This apparatus for making tests on noise gives us a constant pitch of tuning fork accuracy; there is a complete range of intensity variation possible; it is mechanically simple to operate with only loose tubes and battery charge to watch; it will generate and amplify without variation for twenty-four hours at a time; it can be built in portable units; and through the use of the audibility meter it almost automatically compensates for variations in the tonal intensity, due to being placed in a sound-reverberant or in a sound-absorbent room.

DONALD M. CRAWFORD
PSYCHOLOGICAL LABORATORY,
COLGATE UNIVERSITY

SPECIAL ARTICLES

MUTATION, CHROMOSOME NON-DISJUNCTION AND THE GENE[1]

MODERN genetics distinguishes several types of mutations; gene mutation, where only one gene is affected; deficiencies, where a whole series of genes may be dropped out; chromosomal mutations, where the effect is due to irregularities in chromosome behavior or number as in non-disjunction, triploid or sex intergrade formation, etc. For some years flies of unique appearance have sporadically appeared in certain of my experiments, which under the older terminology would be considered mutations, although they appear best considered under the more limited rubric as due to chromosome non-disjunctions and not mutation in the gene sense. The variable nature in the time of appearance of these abnormal forms makes them resemble fluctuating mutations which are of so much interest in connection with the mechanism of mutation. The abnormal flies represent morphological variates extending all the way from male on the one hand to female on the other. Cytological analysis of the chromosomes shows that the sex intergrade forms are the result of a multiplication of the chromosome groups in the mother fly to form eggs with double the ordinary number of chromosomes. The sex intergrades consequently carry three sets of autosomal chromosomes and two sex chromosomes. Another class of females, showing increased size and larger eye pattern, have three full sets of chromosomes or are triploids. Incidentally, therefore, these results furnish independent confirmation of Bridges' hypothesis that sex is determined by a balance of the sex chromosomes and autosomes. In this antagonism of forces the sex chromosomes have a female tendency, while the autosomes have the male tendency. Extensive pathological changes are found in these forms; instead of all male parts going together or all female parts together, all manner of combinations of the two are witnessed. In fact, the study of the unbalanced conditions shows that external appearance is not always a criterion of internal structure, since female-appearing sex intergrades may have testes and male-appearing intersexes may have ovaries.

The frequency with which these mutant forms appear within this stock is many times that in normal stocks. Careful examination of a normal stock of 15,785 flies showed but one triploid mutant and no sex intergrades. On the other hand, examination of 1,775 flies from normal appearing parents in the sporadically mutating stock showed thirty-four sex intergrades and triploids, or a rate of one in fifty-two flies, three hundred times as frequent as in the normal stock. These two sets of flies were grown in the same bottles under as nearly the same conditions as possible. The classification is believed to be accurate, as many of each class have been bred to test genetically the accuracy of the separation, with results which have thus far checked perfectly. Another stock made by outcross and extraction showed in 1,173 flies thirty-seven sex intergrades and triploids, or a rate of one to thirty-one—500 times the normal rate. Besides these exceptional classes two others appear. The first is the familiar exception to sex linkage due to non-disjunction of the sex chromosomes. These appear in large numbers. The second mutant involves the vigor of the fly, the bristles, the eyes and fertility and has some of the characteristics of a dominant.

Genetic analysis designed to determine the causative agent behind this series of phenomena shows that a third chromosome recessive factor controls these events. This factor is inactive in the male, as males homozygous for the factor never produce exceptions. In the homozygous females the exceptions freely occur. With the single dose, heterozygous, or when this factor is absent these mutant flies rarely appear. This factor for mutant production is associated with and probably identical with a factor which causes practically complete linkage or lack of separation of any of the factors in any chromosome in the female. It is evident from these facts that the chromosomes of the male and female Drosophila pass through phases which must be divergent in at least two particulars, chromosomal linkage and disjunction. That one factor should be capable of throwing the whole mechanism of mitosis out of gear, even to altering the behavior of the chromosomes in which it is not located, is an extremely interesting fact. The action of this gene finds expression only in the female's progeny, making the case look like one of maternal inheri-

[1] From the Department of Animal Pathology of the Rockefeller Institute for Medical Research, Princeton, N. J.

tance when, in truth, the causative factor is transmitted by both sexes and under strict Mendelian rules. The location of the factor within the chromosome is of interest, as the results show it to be at or near the point of this V-shaped chromosome where presumably the spindle fiber attachment takes place. This fact may be significant in view of the evidence accumulating to show that the spindle fiber attachment is frequently associated with abnormalities in chromosome behavior. The frequency of occurrence of these mutant forms points to their random distribution within any female's progeny and, therefore, that the non-disjunction of the chromosomes occurs in the last oogonial divisions or later. The non-disjunction generally involves both the paternal and maternal sex chromosomes and not, as might be the case, only paternal or maternal chromosomes.

JOHN W. GOWEN

REGULATING THE STORAGE OF VITAMIN A IN ANIMALS THAT ARE TO BE USED FOR THE DETERMINATION OF THIS VITAMIN

THE following observations and considerations led to a study of the problem of the storage of vitamin A in rats reared under carefully controlled conditions:

(1) In a previous study of this problem by Steenbock, Sell and Nelson,[1] the authors were cognizant of the possible influence of the consumption of the stock diet by the young on the storage of vitamin A.

(2) It is extremely difficult to have a uniform supply of A in any stock diet. The instability of the vitamin and its consequent variation in natural foods, particularly foods in such a state of comminution as to prevent selection from the diet, is one of the problems to be dealt with.

(3) Keeping animals on a diet which is low enough in vitamin A to insure a low storage in the young may interfere with satisfactory reproduction if the level becomes just a little too low.

(4) Some data obtained in studies in this laboratory on a prophylactic technique of vitamin A determination in which the rats were given a single or limited number of feedings of vitamin-containing material were difficult to interpret because of the variations in the time of onset of symptoms of vitamin A deficiency.

(5) If mother rats are kept on a diet which insures a very generous supply of A, so that the milk at all times contains a maximum amount of this vitamin and the young receive no other vitamin A than that which is contained in the mother's milk before they are put on a vitamin A free diet, will such young be suitable for vitamin A studies?

Information on the storage of vitamin A in young rats was obtained under the following conditions: Stock rats were bred when kept on a diet that included a generous supply of cod liver oil known to be very potent in vitamin A. Pregnant females were segregated. Litters of six animals were used, and the number of rats in a litter was reduced when necessary. Mothers were put on an A-free diet, some the day the young were born and others when the young were five, ten, fifteen, sixteen, seventeen, eighteen, nineteen and twenty days old. When the young had attained a weight of from forty to forty-five grams they were weaned and put on the A-free diet. If the mother is put on the A-free diet when the young are sixteen to eighteen days of age and weigh not less than twenty-seven or more than thirty grams, and the young are weaned when they weigh from forty to forty-five grams, the onset of symptoms of vitamin A deficiency in the young seems to be independent of the amount of vitamin A given the mother during the entire period of lactation, provided a certain minimum level is not reached. On such a regimen, for the past six months the animals in this laboratory have shown definite symptoms of vitamin A starvation between the fifth and sixth week after weaning. Ophthalmia from vitamin A deficiency seems to occur with the greatest degree of regularity in rapidly growing animals, and our experience indicates that animals do not grow rapidly if the mother is put on the A-free diet before the young are fifteen days old. It is possible that this retardation in the growth of rats can be eliminated by adjusting the diet of the mother, but for the results desired this seems to be unnecessary. Animals that weigh much more than thirty grams will eat the stock diet. All rats which were put on the A-free diet at the age of nineteen days or more showed a distinct delay in the onset of ophthalmia as compared with those which were put on the A-free diet before that age.

It seems very probable that by following the essentials of the technique outlined herein with rats reared in any laboratory the storage of vitamin A will be comparatively uniform. There is the added advantage of maintaining the stock animals on a diet which is known to be adequate in every respect. There has been no indication that the time the females are kept on the A-free diet (from five to eight days) is long enough to deplete her reserves of A to the extent that it becomes apparent.

E. M. NELSON

BUREAU OF CHEMISTRY AND SOILS,
U. S. DEPARTMENT OF AGRICULTURE

[1] Steenbock, H., Sell, M. T., and Nelson, E. M. *J. Biol. Chem.*, Vol. 56, p. 327. 1923.