

THE “FLY ROOM”

When Daniel Coit Gilman became the first president of Johns Hopkins University in 1875, he assembled a remarkable group of scholars to supervise the graduate work there. Among these were two biologists: W. K. Brooks, who had studied with L. Agassiz, and H. Newell Martin, a student of Michael Foster and T. H. Huxley. These two trained a whole generation of outstanding zoologists; among them Edmund Beecher Wilson and Thomas Hunt Morgan were of especial importance in the history of genetics.

E. B. Wilson (1856–1939) took his Ph.D. at Johns Hopkins in 1881, with a thesis on the embryology of the colonial coelenterate *Renilla*. He then went to Europe, where he worked at Cambridge, at Leipzig under Leuckart, and at Naples. The Naples station, where he returned several times later, greatly influenced him and led to lasting friendships with such men as Dohrn, Herbst, Driesch, and especially Boveri. In 1885 he became the first professor of biology at the newly opened college at Bryn Mawr. In 1891 he became professor of zoology at Columbia University and remained there for the rest of his life. He also spent many summers working at the Marine Biological Laboratory at Woods Hole, Massachusetts. Wilson’s early work was largely in embryology, at first descriptive, and later of an experimental nature; his interest here was chiefly in the analysis of the gradual limitation of the potentialities of the cells of the developing embryo and the extent to which “formative stuffs” were involved in development. The first edition of his great *The Cell in Development and Inheritance* appeared in 1896, the second in 1900, and the third (really a new, much larger, and wholly rewritten book) in 1925. This was the standard work for many years and exerted a very great influence on biology. Wilson’s own studies on chromosomes began about 1905, with the work on the sex chromosomes referred to in Chapter 6, and led to a series of detailed accounts that are models of accuracy and clarity of expression.

The career of T. H. Morgan (1866–1945) resembled that of Wilson in many respects. He took his Ph.D. at Johns Hopkins in 1890 and then went to Europe, where he was also much influenced by a stay at Naples, and made lasting friendships, especially with Dohrn and Driesch. In 1891 he succeeded Wilson as professor at Bryn Mawr and, in 1904, joined him at Columbia. Like Wilson, he wrote a thesis on embryology, and continued in this field, first with descriptive work, and later with the experimental approach. He also studied the chromosomes in connection with sex determination. At Woods Hole he and Wilson were neighbors, and they and their families were very close friends, both at Woods Hole and in New York.

For all that, the two men were very different. As R. G. Harrison (who was a close friend of both) has expressed it:

. . . Wilhelm Ostwald, in his interesting book on great men of science, classified them, according to their talents, as romantics and classics. . . . To the romantic, ideas come thick and fast; they must find quick expression. His first care is to get a problem off his hands to make room for the next. The classic is more concerned with the perfection of his product, with setting his ideas in the proper relation to each other and to the main body of science. His impulse is to work over his subject so exhaustively and perfectly that no contemporary is able to improve upon it. . . . It is the romantic that revolutionizes, while the classic builds from the ground up.

Wilson is a striking example of the classic, and it is interesting to note that for many years his nearest colleague and closest friend was an equally distinguished romantic.

In 1909, the only time during his twenty-four years at Columbia, Morgan gave the opening lectures in the undergraduate course in beginning zoology. It so happened that C. B. Bridges and I were both in the class. While genetics was not mentioned, we were both attracted to Morgan and were fortunate enough, though both still undergraduates, to be given desks in his laboratory the following year (1910–1911). The possibilities of the genetic study of *Drosophila* were then just beginning to be apparent; we were at the right place at the right time. The laboratory where we three raised *Drosophila* for the next seventeen years was familiarly known as “The Fly Room.” It was a rather small room (16 by 23 feet), with eight desks crowded into it. Besides the three of us, others were always working there—a steady stream of American and foreign students, doctoral and postdoctoral. One of the most important of these was H. J. Muller, who graduated from Columbia in 1910. He spent the

winter of 1911–1912 as a graduate student of physiology at Cornell Medical School and then came back to take a very active part in the *Drosophila* work.

There was an atmosphere of excitement in the laboratory, and a great deal of discussion and argument about each new result as the work rapidly developed.

In 1909 Castle published diagrams to show the interrelations of genes affecting the color of rabbits. It seems possible now that these diagrams were intended to represent developmental interactions, but they were taken (at Columbia) as an attempt to show the spatial relations in the nucleus. In the latter part of 1911, in conversation with Morgan about this attempt—which we agreed had nothing in its favor—I suddenly realized that the variations in strength of linkage, already attributed by Morgan to differences in the spatial separation of the genes, offered the possibility of determining sequences in the linear dimension of a chromosome. I went home and spent most of the night (to the neglect of my undergraduate homework) in producing the first chromosome map, which included the sex-linked genes *y*, *w*, *v*, *m*, and *r*, in the order and approximately the relative spacing that they still appear on the standard maps (Sturtevant, 1913).

The finding of autosomal linkage in *Drosophila* has been described by Morgan and Bridges (1919) and by Bridges and Morgan (1923) in their accounts of the mutant genes of the second and third chromosomes. The first test of two autosomal genes was made by Sturtevant (February 1912) and showed that black and pink were independent. It was concluded that they were probably in different chromosomes—though this was only a tentative conclusion, since it was known that linkage could approach independent segregation in the frequency of recombination. In March, 1912, Bridges found that the newly discovered mutant curved (wing-shape) when crossed to black, gave no double-mutant types in F_2 , so it was clear that autosomal linkage could occur. It was evident that by this time there were more autosomal mutants than there were chromosomes, so Bridges and I began a systematic search by testing the available types against each other. These tests quickly yielded results, but about a week before they did, the second case was discovered by C. J. Lynch, who had made a cross of black to vestigial for another purpose and noted the absence of black vestigial in F_2 (Morgan and Lynch, 1912). This was the first published case of autosomal linkage in *Drosophila*; it was soon followed by the discovery (Morgan, 1912) that there is no crossing over in the male for these genes. This relation was soon shown to be general for both the second and the third chromosomes. By the

middle of July, 1912, the tests carried out by Bridges and Sturtevant had shown that this linkage group (the "second") included not only black, curved, and vestigial, but five additional mutant types. In the same month, we also found two additional types linked to pink, thus beginning the study of the third linkage group (Sturtevant, 1913). The fourth and last linkage group was found by Muller in 1914.

Stevens (1908) described the chromosomes of the female of *Drosophila melanogaster* (under the name *D. ampelophila*) as they are now known, but she found the male difficult to study, and interpreted her figures as meaning that there was a rather small X attached to an autosome, and no Y. This interpretation was followed in early genetic literature on the species, until the work of Bridges (at first on XXY females in 1914), and then of Metz (at first on other species of the genus, also in 1914) established the relations now known. Bridges insisted from the first, and rightly, that the Y is J shaped and longer than the rod-shaped X; but the rest of the group was at first unwilling to accept this, since in other animals (even in other species of *Drosophila*) the Y was known to be absent, smaller than the X or equal to it, but never larger. A corollary of the earlier interpretation was that there were four, rather than three, pairs of autosomes, with one of them having some sort of relation to the X.

Bridges' cytological work grew out of his studies of nondisjunction. In the first paper on the sex-linkage of white eyes, Morgan reported a few white sons from the original mutant male, which he supposed represented further mutation; there can be no doubt that they were due to nondisjunction.

Further examples kept appearing, and in 1913 Bridges published an extensive genetic analysis of the phenomenon, giving it the name "nondisjunction." Further studies led to no satisfactory causal interpretation until he looked at the chromosomes and saw that females that gave exceptional offspring were XXY in composition (1914). As Bridges understood, this was really a proof of the chromosome theory and made it inconceivable that the relation between genes and chromosomes was merely some kind of accidental parallelism—especially after the publication of his detailed account in 1916, as the first paper in volume 1 of the newly founded journal *Genetics*.

A further consequence of the cytological work of Bridges and of Metz was that it became clear that *D. melanogaster* had three pairs of autosomes—two large and one small—corresponding to the three autosomal linkage groups, of which two were also large and one was small.

By 1915 the work with *Drosophila* had progressed to the point where the group at Columbia was ready to try to interpret the whole field of

Mendelism in terms of the chromosome theory. The resulting book, *The Mechanism of Mendelian Heredity* (Morgan, Sturtevant, Muller, and Bridges, 1915), is a milestone in the history of the subject.

There had been much reluctance among geneticists to accept the chromosome interpretation. Johannsen, for example, in the 1913 edition of his book, referred to it as "a piece of morphological dialectic"; and Bateson, in a review of *Mechanism* (1916), wrote

. . . it is inconceivable that particles of chromatin or of any other substance, however complex, can possess those powers which must be assigned to our factors [i.e., genes]. . . . The supposition that particles of chromatin, indistinguishable from each other and indeed almost homogeneous under any known test, can by their material nature confer all the properties of life surpasses the range of even the most convinced materialism.

It should be added that by his third edition (1926) Johannsen accepted the chromosome interpretation, and that Bateson thus closed the review (from which the quotation just cited is taken): ". . . not even the most skeptical of readers can go through the *Drosophila* work unmoved by a sense of admiration for the zeal and penetration with which it has been conducted, and for the great extension of genetic knowledge to which it has led—greater far than has been made in any one line of work since Mendel's own experiments."

Not all critics were as generous, nor did they always receive soft answers. In short, there were a good many polemical papers; and there surely would have been more if the work had not had the whole-hearted support of Wilson, who had the respect and admiration of all zoologists, making him an invaluable ally.

With the publication of the *Mechanism* and of Bridges' 1916 paper, this part of the story closes. There was still much exciting and fundamental work to be done with *Drosophila*, and the Columbia laboratory was still the center for such work, but it had become a question of how the chromosome mechanism worked, not of whether it could be demonstrated to be the true mechanism.

There was a give-and-take atmosphere in the fly room. As each new result or new idea came along, it was discussed freely by the group. The published accounts do not always indicate the sources of ideas. It was often not only impossible to say, but was felt to be unimportant, who first had an idea.* A few examples come to mind. The original chromosome

* There are, in the later literature, some examples of a concern about priority in the development of ideas in the early period, but at the time such a concern never inhibited free and open discussion.

map made use of a value represented by the number of recombinations divided by the number of parental types as a measure of distance; it was Muller who suggested the simpler and more convenient percentage that the recombinants formed of the whole population. The idea that "cross-over reducers" might be due to inversions of sections was first suggested by Morgan, and this does not appear in my published accounts of the hypothesis. I first suggested to Muller that lethals might be used to give an objective measure of the frequency of mutation. These are isolated examples, but they represent what was going on all the time. I think we came out somewhere near even in this give-and-take, and it certainly accelerated the work.