

CHAPTER 3

MORGAN: GENES ON THE SAME CHROMOSOME DO NOT ASSORT INDEPENDENTLY

Thomas H. Morgan continued his research and found that other genes also tended to be inherited together, similar to the sex-linkage association he had already observed.

DEVIATIONS FROM MENDEL'S PREDICTED RATIOS

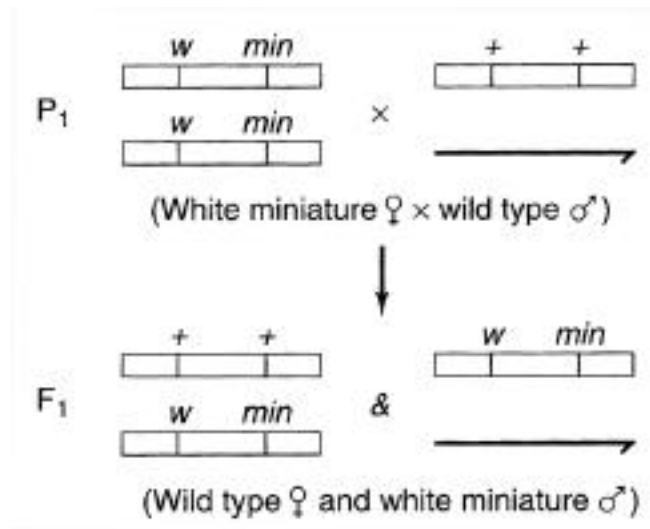
When the chromosomal theory of heredity was first advanced by Sutton in 1903 to explain Mendelian segregation and independent assortment, it almost immediately appeared to suffer from a fatal flaw: four more independently assorting traits were found in the garden pea, in addition to the seven Mendel had reported-yet peas only had seven haploid chromosomes! Either Mendel's factors were not on chromosomes after all, and the correspondence noted by Sutton was a happy accident, or factors *on the same chromosome* could assort independently of one another. The logic was inescapable, however unattractive the alternatives. Squarely facing the issue, the botanist Hugo de Vries in 1903 proposed a formal theory of *factor exchange*. What de Vries proposed was that in prophase I of meiosis, when maternal and paternal homologous chromosomes were closely paired, exchange could take place between factors opposite one another. The only requirements were (1) a mechanism of exchanging the material, (2) proper alignment so that only "like" factors were exchanged, and (3) a means of ensuring accuracy in the equality of exchanged material. Whether or not an exchange of any given gene actually occurred was, in de Vries' model, a matter of chance.

de Vries' model had the great virtue that it could account for any observed deviation from Mendelian proportions in terms of altered probabilities of factor exchange. The model also had the disadvantage of Mendel's theories: it was purely formal, a hypothetical scheme with no known mechanism. Chromosomes had never been shown to exchange parts so readily-they seemed too concrete and solid for such a dynamic view. Largely for this reason, de Vries' proposition of chromosomal recombination did not gain rapid acceptance. In the first reported case of linkage, W. Bateson, E. R. Saunders, and R. C. Punnett (three of the principal figures in the early history of genetics) suggested that preferential multiplication of certain gametes after meiosis (rather than chromosomal exchange) was probably responsible for the discrepancy from Mendelian prediction.

TESTING DE VRIES' HYPOTHESIS

The first clear support for de Vries' hypothesis came six years later, from Thomas H. Morgan's fruit flies. While Morgan confirmed Sutton's chromosomal theory with his analysis of sex linkage by showing that the gene "white-eye" appeared to be on the X chromosome of *Drosophila*, he subsequently detected *other* traits that exhibited sex linkage, such as miniature wing and yellow body. Because there was only one X chromosome in *Drosophila*, all of these traits by the chromosomal theory had to have been on the same chromosome. de Vries' model was thus subject to direct test: one needed only look to see if new combinations of genes arose in crosses. Any *new* combinations between genes on the *same* chromosome could only have arisen by *exchange* between the two X chromosomes of the female (the male has but one).

The test, then, was to cross two of Morgan's sex-linked traits and study their simultaneous assortment (a two-factor, or *two-point* cross). Morgan crossed female flies that were homozygous for both white-eye (*w*) and miniature wing (*min*) with wild-type (+) male flies. As you would expect from sex-linked traits, the F₁ progeny flies show the reciprocal arrangement:



The key to the test was to look at the F₁ females. They had two homologous X chromosomes, which lined up during gametogenesis in prophase I of meiosis. If chromosomes maintained their integrity, as common sense dictated, then the only possible female gametes were ++ and w min (the underline denotes linkage on the same chromosome). If, on the other hand, de Vries' factor exchange occurred, then two other female gametes would occur, + min and w +. How were the female gametes going to be seen? A test cross, of course. In this case, a test cross required a double recessive—the F₁ brothers of the females in question. Morgan analyzed 2441 F₂ progeny of this test cross, with the following results:

Eyes	Wings	♀	♂	Total	
w	min	359	391	750	} 1541 Parental combinations
+	+	439	352	791	
w	+	218	237	455	} 900 New combinations
+	min	235	210	445	
		<u>1251</u>	<u>1190</u>	<u>2441</u>	

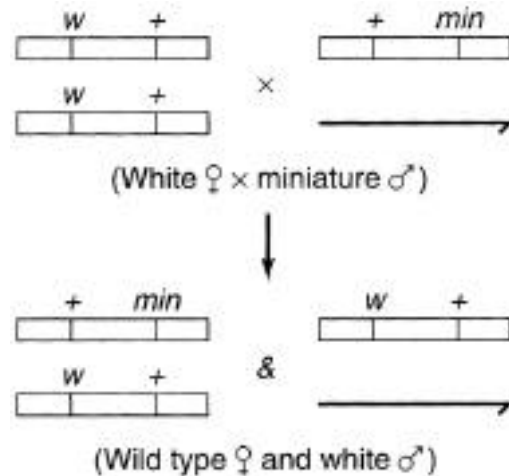
New combinations were obtained! Of the 2441 F₂ progeny, fully 900 (36.9%) represent new combinations of the two factors, or within-chromosome recombinations. Morgan was forced to conclude that in 36.9% of the F₁ females, an exchange of factors had occurred between the two X chromosomes just as de Vries had suggested.

Note that if white-eye is considered alone, the results fit the 1:1 Mendelian test cross ratio (1205 w:1236 +), and similarly for miniature wing (1195 min:1246 +). The real deviation from Mendelian expectation is not in the behavior of either of the traits alone, but rather in the lack of independence of their assortment. If w and min were fully independent, the expected ratio in this test cross should approach 1:1:1:1 for the four combinations. Instead, a great preponderance of the original parental combinations is seen, as if the original combinations tended to stay together, to act linked to one another.

COUPLING VS. REPULSION

Morgan's results clearly indicated that although factor exchange indeed occurred within chromosomes, its effects were limited. Certain combinations of traits tended to stay together in crosses. Could this have been due to some characteristic of the traits themselves? The simple test of this possibility was to put

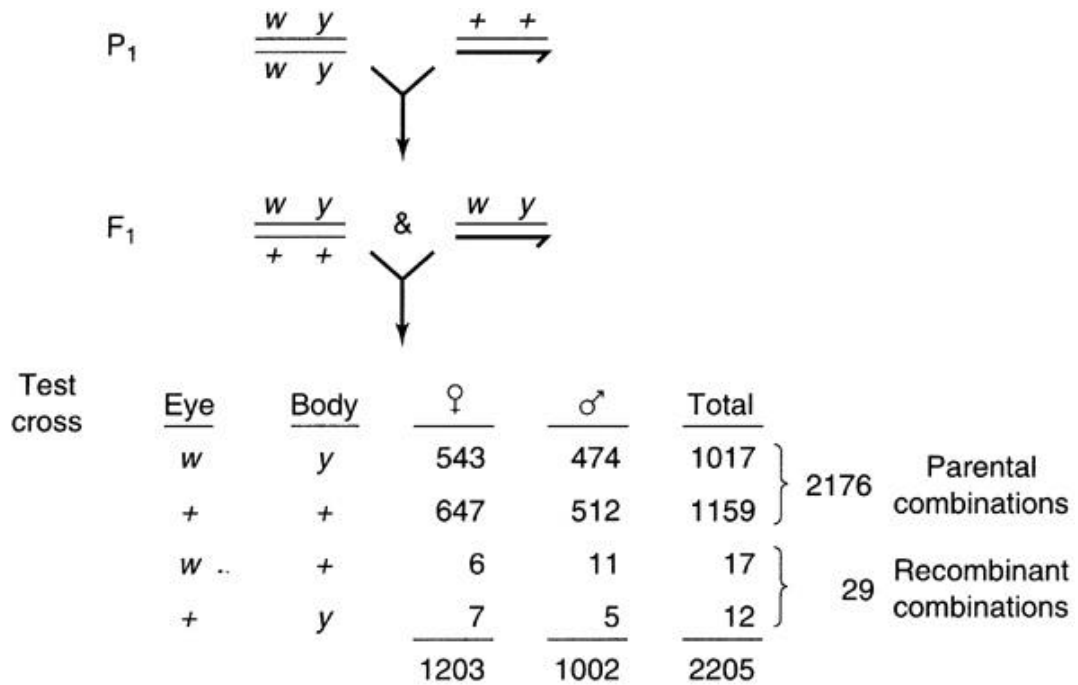
different alleles in combination with one another. Indeed, when a parallel cross was carried out between homozygous white females and miniature males:



and the wild type ($+ \textit{min}/+ \textit{w}$) was test-crossed to a $w \textit{min}$ male, the reverse combinations were maintained: of the test-cross progeny, 62% were either white eye ($w +/w \textit{min}$) or miniature wing ($w \textit{min}/+ \textit{min}$), the parental combinations; while 38% were either wild type ($+ +/w \textit{min}$) or white eye and miniature body ($w \textit{min}/w \textit{min}$), the recombinant types. Thus, it was very clear that particular alleles maintained their association not because of any special attributes of particular alleles, but rather because of their presence together on parental chromosomes. Double heterozygotes in which the dominant alleles are on the same chromosome ($A B/a b$) are said to be in a coupling arrangement, while those in which the dominant alleles are on opposite chromosomes ($A b/a B$) are said to be in repulsion. The identity of the alleles at two loci does not affect the recombination frequency between them: in either coupling or repulsion, the same recombination frequencies were obtained in test crosses (37% and 38% in the case of the $w \textit{min}/++$ and $w ++/\textit{min}$ examples above).

LINKAGE REFLECTS PHYSICAL ASSOCIATION OF GENES

When Morgan examined other genes that exhibited sex linkage, he again observed recombinant types and a tendency for parental combinations to stay together. There was an important difference, however: the frequency with which Morgan observed recombinants, while characteristic for any gene pair, was quite different for different pairs. Thus, when white-eye was compared to another "X-linked" trait, yellow body (*y*), Morgan obtained the following result:



Here the frequency of the character exchange was only 1.3%.

Morgan concluded that characters remained together because they were physically near to one another on the chromosome and were less likely to exhibit de Vries' factor exchange. Morgan called this within-chromosome recombination *crossing-over* when they were far apart. Further, he postulated that the nearer two genes were to one another, the more frequently they would be observed to remain associated together (e.g., the greater the linkage).