The Mechanism of Heredity.[1]

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II.

Linkage and Crossing-over.

MENDEL'S second law has been found to be restricted in its application. Two pairs of characters do not always assort independently. This fact was first observed by Bateson and Punnett in 1905, and called gametic coupling—not that gametes (ripe germ-cells) are coupled, but that when certain genes enter together from one parent they tend to hold together, as though coupled, in later generations. A specific case will serve to illustrate this kind of inheritance.

If a sweet pea with genes for purple flowers and long pollen grains is crossed to a pea of another strain with red flowers and round pollen, the expectation for the two pairs of genes would be in F_2 9 : 3 : 3 : 1. Instead of this ratio there was found approximately 177 : 15 : 15 : 49. Purple long and red round have come out in the second generation in unexpected ratios, or, in other words, the results are explicable only on the hypothesis that the genes that went in together have shown a tendency to stay together instead of freely assorting.

This coupling is often spoken of to-day as linkage, because it applies not only to two genes, but to any number of them. A few further cases may be given; in one the characters, as in the pea, are not sex-linked, and in the other they are. There is a strain of *Drosophila melanogaster* that is black. It gives with the wild fly in the second generation a 3 : 1 Mendelian ratio. There is another strain that has vestigial wings. It, too, gives with the wild fly a 3 : 1 Mendelian ratio. It is easily possible to make a strain that is pure both for black (*bb*) and for vestigial (*vv*). If a black vestigial male (*bv*) is mated to a wild female (B V) (grey long wings) all of the offspring are grey long (Fig. 11). If one of the F_1 sons is mated to a black vestigial female of pure stock, only two kinds of offspring are obtained; half of them are black vestigial, and half are grey long. In other words, the two recessive characters that went in together (black vestigial) have come out together. These characters are completely linked in the male. It may be said, in exactly the same sense, that the other two characters, the dominant ones, namely, grey long (which went in together from the other side), are also linked. Now if the genes for black and for vestigial are carried in the same chromosome, then their partners or allelomorphs (grey long) lie in the other chromosome of the same pair, and if these chromosomes remain intact the result is what is expected to take place.

Linkage is also excellently illustrated in the case of sex-linked characters. As has been shown, white-eye *versus* red-eye colour of Drosophila gives a Mendelian ratio. Another sex-linked character, yellow colour, also gives the same result. If a strain is made up that has white eyes and yellow colour, and if a female of this strain is mated to a wild-type fly (red eyes, grey colour), all the sons will be white-yellow, and all the daughters red-grey (Fig. 12). If these are inbred, the great majority of the offspring (98·5 per cent) are yellow-white and grey-red (half and half). In other words, these characters are linked, but only in 98·5 per cent. of the cases. The remaining 1·5 per cent. is composed of two kinds of individuals, red-yellow and white-grey. It may be said, therefore, in this case, that the white eye of the yellow type has crossed over to the grey type, and in exchange the red eye of the grey type has crossed over to the yellow type.

The four kinds of offspring obtained in this cross can be accounted for, if once in a hundred times an interchange has taken place between the two X-chromosomes of the F_1 female, in such a way that the part containing the gene for white eye is interchanged for a corresponding part of the other chromosome with the gene for red eye.

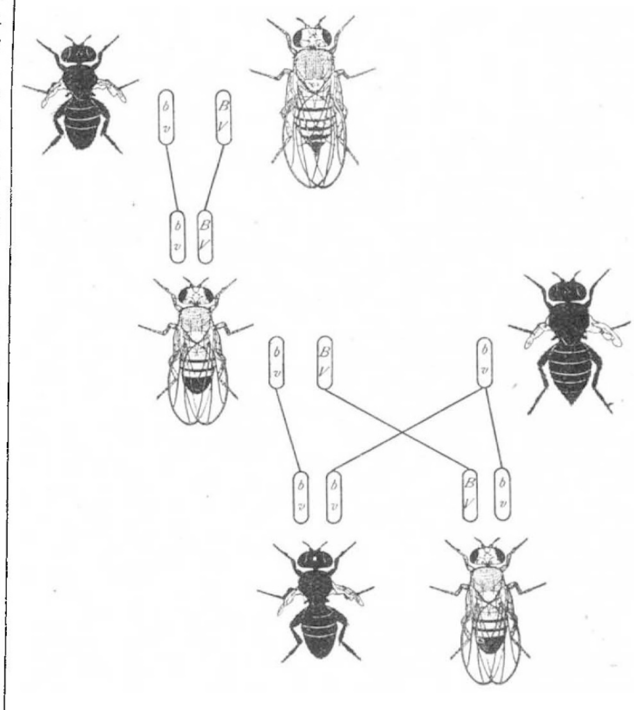

FIG. 11.

Another example of crossing-over may be given, one involving the same characters, black and vestigial, which were used to illustrate complete linkage. It is possible to use the same combinations of characters to illustrate both absolute linkage and crossing-over, because in the male of Drosophila there is no crossing-over, but in the female crossing-over occurs. Therefore, in the first case above, in which this combination was utilised, an F_1 male was back-crossed, while in the present case an F_1 female will be employed. If, as shown in Fig. 13, a black vestigial fly be crossed to a wild-type fly (long wings, grey), the F_1 female will be wild-type. If she is back-crossed to a black

[1] Continued from p. 244.

vestigial male of pure stock, the F_2 offspring will be of four kinds, in the proportions given below :—

Non cross-overs		Cross-overs	
Black vestigial	Grey long	Black long	Grey vestigial
41·5 per cent.	41·5 per cent.	8·5 per cent.	8·5 per cent.
83 per cent.		17 per cent.	

In this experiment 17 per cent. of crossing-over occurs in the F_1 female. As before, the relation of these facts to the chromosomes is illustrated by the rods in the centre of the diagram. The two pairs of elements (genes) involved are indicated by the letters inside the rods.

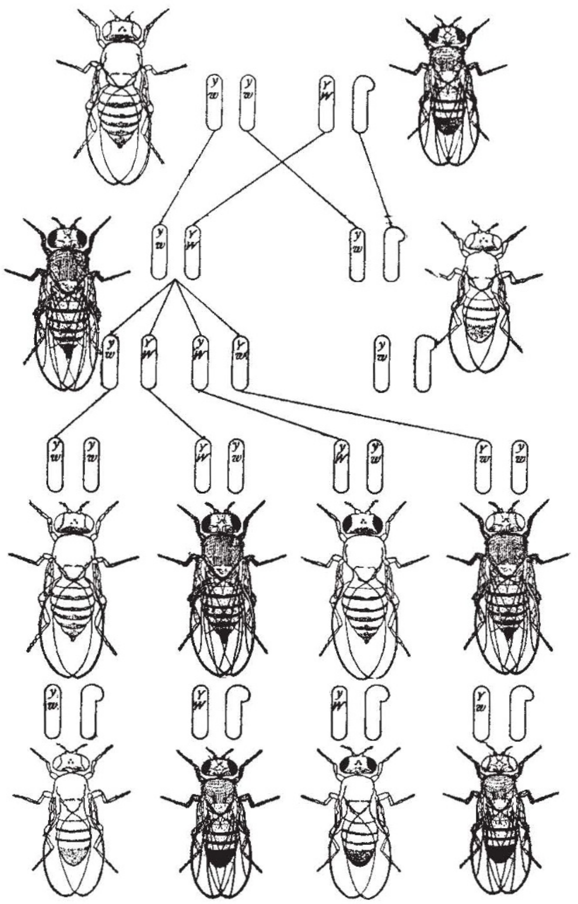

FIG. 12.

Many examples of linkage and crossing-over are known at the present time. Linkage is said to be strong when, as in the yellow-white case, crossing-over takes place in a small proportion of cases. Linkage is said to be weak when crossing-over takes place frequently. Crossing-over may be less than 1 per cent., or even not take place at all (complete linkage), as in the case of the black vestigial male given above. It may take place in nearly 50 per cent. of the individuals of a back-cross, which means that about half of the flies show linkage, and half show crossing-over. This would be, of course, numerically the same result as when the two pairs of characters involved freely assort. A case of this kind could not, in fact, by itself alone be distinguished from a case where the pairs are carried by different chromosomes. It may appear, therefore, incorrect to speak here of linkage, and this would be true were there no other evidence showing that the two characters involved are in the same chromosome. But whenever a number of other characters are known in the same group the linkage of the two characters giving 50 per cent. of crossing-over can still be shown, for if each of the characters is found to be linked to a third one they must be linked to each other.

In Drosophila there are more than one hundred sex-linked characters. If their linkage relations are studied *in series* an important result comes to light. This may be illustrated by the following example. It has been stated that crossing-over takes place in 1·5 per cent. of cases between yellow colour and white eyes. There is another eye character, called echinus,

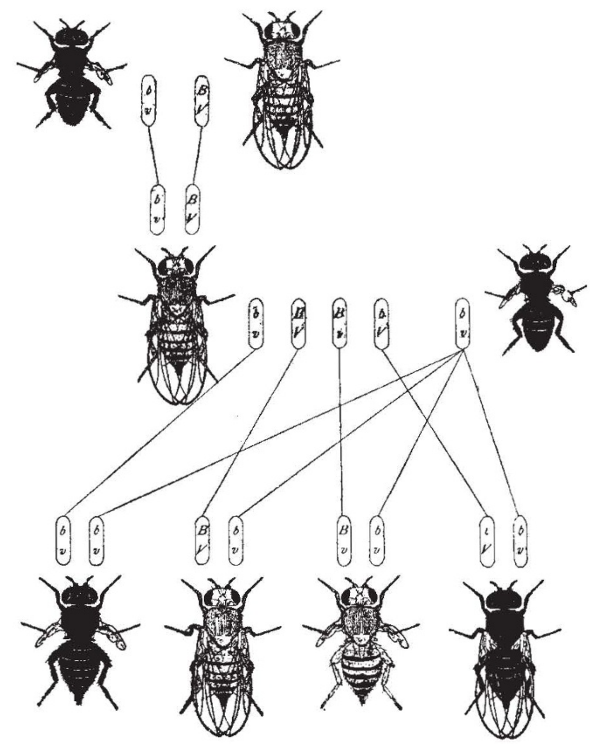

FIG. 13.

that gives 5·5 per cent. of crossing-over with yellow (Fig. 14). If, now, the position of echinus is represented as 5·5 units of distance from yellow, then its " distance " from white must be either $5·5 + 1·5 = 7·0$, if it lies to the " north " of yellow, or else $5·5 - 1·5 = 4·0$ if it lies to the " south." In fact, when the experiment is made, the percentage of crossing-over between white and echinus is found to be 4·0.

There is another sex-linked character, ruby, that gives 7·5 per cent. crossing-over with yellow. If it lies to the north of yellow it must give with echinus $7·5 + 5·5 = 13$; or if to the south of yellow, $7·5 - 5·5 = 2·0$. It is found to give 2 per cent. of crossing-over. Hence, lying south of yellow, it should give with white 6·0, and this is what is found.

Such a method of analysis can be followed step by step until the whole of the sex-chromosome is plotted. This procedure has a twofold significance. First, if a new mutant character is found, its " linkage-group " is first made out ; then its " distance " from any one member of that group is determined. It is then necessary to find its position with respect to another known member of the group (preferably one near by) which determines whether it is north or south of the first member. Once this has been done, the method of inheritance of the new character with all other members of its group can be worked out on paper from the crossing-over data, plotted as distance. In other words, the heredity of this new mutant, with all the other known characters of Drosophila, can be predicted, since, with its normal allelomorph, it will give a 3 : 1 ratio; with any character in another group it will give a 9 : 3 : 3 : 1 ratio; and with other members of its own group it will give a definite result which can be calculated from the "distance" of the plotting.

The second point of significance concerning the plotting of the genes in terms of distances is as follows: the discovered relation of genes, as expressed in distances, is one that holds for points in a line. This means that if the genes in question are represented in space, their relation to each other is that of points in a line. If the line is a chromosome, then the chromosomes are to be thought of as made up of a single line of genes. The reasons for referring the genes to the chromosomes have already been given. The possibility of explaining crossing-over on a chromosome basis will be discussed later.

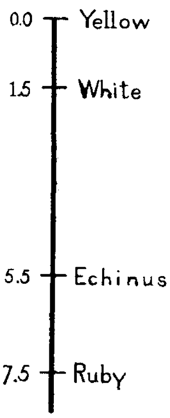

FIG. 14.

There is one situation where, on superficial examination of the data, an apparent disturbance of the linear order may appear, namely, when crossing-over takes place at two levels in the same linked series at the same time (double crossing-over). But by marking intermediate points between the extreme ones all double cross-overs can be detected and the distances corrected for them. When this is done, it at once becomes apparent that the linear order is the correct arrangement of the genes. In fact, far from throwing doubt on the linear order, these cases, where double crossing-over occurs, furnish a strong corroboration of the correctness of the hypothesis.

The use of the word "distance" as an expression for the percentage difference in crossing-over values does, unfortunately, lend itself to misunderstanding, unless one knows just what meaning is attached to the word when used as defined above. An example will make this clear. If crossing-over is more likely to occur in one region of the linear order than in other regions, the plotted "distances" will be relatively too short in comparison with the distances of the remainder of the series. Distance, therefore, must be understood in a relative, not in an absolute, sense. We have been aware of the necessity of this restriction from the beginning of our studies of the linear order of the genes, and have warned others of the danger in numerous publications, but apparently without complete success. It has also been shown that the percentage of crossing-over changes under external (Plough) and internal (Bridges) conditions. As the female gets older, crossing-over becomes less in some cases, hence the "distances" appear to become less. It has also been shown by Sturtevant that genetic factors may exist that affect the crossing-over in certain regions of the linear series, in one case shortening that region to zero, since all crossing-over is suppressed. But the significance of this result, from our present point of view, is that when the shortening factor is removed (by a definite genetic procedure) the original distance of the genes in this region reappears, *and the genes are shown not to have changed their original order*. This reassures us that the linear order stands on a firm basis. A recent attack on the theory of the linear

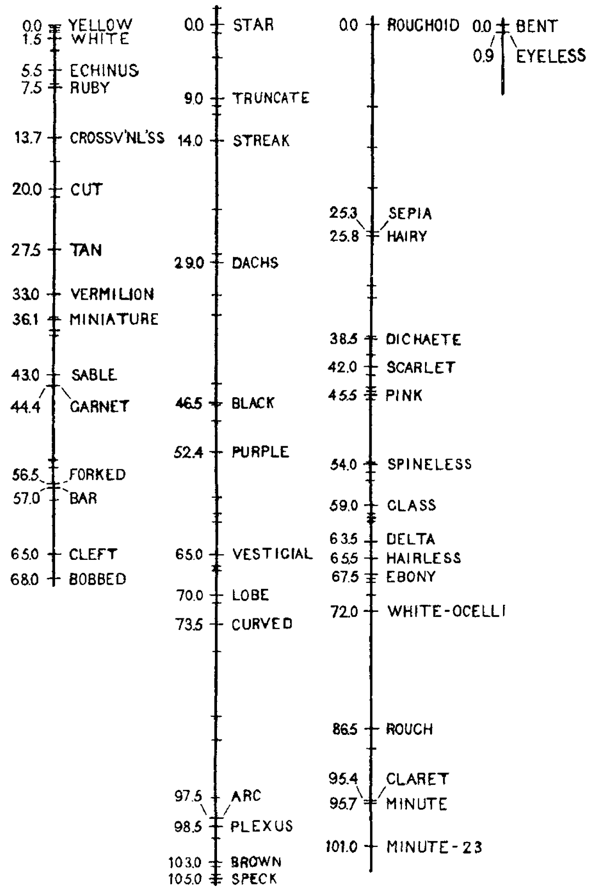

FIG. 15.

order is based on evidence that shows that "through selection" the distances between certain genes changed. The result really has no bearing on the point, because the order of the genes was not shown to have been affected. Moreover, Sturtevant's case, more thoroughly worked out, shows that where even greater changes of distance had taken place the order of the genes had not changed.

The plotting of the linear order of the genes in the four chromosomes of *Drosophila melanogaster* is shown in Fig. 15. The four great groups of linked genes are represented by straight lines with the approximate positions of the genes indicated by short cross-lines. The numbers opposite these cross-lines give the distances from a base chosen as far "north" as possible. The location of some of the genes rests on an immense amount of data; other genes are less accurately placed. Still others, not so well determined, have been omitted from this diagram.

The localisation of the genes has been calculated from numerical data independently of any assumption as to how crossing-over takes place in the animal. Perhaps it might be safer to let the matter rest on the genetic evidence alone in the present uncertain frame of mind of most cytologists concerning the conjugation of the chromosomes at maturation; but there are at least certain facts admitted by a number of cytologists concerning the maturation of eggs and sperm that seem to fall into line with the simple mechanism that the genetic evidence for crossing-over calls for. This evidence may next be considered.

(To be continued.)

Science in Poland.

DURING the past seven years Poland has suffered all the miseries of war. Amid the desolation in which the country was plunged, the votaries of science did their best, until 1919, to uphold the interests of study and education against inimical and contending Governments; since the Polish State was resuscitated they have been engaged in laying the foundation of the work of the future. In 1914 only two Polish universities (Cracow, Lwów) were in existence; in 1922 five large State-endowed universities are actively at work; the University of Warsaw was started in 1915, those of Poznan and Wilno in 1919. Centres of technical teaching and research are springing up; in Warsaw and Lwów important colleges of mechanical and electrical engineering, of applied chemistry, of architecture, etc., are well attended, and in 1919 a High School of Mines was established in Cracow. These institutions are sufficiently equipped with appliances required for practical teaching.

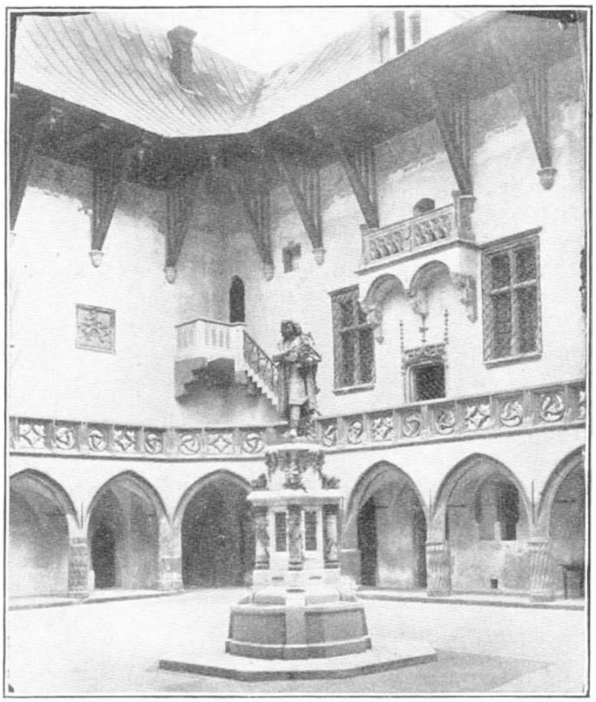

FIG. 1.—Interior Court of the Library of the Jagellonian University, Cracow, with the statue of Copernicus.

Agricultural science also receives a good deal of attention; in addition to faculties or other schools of university rank existing in Cracow, Warsaw, Lwów, and Poznan, a National Institute of Agricultural Research was founded in Pulawy in 1917. This institute is under the direction of Profs. Godlewski and Marchlewski, and shows a remarkable completeness of arrangement. For the study of the mineral resources of Poland, a National Geological Institute was created in 1920 in Warsaw, under Prof. Morozewicz; a branch institution in Cracow, under Dr. Nowak, has for its object the investigation of oil-bearing regions. An Epidemiological Institute, a Central Meteorological Office, and a Natural History Museum have been constituted; but within the brief compass of an article it is impossible to do more than refer simply to the fact of their inauguration.

At the head of Polish educational institutions stands the Jagellonian University of Cracow, founded by Casimir the Great, King of Poland, in 1364. In 1400 the university was restored and enlarged by King Ladislas Jagello, who thus complied with the last wish of his universally honoured and beloved wife, Queen Jadwiga. At the end of the fifteenth century the university was at the height of its influence and fame; there was probably no contemporary school in Europe where mathematics and astronomy were prosecuted with more zeal and success. An undergraduate matriculated in the university in 1491 who was to transmit his name to the remotest posterity. At that time Wojciech Brudzewski (Albertus de Brudzewo) had attained a wide and established reputation as an astronomer, and it was probably by him that young Copernicus was taught to employ his genius.

In the seventeenth and eighteenth centuries the university suffered much from the insecurity of the times, and for many years was on the decline. A new epoch began about 1870; an impulse was given to study, and research, although hampered by financial embarrassments, had greater importance assigned to it than at any previous period. Among the mathematicians of that period are Mertens, Baraniecki, and Zrawski; Rudzki did creditable work in geophysics, especially seismology; Zygmunt Wróblewski and Karol Olszewski, by their activity in the domain of low temperature research, achieved success that shed lustre on the Cracow laboratories; Witkowski, by the pains he took to ensure accuracy, paved the way for much subsequent thermodynamical investigation; Smoluchowski (whose untimely death, in 1917, was a matter of universal regret) accomplished brilliant work, largely influencing progress towards a kinetic theory of matter. Within the precincts of the Jagellonian University, Janczewski, E. Godlewski, Sen., Rostafinski, Raciborski, Rothert, Kulczynski, Prazmowski, Wierzejski, Jentys, Adametz, Majer, Kopernicki, and Talke-Hryncewicz — names well known to students of