Presumably the essential sex-determining mechanism is the same in the two species, but both the male-determining action of the autosomal gene and the female-determining action of the X are stronger in neorepleta.


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**THE MECHANISM OF POSITION EFFECT—EXPERIMENTS ON THE PHENOTYPIC EXPRESSION OF POSITION EFFECTS IN RELATION TO CHANGES IN PAIRING OF NEIGHBORING CHROMOSOME REGIONS**

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Communicated February 21, 1946

In a previous paper we discussed two alternative types of interpretation of the phenomenon of position effect, and expressed a predilection for one of these alternatives, partly on the grounds that it seemed to lend itself more readily than the other to experimental tests. The hypothesis as to the mechanism of position effect that we thereupon elaborated was closely related to some early suggestions of Muller. Briefly stated, it postulated the following chain of events. In an organism such as Drosophila, where somatic pairing occurs, chromosomal aberrations change the pairing relationships of the chromosome regions adjacent to the breaks, or facing the breaks. The forces which bring about pairing may thus achieve a new distribution on either side of a gene located near to or facing a break. Such a change in pairing forces might subject this gene to a changed condition of stress. Now, if we visualize the gene as a complex folded protein molecule, or part of such a molecule, the specific activity of which is determined by the spatial configuration of specific groups on its surface, then a change of stress might be expected to lead to a change in the degree of extension of the folded protein, hence to a change in the spatial relationship of the active group, and so finally to a change in the specific activity of the gene, which change may be manifested phenotypically as a position effect.

We concluded that if this hypothesis were valid it should be possible, given an already existing position effect, to modify its phenotypic expression by further changing the pairing relationships of the chromosome regions in the immediate neighborhood of the affected gene. Moreover, it seemed clear that it would not be necessary for this purpose to alter the
already aberrant chromosome in which the affected gene itself was located, but that the change in pairing, and therefore the phenotypic change, should be obtained equally well by introducing an aberration in the homologous chromosome, opposite and close to the affected gene.

The experiments presented here were designed to serve this purpose.

Experiments and Results.—For the position effects, the white (w) locus was chosen, and three white-mottled stocks (w\textsuperscript{m4}, w\textsuperscript{m5} and w\textsuperscript{258-18}) were used.\textsuperscript{4} The first of these (w\textsuperscript{m4}) involves an inversion in the X-chromosome, with one break to the left of w\textsuperscript{+} and the other in the heterochromatic region of the chromosome, while each of the other two stocks carries a translocation between the X-chromosome and chromosome 4, the break in X being to the right of w\textsuperscript{+}. In all three stocks the males and homozygous females are viable, and the white-mottled eyes are characteristic of these flies as well as of females heterozygous for the rearrangement and for a normal X carrying the mutant allele w.

In order to combine the position effects with an aberration adjacent to the w locus in the opposite chromosome, deficiencies were used, and a comparison was made of heterozygous females (w\textsuperscript{m}/y Hw w) and females (w\textsuperscript{m}/Df w) in which an X-chromosome with a deficiency next to the w locus was substituted for the y Hw w chromosome, the dominant Hw being used as a marker to distinguish the two types (see figure 1; here, and throughout this paper, the following symbols are used: w = white, w\textsuperscript{m} = white-mottled, y = yellow, Hw = hairy wing, Df = deficiency).

Three deficiency stocks were used, w\textsuperscript{258-45}, w\textsuperscript{258-48} and w\textsuperscript{258-14}, in which there are deficiencies of one band, 5 bands and 13 bands, respectively, immediately to the left of, but not including, the w locus (assumed to be associated with band 3 C 2.3)\textsuperscript{4} which was represented by the recessive w.

Crosses of the general type Df w/y Hw w ♀ × w\textsuperscript{m} ♂ were made, so that the w\textsuperscript{m}/Df w and w\textsuperscript{m}/y Hw w F\textsubscript{1} females to be compared developed in the same bottle under the same conditions. Flies were raised at 25°C. except in a few of the initial experiments, which were run at variable room temperatures, probably averaging 26° or 27°C.

The w\textsuperscript{m}/Df w flies and the w\textsuperscript{m}/y Hw w controls were classified individually as to eye-color in four arbitrary groups—light, light intermediate, dark intermediate and dark. As there was no objective control (such as a color chart) for this system of classification, the standards adopted for the four groups may have varied somewhat from time to time. Nevertheless, the method was satisfactory for comparing flies at any one time, and the conclusions drawn from comparison of w\textsuperscript{m}/Df w flies and w\textsuperscript{m}/y Hw w controls from the same bottle are valid.

In eight out of the nine possible combinations between the three white-mottled and the three deficiency stocks, a significant difference\textsuperscript{4} was observed in the distribution of the w\textsuperscript{m}/Df w and w\textsuperscript{m}/y Hw w flies in the four
Diagram showing X-chromosomes (first and third lines) and their pairing (second and fourth lines). A represents combinations with the w-mottled stocks \(w^{15+18}\) and \(w^{23}\); B, combinations with the \(w^{m+}\) stock. A1 and B1, controls; A2 and B2, substitution of an X-chromosome with a deficiency (single line) for a normal X. Maximum pairing is assumed for euchromatic regions (double line), but the non-homologous pairing of heterochromatic regions (solid black) is not indicated.
eye-color classes. In some combinations the flies with deficiencies were generally lighter in eye-color than the controls, in other combinations they were darker. These differences are summarized in table 1.

It is obvious from this table that in general our expectation was fulfilled: on substitution of a chromosome with a deficiency near to \(w\) for a chromosome which was structurally normal in the \(w\) region, a modification of the phenotypic expression of the position effect was obtained.

There remains the question whether the phenotypic changes are indeed related to changes in pairing in the \(w\) region, or whether they should be attributed to some other cause, for any of the following explanations seem plausible.

1. As the stocks used were not isogenic, the differences may be due to modifying genes distinguishing the three deficiency chromosomes from the \(y\ Hw\ w\) chromosome. These modifiers could be located (a) in the \(X\)-chromosome, but not closely linked with the \(w\) locus; (b) in the deficient region of the \(X\)-chromosome (and
thus closely linked with \( w \) and affecting the total balance of + and - modifying genes through their presence or absence; or (c) closely linked with \( w \), but not in the region of the deficiency.

2. The differences could be due to differences in competitive action of the \( w \) alleles in the deficient chromosomes, like that postulated by Stern in the case of cubitus interruptus alleles.

These possibilities will be considered in order.

1. (a) To make all stocks as isogenic as possible, they were all outcrossed repeatedly to a single stock of \( y Hw w \). The crosses were also made in such a way as to select for viability of the \( w^m/Df w \) combinations, which in some cases was rather poor. The procedure adopted was to obtain each \( w^m/Df w \) combination, outcross it to \( y Hw w \) males, and in the next generation breed together \( Df w/y Hw w \) females and \( w^m \) males. Then the \( w^m/Df w \) females were selected and outcrossed to \( y Hw w \) males a second time, and so on. This procedure should have two results: (1) replacement of autosomes of the \( w^m \) and \( Df w \) stocks by those of the \( y Hw w \) stock, and (2) replacement by crossing-over of parts of the \( Df w \) and eventually of the \( w^m X \)-chromosomes by the \( y Hw w X \). Although the \( y Hw w \) stock itself was not strictly isogenic, it should thus serve to give both \( w^m/Df w \) and \( w^m/y Hw w \) flies a similar range of variation in genetic background, with the added reservation that in regions close to the breaks the substitution of genes from the \( y Hw w \) stock could not be expected at all, owing to the low frequency of crossovers in these regions.

The extent to which different combinations were outcrossed and the results of the outcrossing, are shown in table 2. The most important of these results is that of the \( w^{m5}/w^{35s-14} \) combination. A comparison of tables 1 and 2 shows that though at first the eyes of \( w^{m5}/w^{35s-14} \) were darker than those of \( w^{m4}/y Hw w \), after eight generations of outcrossing \( w^{m5}/w^{35s-14} \) became lighter than \( w^{m5}/y Hw w \). This must mean that the original \( w^{35s-14} X \)-chromosome carried modifiers for dark eye-color which were effectively removed by crossing-over in the course of several generations of outcrossing to \( y Hw w \), and that the difference in the opposite direction which then became apparent had been masked by these modifiers at an early stage, before their substitution by genes from the \( y Hw w X \)-chromosome. This later difference therefore cannot be attributed to modifiers in any other part of the \( X \)-chromosome than the close neighborhood of \( w \).

Other combinations which were outbred for several generations continued to show the same difference between the \( w^m/Df w \) and \( w^m/y Hw w \) flies that appeared at the first cross.

In two cases \( (w^{35s-18}/w^{35s} \text{ and } w^{m4}/w^{35s-48} \) combinations) after crossovers had occurred between the \( Df w \) and \( y Hw w \) chromosome to the left of the deficiency, the crossover chromosome consisting of the left end of the deficiency chromosome (but without the deficiency) and the right end
of the \( y \) \( Hw \) \( w \) chromosome (without \( y \) \( Hw \)) was tested by making up the combination \( cros\text{o}ver/\ y \) \( Hw \) \( w \) and mating to \( w^m4 \) or \( w^{258-18} \) males. The distribution of eye-colors in \( w^m/cros\text{o}ver \) and \( w^m/y \) \( Hw \) \( w \) females of the next generation did not differ significantly, showing that the left end of the deficient \( w^{258-48} \) \( X \)-chromosome was not distinguishable from that of the \( y \) \( Hw \) \( w \) chromosome with regard to modifiers of the position effects.

It may be concluded from the outbreeding experiments that the final differences observed between \( w^m/Df \) \( w \) and \( w^m/y \) \( Hw \) \( w \) flies were not due to any difference in such modifiers as could be separated from the \( w \) region by crossing over. This conclusion is substantiated, as far as the region to the left of \( w \) is concerned, by the tests of crossovers just described.

<table>
<thead>
<tr>
<th>( w^m ) combination</th>
<th>( w^{258-45} )</th>
<th>( w^{145-45} )</th>
<th>( w^{258-48} )</th>
<th>( w^{558-14} )</th>
<th>( w^{258-14} )</th>
<th>( w^{158-14} )</th>
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<tbody>
<tr>
<td>( Df ) ( w ) Light</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Light intermediate</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>14</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Dark intermediate</td>
<td>150</td>
<td>80</td>
<td>2</td>
<td>130</td>
<td>1</td>
<td>99</td>
</tr>
<tr>
<td>Dark</td>
<td>386</td>
<td>250</td>
<td>64</td>
<td>165</td>
<td>21</td>
<td>222</td>
</tr>
<tr>
<td>( y ) ( Hw ) ( w ) Light</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Light intermediate</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>2</td>
<td>29</td>
<td>0</td>
</tr>
<tr>
<td>Dark intermediate</td>
<td>74</td>
<td>48</td>
<td>98</td>
<td>59</td>
<td>86</td>
<td>38</td>
</tr>
<tr>
<td>Dark</td>
<td>633</td>
<td>323</td>
<td>156</td>
<td>325</td>
<td>76</td>
<td>355</td>
</tr>
<tr>
<td>No. of generations</td>
<td>10</td>
<td>10</td>
<td>13</td>
<td>14</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>( \chi^2 )</td>
<td>63.3</td>
<td>15.5</td>
<td>31.1</td>
<td>80.5</td>
<td>24.7</td>
<td>60.1</td>
</tr>
<tr>
<td>( n )</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>( P )</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

(b) The loss of dominant modifiers in the deficient chromosomes could result in a difference in phenotype of flies carrying these chromosomes as compared with those having a complete \( y \) \( Hw \) \( w \) chromosome. Inspection of the tables, however, shows that the same deficiency (e.g., \( w^{258-48} \)) may modify different position effects in opposite directions. In other words, on the assumption of a change in balance of dominant modifiers, we would also have to assume that these modifiers have a different and specific action on different position effects. While this interpretation does not appear probable to us, it obviously cannot be excluded altogether.

There is another possibility, however, namely that the deficiencies uncover recessive modifiers in the opposite chromosome, near to the affected \( w \) locus. In this case, the reaction of different position effects to the same deficiency would be attributable not to specific action of the same
modifiers, but to the presence of different modifiers closely linked with the affected \( w \) loci of the different white-mottled stocks.

If this were so, we would assume for instance that in the \( w^{255-18}/w^{258-45} \) combination, the deficiency uncovers recessive modifiers which darken the eye-color, while in \( w^{m4}/w^{258-48} \) one or more recessive modifiers for lighter color are effective. These modifiers, then, should also be effective in the hemizygous males and homozygous females of the position effect stocks; but this is not the case, for \( w^{258-18} \) and \( w^{m4} \) \( \sigma \)'s were scored after 13 and 12 generations of outcrossing, respectively, and in both cases (not in \( w^{m4} \) only) proved to be lighter than the corresponding \( w^{255-18}/yHw w \) or \( w^{m4}/yHw w \) \( \sigma \)'s.

We consider, therefore, that this possibility can be discarded.

It may be added that the probability that differences are due to modifiers in the deficient regions is considerably reduced by the fact that such differences are obtained even with the single band deficiency of \( w^{258-45} \).

(c) It will be seen that the assumption of very closely linked modifiers outside of the deficiency differing from those of the \( yHw w \) chromosome again requires the additional assumption of specific and opposite action of these genes on different position effects. We are left in doubt as to this possibility, as in the case of possibility 1(b) above.

2. Stern\(^6\) has obtained results with alleles at the cubitus interruptus \((ci)\) locus which he interprets on the supposition that some of these alleles compete with one another for the use of a common substrate, and that differences in ability to combine with this substrate or to convert it into a new end-product are the cause of different degrees of phenotypic expression of the cubitus interruptus effect in flies carrying different combinations of alleles.

In order to test the \( w \) alleles in our deficiency chromosomes for such a competitive effect, females of the constitution \( w^{259-14}/yHw w, w^{258-45}/yHw w \) and \( w^{258-48}/yHw w \) were mated with apricot \((w^a)\) males, and in each case a comparison was made between the \( w^a/Df w \) and \( w^a/yHw w \) progeny.

It was impossible to distinguish between the two types in any case, so that there is no evidence that any of the deficiencies used have any effect on the expression of the \( w^a \) allele.

**Summary and Conclusion.**—On the assumption that pairing conditions affect the manifestation of position effect, experiments were performed in which the eye-colors of flies, carrying a white-mottled \( X \)-chromosome and either a normal unbroken \( X \) or one with a deficiency next to the \( w \) locus, were compared. The eye-colors appear to be different. While these results can be regarded as supporting the hypothesis which the experiments were designed to test, it cannot be completely excluded at present that they are due to the action of modifiers, or to competition between alleles.\(^7\)
THE DISTORTION OF ANGLES IN GENERAL CARTOGRAPHY*

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Communicated March 8, 1946

1. Azimuthal Curves.—Let a surface $\Sigma$ be mapped in a point-to-point fashion upon a plane $\pi$ with cartesian coordinates $(x, y)$ such that point $s$ of $\Sigma$ and $\pi$ will correspond if they are represented by the same (curvilinear) coordinates. Recently we have introduced the term cartogram, to denote any particular mapping of a surface $\Sigma$ upon a plane $\pi$. The cartogram is conformal or general according as the transformation is or is not conformal.

We define the azimuthal ratio $\alpha$ in the following manner. Let $d\theta$ denote the angle between two infinitesimally consecutive directions at a fixed point $p(x, y)$ on the plane $\pi$, and $d\theta$ the angle between the corresponding consecutive directions at the associated fixed point $P(x, y)$ on the surface $\Sigma$. By the azimuthal ratio $\alpha$, we shall mean the value of the fraction: $\alpha = d\theta/d\theta$. That is, it is the instantaneous rate of change of the inclination at the point $P(x, y)$ on the surface $\Sigma$ with respect to the inclination at the corresponding point $p(x, y)$ on the plane $\pi$.

Our azimuthal ratio $\alpha$ is a function of the lineal element $(x, y, y')$. It is independent of the slope $y' = dy/dx$ if, and only if, the cartogram is conformal, in which case $\alpha = 1$.

An azimuthal curve is the locus of a point on the plane $\pi$ (or on the surface $\Sigma$) along which the azimuthal ratio $\alpha$ does not vary. In a general cartogram, there are $\sim^2$ azimuthal curves. (In this connection, conformal cartograms are of no interest since every curve is azimuthal because of the fact that $\alpha = 1$.)

In the present article, we shall derive some of the geometrical properties of systems of $\sim^2$ azimuthal curves. Also we shall compare and contrast these with our properties of scale curves which were developed elsewhere.

2. The formula for the Azimuthal Ratio $\alpha$.—To derive this formula, we