SPECIAL ARTICLES

THE BAR "GENE" A DUPLICATION

THE nature of the Bar gene has been the subject of extensive investigation and speculation since February, 1913, when Tice[1] found this reduced-eye mutant as a single male in the progeny of normal-eyed parents. The eye-reduction behaves as a sex-linked dominant, with a locus at 57.0, and has been one of the most important of all the sex-linked characters of *D. melanogaster*. A remarkable peculiarity of the mutant is that occasionally the homozygous stock gives rise to a fly indistinguishable in appearance and genetic behavior from wild-type.[2] More rarely the stock gives rise to an even more extreme reduction in eye-size, a type which was called Ultra-Bar by Zeleny,[3] who found it.

Sturtevant and Morgan[4] and Sturtevant[5] found that these two-way changes were the result of a novel type of "'unequal" crossing-over, by which the two genes originally present in the two parental chromosomes both emerged in the same chromosome (Bar-double) while the other resultant chromosome was without Bar (Bar-reverted). The change from Bar to Bar-double was considered to be a single gene duplication, while the converse change, from Bar to Bar-reverted, corresponds to a one-gene deficiency. Since the Bar-reverted type proved to be indistinguishable from the normal unmutated wild-type, the gene present in Bar and lost in Bar-reverted must have itself correspond to a new addition or one-gene duplication.[6]

Sturtevant[5] found the unexpected relation that two Bar genes in the same chromosome (BB/B$^+$) gave a greater reduction in the size of the Bar eye than did two Bar genes in opposite chromosomes (B/B), an intensification of action which he formulated as a "position effect." Dobzhansky[7] interpreted his allelic Baroid mutant as a position effect due to the substitution of material at or near the Bar-locus (in the normal X) by material translocated from the right limb of chromosome 2, and the reduction in the Bar eye to the interaction between a gene in the X chromosome and the duplication.

A chance to clear up some of the puzzles as to the origin and behavior of Bar was offered by the salivary chromosomes. Study of the banding in a stock of Bar (forked Bar) showed that an extra, short section of bands is present in excess of the normal complement, forming a duplication. The insertion point of this duplication is in the bulbous "turnip" segment, not far from the basal end of the X.[8]

[1] S. C. Tice, *Biol. Bull.*, 26: 221–51, 1914.
[2] H. G. May, *Biol. Bull.*, 33: 361–95, 1917.
[3] C. Zeleny, *Jour. Exp. Zool.*, 30: 293–324, 1920.
[4] A. H. Sturtevant and T. H. Morgan, SCIENCE, 57: 746–7, 1923.
[5] A. H. Sturtevant, *Genetics*, 10: 117–47, 1925.

The exact point of the insertion is ambiguous, for a reason which will appear below. The normal X in this region (see revised map in Fig. 1) shows in sub-section 16A a heavy band, which in well-stretched chromosomes, or with certain fixations, is a clear doublet, usually with the halves united in a capsule, but occasionally completely separate. This is followed by a very faint dotted line, which can be seen only in the most favorable conditions. Next follows a fairly weak line which is distinctly "dotted" in texture, with the separate dots loosely connected across the width of the chromosome. Next follows closely a still fainter, diffuse, continuous-textured doublet, with the doubleness generally appearing as mere broadening. The last line of sub-section 16A is again a very faint dotted singlet. Sub-section 16B starts with a sharply discontinuous line of fairly heavy dots or vesicles and is a line very easy to recognize. The greatest width of the bulbous segment 16A is at the two fairly weak bands, while a very sharp change in size occurs at the transition from 15F to 16A.

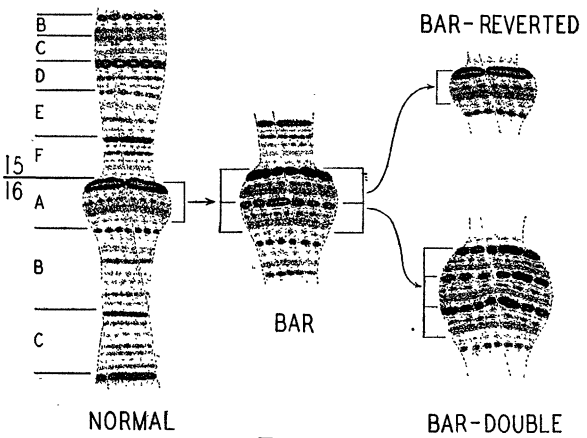

FIG. 1

In the Bar chromosome the condition may be described observationally as the repetition of section 16A, with the exception of the final very faint dotted line. But the whole region of this bulb has undergone changes in the Bar chromosome as follows: the "puff" of the bulbous segment is more pronounced and its size is increased; the banding is more discontinuous by being broken into blocks and vesicles, and the regularity of synapsis is disturbed by oblique junctions. Thus, in Bar the heavy doublet following the last faint dotted line of 15F is more segmented than normal and more rarely shows its doubleness clearly. This tendency is more pronounced in the heavy broken line of

[6] S. Wright, *Amer. Nat.*, 63: 479–80, 1929.
[7] Th. Dobzhansky, *Genetics*, 17: 369–92, 1932.
[8] C. B. Bridges, *Jour. Hered.*, 26: 60–4, 1935.

the repeat seriation to the right. All the lines of the repeat seriation to the right differ from the corresponding lines of the initial seriation by being somewhat less intense, more broken, more diffuse and more confused in their synapsis relations.

In a forked non-Bar stock recently derived from the above forked Bar stock by breeding from the rare Bar-reversions, the banding was found to be precisely identical with that of unrelated normals as far as could be observed in excellent permanent preparations of well-stretched chromosomes.

In a forked Bar-double stock, similarly derived from the same f B stock by breeding from the very rare "Ultra-Bar" type of eye, it was found that the extra section observed in Bar was present still again, giving a thrice-repeated seriation in direct sequence. The changes differentiating Bar from normal were carried further in Bar-double, as follows: The size and puffiness of the bulbous regions was still greater, as well as the blockiness of the banding and irregularity and obliqueness of the synapses. These disturbances were greatest in the middle one of the three seriations.

These findings enable the Bar "gene" to be reinterpreted as a section of inserted genes—a duplication. The production of Bar-double and of Bar-reverted is seen to be the insertion of this extra section twice, or conversely, its total loss—both presumably by a process of unequal crossing-over. That the section of bands should behave as a unit in this process is perhaps accounted for by the observation of oblique synapsis, especially frequent in Bar-double, where presumably one entire sequence synapses with another of a different position in the series of three. The oblique synapses were even more frequent in BB/B$^+$, where one series in B$^+$ has a choice of three series in BB, apparently usually synapsing with one or the other end series.

According to this interpretation the source of the duplication is the material directly adjacent to the repeat. But whether the point of insertion preceded the heavy doublet of 16A1 or the very faint final singlet of 16A5, can not be determined. If Bar is itself a repeat, a reason is thereby provided for its unique behavior of giving rise to Bar-double and Bar-reverted by oblique synapsis. Perhaps half of the Bar-reversions carry the original series and the other half the subsequent repeat restored to its original position.

On this interpretation, the "position effect"—the reinforcement of the action of one Bar gene by another in direct sequence next to it—has a visible cytological accompaniment in the increased size and puffiness, and the change in the character of the banding of both series in Bar as compared with normal and of all three series in Bar-double as compared to Bar itself. Part of this is presumably due to the "rounding-up" tendency of the synaptic attraction *along* the chromosome in addition to the oblique attractions and the straight-across attractions.

The Bar-eye reduction is thus seen to be interpretable as the effect of increasing the action of certain genes by doubling or triplicating their number—a genic balance effect. But "position effects" are never excluded when duplications or other rearrangements are present, either in the wedging further apart of genes normally closer, or by the interaction with new neighbors. The respective shares attributable in the total effect to the genic-balance change and to the position-effect change seems to be at present a matter of taste.

Study of the Baroid translocation apparently shows that the break in X comes between the two halves of the heavy doublet of 16A1. The break in 2R follows directly after the heavy capsular doublet of 48C1. Thus a demonstrable basis is laid for Dobzhansky's interpretation of the Baroid eye-reduction as a position effect.[7]

The previously reported finding[8] of the presence of "repeats" as a normal part of the chromosomes of *D. melanogaster,* and the suggestion that unequal crossing-over is probably the mechanism of production of some short repeats, thus have received ample verification by these direct observations on these processes in the case of Bar and its derivatives.

CALVIN B. BRIDGES

CALIFORNIA INSTITUTE OF TECHNOLOGY,
FEBRUARY 21, 1936

A NEW METHOD FOR TESTING THE SENSE OF SMELL AND FOR THE ESTABLISHMENT OF OLFACTORY VALUES OF ODOROUS SUBSTANCES

IN a series of experiments we have found that if odors are injected into the nasal passages in sufficient volume and with sufficient force, they can be recognized even when the breath is being held, and in papers recently published[1] two procedures for the examination of the sense of smell were described, which are based upon this new principle.

The apparatus used consists of a wide-mouthed bottle, which is closed by a rubber stopper through which pass glass inlet and outlet tubes. The end of the outlet tube has a rubber connection for the attachment of a nosepiece, and the rubber connecting tube is closed by an ordinary pinchcock. The nosepieces are Y shaped, so that the nosetips at the ends of the branches of the Y can be inserted into the nostrils. In

[1] *Bulletin* of the Neurological Institute of New York, Vol. IV, Nos. 1 and 2, 1935.