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Theoretical Genetics - Paper Presented at the Fifty-Fifth Annual Meeting

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THEORETICAL GENETICS

E. W. TIMM

The first task of genetics was to determine the laws which govern the transmission of characters from parent to offspring and to locate the material basis for this regular behavior. The task was quickly accomplished so that 20 years ago the gene-chromosome theory of heredity was well established; it has since been the ABC of genetics and provides the framework upon which more recent work rests. The substance of the theory, as you will recall, is that the characters observed in an adult individual are determined by genes which are arranged in a linear order in the chromosomes.

It is true that the environment influences the developmental process but it cannot carry the individual beyond the limits set by the gene constellation, commonly referred to as the genotype, so that, in general, the end result of the developmental process, i. e. the appearance of the individual or its phenotype, is determined by the interaction of the genotype with the environment.

To anticipate what will be developed later, we may translate this into other words. The chromosomes consist of a linear array of biochemically differentiated units, each with its own catalytic effect on one or more developmental processes. These highly integrated processes have undergone selection since the origin of life; more complex processes have evolved, so that today we have the amazing array of diverse plant and animal forms which are so beautifully adapted to their several ecological stations. This diversity of form is one of the most striking features of nature, but scarcely less striking is the discontinuity of the diversity. All living individuals do not form a single continuous frequency distribution but rather are grouped into discrete frequency distributions which are commensurate with the number of the lowest taxonomic units recognized. This demonstrates that all possible permutations and combinations of the biochemical units within the chromosomes are not equally harmonious; selection has preserved only the relatively more harmonious ones.

The most obvious deduction from the gene-chromosome theory is that there should be a one-to-one correspondence between the cytological behavior of the gene-bearing chromosomes and the mode of inheritance. Abundant evidence on the correctness of this deduction provides a mass of incontrovertible evidence as to the correctness of the theory. For example, when a segment of

one chromosome becomes transposed to a non-homologous chromosome the genes in the transposed section are found by breeding experiments to be linked with genes in the non-homologous chromosome; when a section of a chromosome becomes inverted with respect to its two ends the linear order of the genes is likewise found to be inverted.

A recent technique developed by Painter (9) has greatly facilitated studies of this kind. The giant chromosomes in the salivary glands of Diptera larvae had been known as a cytological curiosity for several decades, but it remained for Painter to point out their usefulness for genetic studies. The salivary gland chromosomes are extended to about 100 times their length at meiotic metaphase and show characteristic banding patterns which can be readily identified by the experienced technician; and furthermore, the homologous chromosomes are paired in this somatic tissue, even more completely than at the prophase of the reduction division. However, the pairing is very specific, so that only homologous sections pair and thus chromosome abnormalities may be identified by interruptions in the pairing sequence. By correlating chromosome aberrations with the behavior of the genes involved it has been possible to assign the genes to definite loci within the chromosomes.

A striking use of the salivary gland technique was made by Sturtevant and Dobzhansky (4, 11) in elucidating the phylogenetic relationship of various naturally occurring populations of *Drosophila pseudoobscura*.

If in a strain having a gene arrangement (1) ABCDEFGHI the segment BCDE becomes inverted we will have the arrangement (2) AEDCBFGHI; if now the segment DCBFGH becomes inverted the arrangement becomes (3) AHGFBCDI. These two inversions are overlapping, one inversion has its two limits respectively inside and outside the limits of the other. Overlapping inversions may be recognized by the pairing configuration in the salivary gland chromosomes. If the above three arrangements are found in different strains it is possible to interpret the relationship in three ways.

1. (1) → (2) → (3)
 2. (3) → (2) → (1)
 3. (2) → (3)
- ↘
(1)

The changes (3) → (1) or (1) → (3), however, may be ruled

out since they would involve four simultaneous breaks and a resulting reunion having a very low probability of occurring.

Sturtevant and Dobzhansky examined the gene arrangement in specimens of *D. pseudoobscura* collected throughout the geographical distribution area of the species. Seventeen different gene sequences were found in the third chromosome, all of which could be derived from others by inversions. This made possible the construction of the following phylogenetic chart based on the gene arrangements in the third chromosome. (Fig. 1).

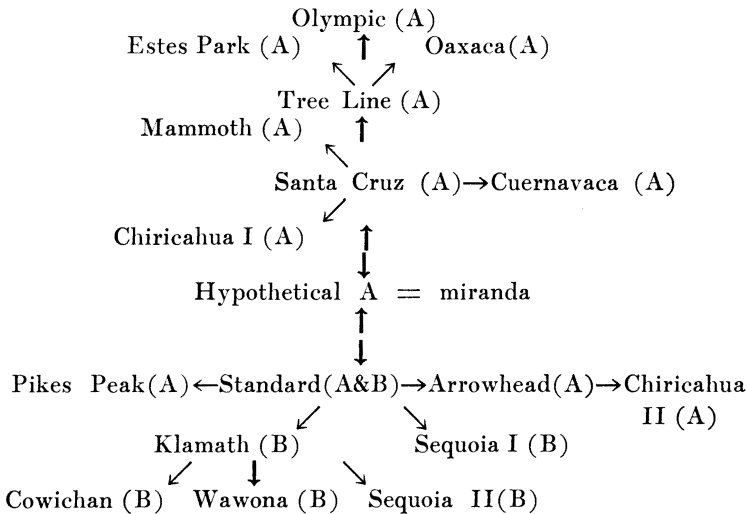


Fig. 1. A phylogenetic chart of the gene arrangements encountered in the third chromosome of race A and race B of *Drosophila pseudoobscura*. (After Dobzhansky)

The two configurations corresponding to Santa Cruz (A) and Tree Line (A), first postulated as theoretically necessary configurations in the early stages of the investigation, were only found later when more flies were examined. One configuration, Hypothetical A, has not been found in *D. pseudoobscura* but obtains in the related species *D. miranda*, a situation which is in itself suggestive. The species, *D. pseudoobscura*, is separated into Race A and Race B, morphologically indistinguishable, but giving sterile hybrid males. Eleven of the gene sequences were found only in race A, five only in race B, while one, Standard (A & B), occurs in both races; hence it is probable that this is the ancestral configuration.

The word "probable" should be underscored for while this technique gives the relationship of the various configurations it cannot identify the parent configuration.

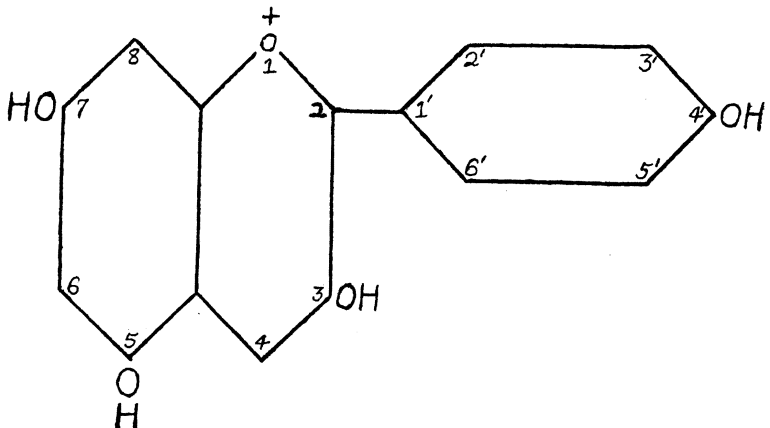
The significance of this work should be emphasized. It is an accurate method and the only method thus far devised for determining the sequential relationships of chromosomal diversification within a species.

Let us return to the consideration of the gene.

As a biochemical unit the gene takes part in three types of chemical reactions. Firstly, there is the reduplication of an exact model of the gene between successive cell divisions; secondly the gene has a catalytic effect on the chemical reactions within the cells, the sum of which we see as development; and lastly, the gene may undergo a change in its characteristic structure, it may partake as a reactant in a reaction which gives as its product the mutated gene.

With respect to reproduction of the gene little is known except that the gene apparently acts as an autocatalyst but whether the gene grows by accretion and then splits or whether the new model is deposited alongside the existing gene remains a riddle.

The problem of gene action in development is a question of bridging the gap between the genes and the characters of the individual. Attempts to close this gap may be made by tracing visible characters back to the qualitative and quantitative nature of chemical substances producing them. One of the best examples of the latter type of approach is found in the recent work of Scott-Moncrieff, Lawrence and Price (6, 10) on the anthocyanin pigments responsible for the red to blue flower colors. The basic pattern of the anthocyanin molecule is shown:



A sugar residue is always attached at 3.

Genes are known which alter the position in the red-blue scale of flower color by altering the constitution of this basic pattern in the following ways:

1. Oxidation at 3', i. e. in effect, substituting an hydroxyl group for the hydrogen atom at 3'.
2. Oxidation at 5' when 3' is already oxidized.
3. Oxidation at both 3' and 5'.
4. Methylation of the hydroxyl at 3'.
5. Methylation at both 3' and 5'.
6. Substitution of a second sugar residue at 5.

Oxidation and substitution of an additional sugar residue increase blueness, while methylation decreases blueness. The pH of the cell sap is also under genetic control and since most anthocyanins act as indicators, a higher pH increases the blueness. Lastly the color may be affected by the presence of copigments, flavones and tannins, which, while ranging from colorless through ivory to yellow when present alone, alter the color of the anthocyanins when the two are present together. Genes control the presence or absence of the copigments.

The remaining gap in the developmental process here involved requires that the genes act as enzymes controlling the synthesis of the various anthocyanin patterns or that they act as super-enzymes, producing enzymes, which in turn control the anthocyanin synthesis. No principles foreign to chemistry need be invoked. This example of a direct chemical analysis of gene action is presumably characteristic of gene action in general; genes produce their effects by controlling the nature and rate of cellular reactions. However, it must be emphasized that in no case have all the intermediate stages been elucidated. Here remains a wide field for future research.

The exactness of any definition of gene mutation is not entirely satisfying. Certain chromosomal aberrations, as judged by their effect on the phenotype, may be erroneously classed as gene mutations, as was the case with DeVries' classical observations on *Oenothera*. In fact it has recently been emphasized that gene mutations actually comprise the residue after all changes for which a mechanical basis has been proven are eliminated. Furthermore, some of the residue may consist of small chromosomal rearrangements which are below the limit of visibility and thus escape detection. Perhaps the advent of the electron microscope will aid in solving this problem by lowering the limit of visibility. Considerations along these lines have led Goldschmidt (5) to sug-

gest that the concept of the gene as a unit must be discarded and that we must focus our attention on the whole chromosome or chromosome complex. This radical change in outlook seems a bit hasty. Even Goldschmidt's suggestion must presuppose linear differentiation of the chromosome; if the units are identical it is hard to conceive of any change being effected by shifting their relative positions. This linear differentiation is what we mean by genes. However, admitting this difficulty, let us examine the properties of the mutation process.

Mutations occur spontaneously at rates which differ widely for different genes. Stadler (quoted in Demerec (2)) has determined the spontaneous rate for a number of genes in maize. (Table 1). The results serve to illustrate the range of rates obtaining. As in a chemical reaction, the rate increases with temperature. Muller (8) determined the temperature coefficient for the incidence of sex-linked lethal mutations in *Drosophila melanogaster* and gives the value of about 5 after correcting for unequal life cycles at the two temperatures.

Table 1—Frequency of Spontaneous Gene Mutations in Maize (after Stadler from Demerec)

Genes	Number of Gametes Tested	Mutations Observed	Mutation Rate Per 1,000,000 Gametes
R (color factor)	554,786	273	492
I (color inhibitor)	265,391	28	106
Pr (purple)	647,102	7	11
Su (sugary)	1,678,736	4	2.4
Y (yellow)	1,745,280	4	2.2
Sh (shrunk)	2,469,285	3	1.2
Wx (waxy)	1,503,744	0	0

Muller's discovery in 1927 (7) that the mutation rate could be increased in *Drosophila* by subjecting the flies to X-rays stimulated work in this field. Briefly, subsequent work showed that the mutation rate is proportional to the amount of ionization produced by the radiation, i. e. it is directly proportional to the dosage in r units for wave lengths from gamma-rays to soft X-rays and also for beta-rays, it is independent of wave-length in this range, and it is independent of the time over which the dose is given.

These facts are in harmony with our model of the gene as a chemical structure potentially capable of undergoing reactions which would result in an altered chemical structure and would thus alter the catalytic properties of the gene. On this hypothesis the rate of mutation is governed by the height of the energy barriers which separate the alternative structures. An individual

gene mutates when the requisite amount of energy is available in the proper bonds. This may occur due to energy fluctuations according to the Maxwell-Boltzmann Distribution Law which is reflected in the temperature coefficient, or the energy may become available as a result of ionizations produced by radiation.

It is not unlikely that the height of the energy barriers and hence the mutation rate has been fixed by selection. In fact, a gene affecting mutability has been reported in a Florida strain of *D. melanogaster* (3). A certain amount of variability is essential to provide the raw materials for evolution, but a relative stability is also necessary to safeguard progress which has already been made.

In conclusion, we may inquire whether gene mutations and chromosome aberrations are sufficient as the raw materials for evolution. It is common knowledge that most mutations, in the broad sense, those occurring spontaneously as well as those induced by radiation, having deleterious effects. This is understandable, for the normal genotypes in a species at a given time level exist because they are efficient in controlling the life processes. The highly integrated mechanisms have passed the test of selection. Only rarely is it to be expected that a random change in this system will better adapt an individual. Cases are known where two or more mutant genes having a deleterious effect when present singly are beneficial when present in combination. This serves to emphasize that it is the system, rather than the individual gene upon which selection acts. An illuminating example of the effect of environment for these considerations is to be found in the Crustacean, *Daphnia longispina*, which has a temperature optimum of 20° and is inviable at 27°. Banta and Wood (1) discovered a mutant which had its optimum between 25° and 30° and could not survive at 20°. It is apparent that statements concerning the relative value of a mutation are meaningless unless a given environment is assumed. Hence, we may picture mutation as supplying a reservoir of variability which is constantly available to the species and which may be vital to its survival in a changed environment.

In this brief interval it has been impossible to cover even a small fraction of the recent advances thoroughly and critically. We can only allude in closing to the many cytogenetic advances which give us a clearer picture of chromosome structure and mechanics; to the insight gained into the chemical nature of chromatin by X-ray studies of proteins and ultra-violet spectro-

scopy applied to cells; to the extension of the principles of heredity to the lower plant and animal forms as well as to those having unusual chromosome cycles; to the induction of polyploidy by colchicine, heat treatment and other manipulation, thus making the experimental production of new species possible; to the extensive work on the various aspects of evolution, the analysis of variation in natural populations and the mathematical treatment of population genetics; and to the bearing of experimental embryology upon genes in development.

The wealth of information accruing from these and other sources contributes toward a more complete understanding of life as an highly integrated state of matter, having a labile continuity in time.

BIBLIOGRAPHY

1. Banta, A. M., and T. R. Wood. A thermal race of Cladocera originating by mutation. *Verhandlungen des V. Internationalen Kongresses für Vererbungswissenschaft* (Berlin) 1:397-398. (1927)
2. Demerec, M. What is a gene? *Jour. Heredity* 24:369-378. (1933)
3. Demerec, M. A mutability stimulating factor in the Florida stock of *D. melanogaster*. *Genetics* 22:190. (1937)
4. Dobzhansky, Th. *Genetics and the origin of species*. Columbia University Press, New York. (1937)
5. Goldschmidt, R. *Physiological Genetics*. McGraw Hill. New York. (1938)
6. Lawrence, W. J. C. and J. R. Price. The genetics and chemistry of flower colour variation. *Biol. Rev.* 15:35-58. (1940)
7. Muller, H. J. Artificial transmutation of the gene. *Science* 66:84-87. (1927)
8. Muller, H. J. The measurement of gene mutation rate in *Drosophila*, its high variability, and its dependence upon temperature. *Genetics* 13:279-357. (1928)
9. Painter, T. S. A new method for the study of chromosome aberrations and the plotting of chromosome maps in *Drosophila melanogaster*. *Genetics* 19:175-188. (1934)
10. Scott-Moncrieff, R. The genetics and biochemistry of flower colour variation. *Ergebnisse der Enzymforschung* 8:277-306. (1939)
11. Sturtevant, A. H. and Th. Dobzhansky. Inversions in the third chromosome of wild races of *Drosophila pseudoobscura*, and their use in the study of the history of the species. *Proc. Nat. Acad. Sci.* 22:448-450. (1936)

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