

The Mechanism of Heredity.

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I.

Mendel's Two Laws of Heredity and their Mechanism.

AT the time when Mendel discovered his two fundamental laws of heredity, no mechanism was known in plants or animals that would explain how such processes as those invoked by him could be brought about; but between 1865 and 1900 (when Mendel's "Principles" were recovered), the study of the ripening process (maturation) of the egg and sperm-cell had progressed so far that such a mechanism was ready at hand.

Mendel's first law—the law of segregation—may be illustrated by the following example: A tall edible pea crossed to a short pea gives tall (hybrid) offspring. These, if self-fertilised, produce on an average three tall to one short. Mendel pointed out that a very simple hypothesis will account for this ratio of 3:1 in the second generation ( $F_2$ ). The original tall parent contributes one element (T), and the short parent another element (t) to the hybrid. If at the time when its germ-cells mature these elements separate (segregate), so that half the eggs come to contain the element for tallness (T), and the other half the element for shortness (t), and if a similar process takes place in the pollen of the hybrid (half the pollen grains bearing T and half t), then chance fertilisation of any egg by any pollen grain will be expected to give three kinds of individuals, namely TT, Tt, tt, in the ratio of 1:2:1. The first two kinds (TT and Tt) will be tall plants, because the one (TT) is pure for tallness, and because in the other (Tt) tallness dominates shortness as seen in the hybrid. Hence the second generation will be made up of three tall to one short.

The unique feature of the situation, the segregation in the germ-cells of the hybrid of the elements derived from each parent, finds a parallel in the distribution of the maternal and paternal chromosomes of the hybrid. For example: every cell of the hybrid contains one chromosome (a) from one parent, and one chromosome (A, the mate of the former) from the other parent. But this condition is not permanent in its germ-cells, for when they arrive at the final ripening stage, the two chromosomes (aA) come together, conjugate, and then "segregate," i.e. they pass into opposite cells. As a result, half the eggs contain chromosome a, half chromosome A. They behave like Mendel's pair of "characters." Hence if the materials responsible for the difference between T and t are carried by the members of the same pair of chromosomes, A and a, they must follow Mendel's first law.

Mendel's second law applies to the independent behaviour of two or more pairs of characters: the

members of each pair assorting independently of the members of other pairs. It has been generally supposed by cytologists that at the ripening of the germ-cells the members of the pairs of chromosomes separate independently, in the same way that Mendel supposed the individual pairs of characters to be distributed. Proof was difficult to obtain from direct observation, but recently this evidence has been abundantly and convincingly obtained by Miss Carothers. If then the chromosomes carry the materials (genes or differentials) for the hereditary characters, they behave in such a way as to ensure the success of Mendel's second law.

Had we only this parallelism to go upon we should be justified, I think, in accepting the chromosome theory of heredity as a working hypothesis, but further evidence has been steadily accumulating. It may be briefly summarised, yet

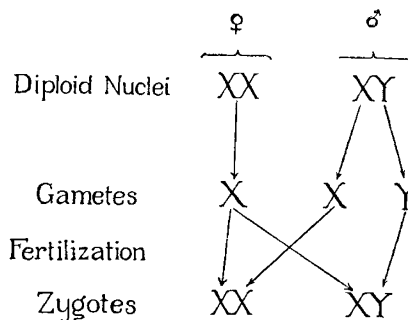


FIG. 1.

must be given in some detail; for it is the exact correspondence between fact and theory that furnishes the essential data for the conclusions arrived at.

(1) In some groups of animals it has been shown that one pair of chromosomes (XY) acts as a differential with respect to sex determination (Fig. 1). The female has two like chromosomes, called X and X; the male has one X, and often another chromosome called Y. Thus  $XX = \text{♀}$ ;  $XY = \text{♂}$ . These chromosomes segregate at maturation, as do the others. Every egg eliminates one X in one of its polar bodies; half the sperms are X-bearing, half Y-bearing. Any egg (X) fertilised by an X-sperm = XX (♀); any egg (X) fertilised by a Y-sperm = XY (♂). Thus sex is here determined by a process that automatically gives equal numbers of males and females.

A son always gets his single X from his mother; a daughter gets one X from her mother, another from her father. Certain characters follow in their heredity the course taken by these chromosomes. For instance, if the mother is aa, and the father is A, each son will be a, each daughter will be aA.

Many examples of this sort could be given, and further tests of the different kinds of individuals that appear in such crosses could also be cited to show that the distribution of the sex-linked characters follows the distribution of the X-chromosomes. This evidence is so significant that it may be further illustrated by a concrete case. If a white-eyed female of the vinegar fly, *Drosophila melanogaster*, is bred to a red-eyed male (Fig. 2), the sons are white-eyed, and the daughters are red-eyed (red dominates white). If these are inbred there appear in the next generation white-eyed daughters, red-eyed daughters, white-eyed sons, and red-eyed sons in the ratio of 1:1:1:1.

The distribution of the X- and Y-chromosomes is illustrated by the rods in the middle of the diagram. The white rod stands for the X that carries the differential for recessive white eyes. The black rod stands for the X that carries the

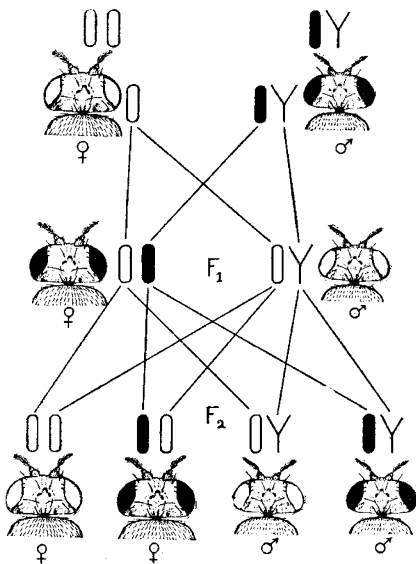


FIG. 2.

differential for dominant red eyes. The Y-chromosome is represented by that letter. It is obvious from the way in which these chromosomes are distributed that there should be both red-eyed and white-eyed grandchildren in equal numbers.

The reciprocal cross gives a different result (Fig. 3). Thus, when a white-eyed male is bred to a red-eyed female, both the sons and the daughters have red eyes. If these are inbred, there appear in the next generation red-eyed daughters, red-eyed sons, and white-eyed sons in the ratio of 2:1:1. Here also it is evident from the distribution of the X's why, in the second generation, the only white-eyed flies present are males. These carry a single white-producing X that traces back to the grandfather. All the granddaughters have red eyes, but are of two kinds, one pure for red, and the other carries both a red and a white rod. If these second-generation females are tested it is found, in fact, that half of

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them carry two red-producing chromosomes, and the other half a red and a white one. Evidence like this from sex-linked inheritance, where both the genetic and the chromosomal histories are known, furnishes by itself very strong evidence in favour of the chromosomal interpretation of heredity, but there is further evidence that makes the case even stronger. This evidence may now be briefly stated.

(2) Individual females of the fly *Drosophila* are

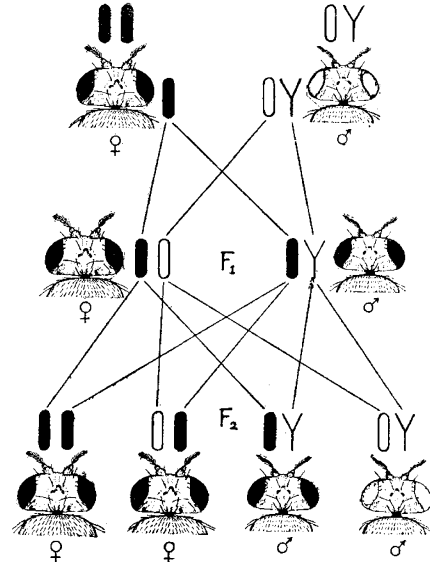


FIG. 3.

sometimes met with that break the rule for sex-linked inheritance. A genetic study by Bridges of this exceptional behaviour led to the prediction that they must have an extra sex-chromosome. Cytological examination showed, in fact, that there is in these females an X- and another X- and a Y-chromosome (Fig. 4). The genetic behaviour of the "non-disjunctional" females is so important for the chromosome theory that it must be followed through carefully. It will be simpler to give the genetic and the chromosome histories together.

When an egg containing the three chromosomes XXY matures, the two X's may conjugate, leaving the Y free to go to either pole of the polar spindle (this happens in 92 per cent. of the cases), or else an X and the Y may conjugate, leaving the other X to go to either pole. As shown in the diagram (Fig. 5), four kinds of eggs result (and four kinds of polar bodies are extruded). If the non-disjunctional female in question has white eyes, the history of her white-bearing X's can be followed when she is fertilised by a male with a red-bearing X-chromosome. Considering first the fertilisation of her four kinds of eggs by the red-producing X-sperm of the male, it is evident that there will be produced four kinds of individuals, viz. XXY, XX, XXX, and XY.



XXY ♀  
FIG. 4.

Two of these red-eyed females are both hybrid for white; one of them should be a non-disjunctional female (XXY) and repeat the same process. Such

sperm and give rise in this way to non-disjunctional daughters (XXY). This, in fact, has been shown to occur.

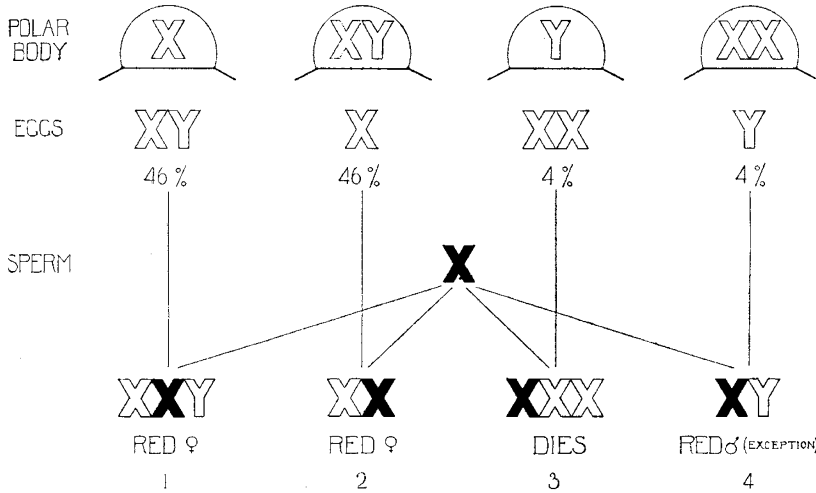


FIG. 5.

is the case. The females with three X's generally die, but occasionally one emerges that can be identified as such by certain peculiarities, and when the

too, involves the sex-chromosomes. We have a stock that gives results diametrically opposite to ordinary sex-linked inheritance. The females

cells of such a female are studied it is found that three X's are present (Fig. 6). Lastly, there is a male, XY, with red eyes, an "exceptional male," since his mother had white eyes. He arises from a Y-egg fertilised by an X-bearing sperm—the so-called female-producing sperm. Here such a sperm makes a male because the combination of one X with the rest of the chromosomes is a male in these flies, quite irrespective of the origin of the X-chromosome. The result shows convincingly

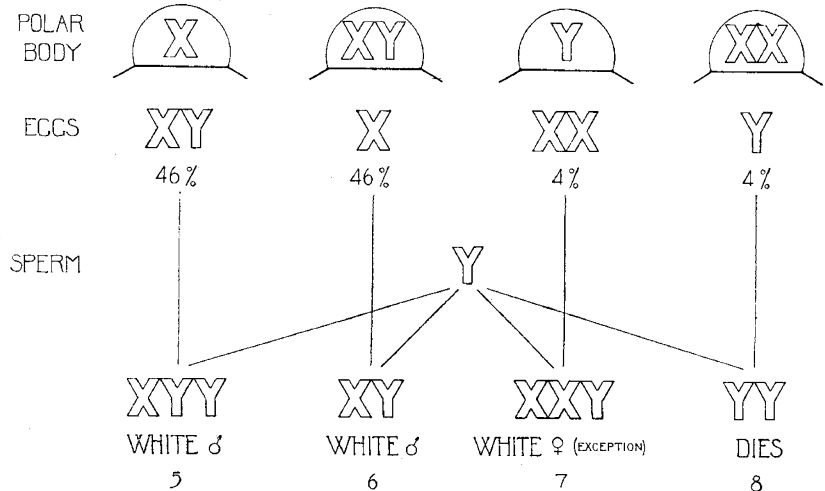


FIG. 7.

that the X-sperm normally gives rise to a female because it carries an X (the egg supplying another X), and not because its X is carried by a "female-producing" sperm.

are yellow (recessive), and give, when bred to a normal grey male, yellow daughters and grey sons. A study of this stock by L. V. Morgan, who discovered it, showed that all the results could be explained by the assumption that two X-chromosomes, bearing yellow, had become stuck together. Sections of these females verified the prediction. Two united X-chromosomes and a Y are present in the yellow females (Fig. 8). At maturation of the eggs both X's pass out together into the polar body at the reduction division, or else both remain in the egg. Thus the mature eggs are XX or Y. Fertilised by a normal "grey" X-sperm, the XX egg gives an XXX grey female (which dies as a rule) and an XY



XXX ♀

Fig. 6.

There remains to be considered the case where the same series of eggs is fertilised by the other kind of sperm, the Y-bearing sperm. In the lower line of Fig. 7 the outcome is shown. Two kinds of males appear, both white-eyed, but one XYY and the other XY. The latter, XY, is found to be a normal male; the former is expected, in some cases, to transmit both an X and a Y through his "female-producing"

grey male. Fertilised by a Y-sperm, the two kinds of eggs give XXY yellow females and YY individuals (which die). Thus, of the four kinds of individuals expected, half the females (XXX) and half the males (YY) die, and a sex ratio of 1:1 remains. It has been stated above that XXX females appear at rare intervals. These are grey and are recognisable as XXX individuals by certain stigmata, and have been shown in sections to possess the three X's.

(4) *Drosophila*, and presumably other animals belonging to the XX-XY type, are so constituted that they can develop with one X or with two X's, provided the other chromosomes are present in duplex. In short, sex determination has been



FIG. 8.

regulated along these lines. Failure to obtain similar situations in the case of the other chromosomes led us to suppose that an individual lacking one or both members of a pair could not "come through"; but we had no actual proof that this was the explanation of their absence. Nevertheless, it was anticipated that it might be possible for individuals lacking one or containing three of the very tiny IV-chromosomes (Fig. 9) to survive. Recently Bridges has found such individuals, and we now realise that they must have been rather frequently met with in the past, but were not recognised as such. A fly with only one of the IV-chromosomes is small, pale, hatches late, has small, slender bristles and a dark trident. The

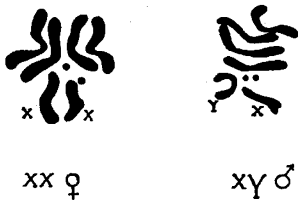


FIG. 9.

wings are blunt and slightly spread, and the eyes large and roundish. If a female, it is expected to contain two kinds of mature eggs (*i.e.* eggs after the polar body has been extruded)—one kind with the other kind without, a IV-chromosome. The egg with one IV-chromosome gives a normal result when fertilised. The egg without a IV-chromosome, if fertilised by a sperm carrying a recessive IV-chromosome character, produces an individual ( $\sigma$  or  $\text{♀}$ ) showing the recessive character of the father, because the single IV-chromosome of this individual came from the father that carried the recessive in question. A male that has only one IV-chromosome in its cells produces two kinds of sperm, one with IV and one without IV. Mated to a normal female, the results are in

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principle the same as above. A male and a female, each with only one IV-chromosome, when mated, might be expected to give some individuals (25 per cent.) without a IV. None such appear, and the ratios show that they die.

Individuals with three IV's are also known. Their characteristics are the opposites of those shown by the haplo-IV's. For example, they are dark with a very faint trident, long-bristled, and have small, smooth eyes. Their wings are long and narrow. Females of this kind produce two kinds of eggs, one kind with two IV's, the other kind with one IV. Mated to a normal male, with a IV-chromosome recessive character, such females produce daughters and sons of two kinds, namely, one kind with three IV's, like the mother, and the other kind normal.

If these males and females, triploid for IV, are mated, the recessive character appears in only 4 per cent. instead of the Mendelian 25 per cent. of the offspring, as would be expected when one recessive and two dominant characters are involved.

Many combinations between triploids and haplo-IV's are possible, and unique ratios are expected. These have also been worked out. Cytological preparations of triplo- and haplo-IV's show in



FIG. 10.

one case three small chromosomes, and in the other only one.

(5) Complete triploid individuals having three of each kind of chromosome have recently been found by Bridges (Fig. 10). The triploid flies are larger and coarser than normals, and also have large, rough eyes. Their eggs, as shown by genetic tests, contain all possible combinations of chromosomes, behaving as though non-disjunction takes place independently in each set of three.

Amongst the offspring of a triploid female (mated to a normal male) there is one class that has three II's, three III's, and three IV's, but with two X-chromosomes. This individual is an intersex, more like a male than a female. There is another class that has three II's, three III's, but only two IV's. It also is an intersex, but more like a female.

Thus sex itself, in this animal, is shown to be an expression of a balance between the X-chromosomes and the rest of the chromosomes. The results show that the differentials which determine sex are not confined to the sex-chromosomes alone. Some appear to be in the II- and III-chromosomes, and others in the IV-chromosome.

(To be continued.)