernible* position effect in two demonstrably separate loci, this genetic criterion of a minute rearrangement is only sometimes provided. It is therefore evident that a minute inversion involving only a few genes (or sometimes only one gene ?) would often be not only cytologically but also genetically indistinguishable from an intragenic mutation, by any methods at present in use.

C. A. Offermann has directed our attention to the fact that there is evidence from another direction that a considerable proportion (if not all) of the apparent 'gene mutations' produced by X-rays are really the effects of changes in position caused by minute intergenic rearrangements. This evidence lies in the fact that the frequency of production by X-rays of readily demonstrable (gross) gene rearrangements is vastly greater in spermatozoa than in other cells, and that, corresponding with this, the frequency of production of apparent 'gene mutations' is also considerably raised in spermatozoa, as compared with other cells—although not nearly as much raised as is the gross rearrangement frequency (see Muller and Altenburg, 1930). Now exactly such relations are to be expected, if most of the induced 'gene mutations' are fine rearrangements, and if we accept the very probable hypothesis that rearrangements, like cross-overs, require contact between two chromonemata (or two portions of one chromonema). For the chromosomes are very much more crowded together and are more condensed in spermatozoa than in other cells. The much greater degree of crowding together would

give vastly more chance for juxtaposition of parts that ordinarily lie widely separated, and so would lead to a far higher frequency of gross rearrangements, while the greater degree of condensation would give more chance for contacts on the part of the very fine loopings that would be responsible for the minute rearrangements.

As our studies of mutations in the *X* and other chromosomes have shown that apparent replicas of practically all known 'natural mutations' in *Drosophila* may also be obtained by X-rays, the further question is raised as to what proportion of 'natural mutations' in *Drosophila* may really be minute rearrangements. This question is of moment because the range of possibilities of phenotypic change through intergenic rearrangements alone must be far from adequate for any indefinitely continued evolution. The latter must depend for the most part upon intragenic change, and hence it is important for the study of evolution, though at present seemingly so impossible, to be able to distinguish some at least of the intragenic mutations from the minute intergenic types of rearrangement. The matter acquires a greater urgency for geneticists when it is realised that they may now expect to have to meet attacks from orthogeneticists and Lamarckians, who may see in the present uncertainty regarding the 'building blocks of evolution', an opportunity of reintroducing teleological notions of evolutionary causation.

In this connexion, it must not be forgotten that all the cytogenetic investigations of species-crossing have agreed in showing that species differences in general reside in chromosomal differences and are therefore fundamentally *Mendelian* in their inheritance. When the chromosomes in species-crosses are able to undergo reduction, the species differences show spread of variation and eventual return to either parent species, whereas, when chromosome segregation is prevented—whether by asexual reproduction, by division of chromosomes at both maturation divisions (as in butterfly hybrids), or by the somatic origination of allotetraploidy—the hybrids breed true. Now Mendelian differences have been found to originate only by a sudden process—mutation. Since mutations involving intergenic changes are necessarily inadequate to provide most of the material for species divergence, it logically follows that a part of the mutations must be intragenic. It is only to be expected that many of these would be similar, in their phenotypic consequences, to effects of intergenic origin, and that discrimination between the two classes of change would present considerable difficulties. Such discrimination must, however, be eventually attempted.

BIBLIOGRAPHY

Alverdes, F., "Die Entwicklung des Kernfadens in der Speicheldrüse der Chironomus-Larve", *Zool. Anz.*, **39**; 1912. "Die Kerne in den Speicheldrüsen des Chironomus-Larve", *Arch. Zellf.*, **9**; 1913.

Carnoy, J. B., "La Biologie Cellulaire", Lierre (see p. 232, 233); 1884.

Koltzoff, N., "The structure of the chromosomes in the salivary glands of *Drosophila*", *Science*, **80**, 312–313; 1934.

Muller, H. J., "Types of visible variations induced by X-rays in *Drosophila*", *J. Gen.*, **22**, 299–334; 1930.

Muller, H. J., and Altenburg, E., "The frequency of translocations produced by X-rays in *Drosophila*", *Genetics*, **15**, 283–311; 1930.

Muller, H. J., and Prokofyeva, A., (i) "Continuity and discontinuity of the hereditary material", *C.R. Acad. Sci. U.S.S.R.* (in press); (ii) "The cytogenetic resolution of the ultra-fine structure of a restricted portion of a *Drosophila* chromosome" (in press; 1934).

Painter, T. S., "A new method for the study of chromosome rearrangements and the plotting of chromosome maps", *Science*, **78**, 585–586; 1933. "A new method for the study of chromosome aberrations and the plotting of chromosome maps in *Drosophila melanogaster*", *Genetics*, **19**, 175–188; 1934.

Sturtevant, A. H., "The effects of unequal crossing over at the bar locus in *Drosophila*", *Genetics*, **10**, 117–147; 1925.

Obituary

SIR HORACE LAMB, F.R.S.

HORACE LAMB was born at Stockport in 1849. His childhood was passed mostly in a household where the strictness of the religious ideas prevailing at that time left little scope for his naturally happy nature and his great vitality. These qualities, which so endeared him to his friends in later years, began to appear at school. At Stockport Grammar School, he had the good fortune to come under a sound and kindly scholar named Hamilton, who quickly appreciated his merits, and finally sent him up to Cambridge, where in 1867 he gained a classical scholarship at Queens' College. At that time his allegiance was almost equally divided between classics and mathematics, but his visit to Cambridge, when he sat for the scholarship examination, turned the scale in favour of mathematics. On his return to Stockport he decided not to take up his classical scholarship but to sit for a mathematical one at Trinity in the following year. His interest in classics and literature, however, remained with him all his life, and had a profound influence on his children, all but one of whom turned to literature or art rather than to science.

The year of preparation for the mathematical scholarship was spent at Owen's College, Manchester, where, under Prof. Barker, Lamb first experienced the recondite joys of the higher mathematics. At Trinity, which he entered in 1868, he graduated as second wrangler, and was elected to a fellowship. At that time, and for some years afterwards, Cambridge mathematics was dominated by the tripos examinations. A young man's ability was judged entirely by his place in the tripos, and his competence as a mathematician by the ingenuity of the questions which he set when in due course he appeared as a tripos examiner. Among the more old-fashioned, it was considered rather pushing to publish original mathematical work. The proper way in which a lecturer could make known any theorem which he might discover in his teaching was to set it as a tripos question. The science of hydrodynamics was