Perspectives

Anecdotal, Historical and Critical Commentaries on Genetics

Edited by James F. Crow and William F. Dove

A Diamond Anniversary: The First Chromosome Map

SEVENTY-FIVE years ago this month A. H. STURTEVANT (1913) published the first linkage map. It involved five *X*-chromosomal loci in *Drosophila ampelophila*, now called *Drosophila melanogaster*. This was early genetics at its most exquisite. From seemingly irrelevant counts of the number of different kinds of offspring from various matings, and with no idea of the nature of the genes, STURTEVANT could nevertheless infer their sequence and relative distances apart on the chromosome.

These quiet beginnings stand in abrupt contrast to the current hubbub over the human linkage map and the proper definition of a map (ROBERTS 1987). With its rival factions and the glare of publicity, the mapping race is almost a genetic Olympics. One other contrast: the 1913 Drosophila paper had one author, the 1987 paper on the human map has 33 (DONIS-KELLER *et al.* 1987).

STURTEVANT was still an undergraduate student at Columbia University when he had the key idea. In his words (1965):

> In the latter part of 1911, in conversation with MORGAN . . ., 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.

The first publication in 1913 was a masterpiece of clarity. Here is a sample:

> By determining the distances . . . between A and B and between B and C, one should be able to predict AC. For, if proportion of cross-overs really represents distance, AC must be, approximately, either AB plus BC or AB minus BC.

Figure 1 shows STURTEVANT's original map, together with the current distances as given by LINDSLEY and GRELL (1968). Considering the primitive laboratory conditions and large distances between markers, the agreement is remarkable. This pathbreaking paper and 32 more of STURTEVANT's most important contributions have been reprinted (STURTEVANT 1961).

STURTEVANT and C. B. BRIDGES were both students in MORGAN's course in elementary zoology at Columbia in 1909. They were both given places to work in the "fly room" and immediately became members of the research team. This room was only 16 by 23 feet and, somehow, eight desks were crowded into it. The room also included fly food preparation, with an always-present stalk of bananas. It soon became filled with additional geneticists, notably H. J. MULLER who joined the group in 1912. Included in this close-packed area was PHOEBE REED, who washed glassware, prepared media, and later became MRS. STURTEVANT.

Each of the researchers made important contributions, of both data and ideas, to the rapid mapping of the Drosophila genome. MULLER introduced the ideas of coincidence and interference. BRIDGES concerned himself with the technology, working out standardized culture conditions and mating systems designed to minimize viability complications. Curiously, the MORGAN school made no use of mathematical mapping functions, which would have been very useful in the early days when distances between known genes were large. Such functions were developed in England (HALDANE 1919) but did not make it across the Atlantic for many years.

The free exchange of data, the continuous discussion of each other's results and the scientific excellence of the group created a situation in which new results came at an enormous rate. Within a few years the rules of transmission genetics and the mechanical basis of sex-linked inheritance, crossing over, nondis-

b	**c**	**p**	**r**	**m**
0.0	1.0	30.7	33.7	57.6
0.0	1.5	33.0	36.1	54.5
y	**w**	**v**	**m**	**r**

FIGURE 1.—STURTEVANT's original linkage map of the Drosophila *X* chromosome, with his placements and the symbols used at the time (*upper*) compared to the current locations and symbols (*lower*). The loci are *yellow* body, *white* eyes, *vermilion* eyes, *miniature* wings and *rudimentary* wings.

junction and chromosome aberrations were worked out.

There was always complete openness, with no ideas or data held back. MULLER suggested measuring distance as percent recombinants; MORGAN first suggested that "crossover reducers" might be inversions, a point that was confirmed by STURTEVANT when he found that the gene order in *Drosophila simulans* differed from that in *D. melanogaster*. STURTEVANT suggested to MULLER that lethals might be an objective way to measure mutation rates. However, it is very difficult to trace the origins of many of the ideas, since all were discussed freely from the beginning.

STURTEVANT's work did not stop with chromosome mapping. He did a key early experiment in multigeneration selection. His finding that the *vermilion* eye-color gene was nonautonomous in gynandromorphs paved the way for the studies by BEADLE and EPHRUSSI on Drosophila eye pigments. These in turn led to the Neurospora studies of BEADLE and TATUM and the beginnings of modern biochemical genetics. STURTEVANT's analysis of cell lineage by using mosaic flies was the direct antecedent of fate mapping as developed by GARCIA-BELLIDO and MERRIAM (1969); in fact, their analysis was based on 379 drawings that STURTEVANT had prepared from a high-nondisjunction strain of *D. simulans*. BENZER later used fate-mapping to study neurological mutants. Recognizing the origins of the idea, he coined the term "sturt" to measure abstract embryological distances. STURTEVANT's discovery of the sex-transforming mutant *tra* is a forerunner of recent work by BAKER, CLINE and others on sex differentiation. He inspired a school of chromosome mechanics carried on by COOPER, NOVITSKI, LINDSLEY and SANDLER. In a totally different area, STURTEVANT was the first to measure the frequency of concealed lethals in natural populations and to note that their frequency was less than expected; he suggested what has turned out to be the correct mechanism, that "recessive" lethals are not completely recessive.

Although Drosophila was his major interest, STURTEVANT also studied the genetics of other organisms. He started out with an interest in horses and his first paper was on color inheritance in the American harness horse. He showed that the puzzling inheritance of the Himalayan coat color in rabbits could easily be explained by multiple alleles. He demonstrated that the strange inheritance of direction of coiling in snails fell into place when one assumed that the direction was determined by the genotype of the mother rather than of the individual itself. He had a long-time hobby of iris breeding and some of his products still adorn the Caltech campus.

STURTEVANT was also deeply interested in insect taxonomy and biogeography and he knew the native plants. He was an excellent taxonomist and wrote monographs and original descriptions of a number of insects. Of all the MORGAN group, he was the one with the greatest interest in *D. melanogaster* as an organism and in its relationship to other species. He was also interested in the history of genetics and his book on the subject has become a classic (STURTEVANT 1965).

No discussion of STURTEVANT is complete without a discussion of his contributions to others. He was most generous with his time and usually had useful, often key suggestions about experiments and their interpretation. He read widely, spending a regular part of each day in the library, and it showed. Until shortly before his death, he kept up with the ever-growing literature of genetics. This knowledge was of enormous value to his colleagues.

The relationship between STURTEVANT and DOBZHANSKY is a matter of endless fascination for historians of genetics. According to DOBZHANSKY, STURTEVANT was an early hero and saved his lifed by making it possible for DOBZHANSKY to stay in the United States rather than having to return to Russia where he was in dangerous disrepute. The two enjoyed an active collaboration and were pioneers in the genetic study of natural populations; their joint paper on inferrring phylogenetic relationships from overlapping inversions is a classic. Together they started *Drosophila pseudoobscura* on its way to fame. Then something went wrong. One possibility is that STURTEVANT, whose careful work was always absolutely reliable, became disillusioned with the work of DOBZHANSKY, who in his enthusiasm to get things done quickly was less careful. In any case, there was a schism and STURTEVANT, who had outlined a whole program of research in evolutionary genetics of *D. pseudoobscura* (PROVINE 1981), ceased to work on this species, leaving the field to be developed by DOBZHANSKY.

STURTEVANT was an interesting conversationalist and enjoyed telling stories from the early days of Drosophila genetics. He especially liked to relate the "omelet incident" in the fly lab at Columbia. He and his associates were playing bridge on a Saturday afternoon when a package arrived addressed to E. B. WILSON. They found that it contained an ostrich egg and, thinking that WILSON wanted the embryo, removed this and fixed it. Then, what to do with the rest of the egg? The obvious answer was to make an omelet, which they did; it provided an enjoyable meal. Soon after, WILSON appeared asking if he had received a package. It turned out that WILSON wanted not just the embryo, but the whole egg to use as an illustration of the largest single cell. He was not pleased. A possible rift between the MORGAN and WILSON groups at Columbia was averted by the timely intervention of an ostrich at the Bronx Zoo, which produced an egg at the opportune moment.

STURTEVANT enjoyed talking about his scientific friends. Knowing this, I once asked him if he could provide me with some anecdotes about my crusty and earthy major professor, J. T. PATTERSON, that could

be used in dedicating the new Patterson Building at the University of Texas. He replied that he knew dozens of anecdotes by and about PATTERSON, none of which was suitable for such an occasion.

STURTEVANT did more than his share for GENETICS. In addition to serving on its Editorial Board, he reviewed many manuscripts and was especially valuable when decisions were difficult. On one occasion he was sent two manuscripts to review, one by a young cytogeneticist and one by DOBZHANSKY. His reply went somewhat as follows (I am quoting from memory): "The first paper is not quite up to GENETICS standards but is a good effort by a young investigator who should be encouraged. I say, reject with regrets. The DOBZHANSKY paper is not his best but I suppose has to be published. I say, accept with regrets."

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