

Table 1. Phytotoxicity (percentage kill) of uracils applied at 2 lb/acre.

Crab-grass	Sorghum	Wild oats	Nutsedge	Mustard	Bean
<i>3-Butyl-6-methyluracil (I)</i>					
100	70	100	0	100	100
<i>5-Bromo-3-isopropyl-6-methyluracil (II)</i>					
100	100	100	100	100	100
<i>5-Bromouracil</i>					
0	0	0	0	0	0
<i>6-Methyluracil</i>					
0	0	0	0	0	0
<i>Uracil</i>					
0	0	0	0	0	0

lized from 20-percent aqueous ethanol. Melting point, 158° to 159°C. Analysis calculated for $C_8H_{11}BrN_2O_2$: C, 38.88; H, 4.49; Br, 32.34. Found: C, 39.02; H, 4.64; Br, 31.96.

These two substituted uracils are unusually phytotoxic to many plants. Some examples are given in Table 1. Compound II is active against a wider range of plants than compound I. Compound I has some interesting selective properties. For example, it has provided kill of many annual weed species without damage to peas and peanuts, even when applied at twice the rate needed to kill the weeds. Compound II has not shown this particular type of selectivity.

Since compound II is effective on a wide range of both annual and perennial weeds, it is particularly attractive as an industrial herbicide where it is desirable to kill all plants. It is especially phytotoxic to perennial grasses which have been previously difficult to control economically.

The approximate lethal dose by oral administration to the male white rat is at least 7500 mg/kg for compound I and 3400 mg/kg for compound II, as determined by the Haskell Laboratory for Toxicology and Industrial Medicine of the Du Pont Company (2).

HARRY C. BUCHA, WILLIS E. CUPERY,
JAMES E. HARROD, HARVEY M. LOUX,

LINUS M. ELLIS

Industrial and Biochemicals Department
and Central Research Department,
E. I. du Pont de Nemours and Company,
Wilmington, Delaware

References and Notes

- O. Mumm and E. Gottschaldt, *Chem. Ber.* **55**, 2068 (1922).
- Helpful discussions have been held with Drs. G. D. Hill, R. S. Johnson, B. C. Pratt, and H. S. Rothrock. This report is contribution No. 749 of the Industrial and Biochemicals Department and Central Research Department, E. I. du Pont de Nemours and Company.

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Patterns of Gene Pleiotropy in Morphogenetic Processes

Abstract. Selection for an increase and decrease in the expression of the *ocelli-less* mutant in *Drosophila subobscura*, variable for the number of ocelli and bristles, has revealed the pleiotropic nature of the mutant. In addition to modifying a morphogenetic system responsible for the formation of ocelli and bristles, it also modifies another morphogenetic system determining the positions of these structures, at the extreme range of the mutant expression.

This investigation is an attempt to deduce the nature of the development processes and their genetic control by studying the range of adult variation as the end product of these processes. The pattern chosen for study was that of the macrochaetae and ocelli (Fig. 1, top) on top of the head in *Drosophila*. The number and arrangement of these structures is highly uniform in *Drosophilidae*, but several mutants are known to alter their number and arrangement.

The sex-linked recessive mutant, *ocelli-less*, in *Drosophila subobscura* removes the head bristles and ocelli. In the foundation population, homozygous for the mutant, the flies had varying combinations of bristles and ocelli. The three pairs of orbital setae and the pair of vertical setae II were not much affected by the mutant. In a few flies the bristles were repeated (two or more bristles lying close together at a site normally occupied by one) unilaterally as well as bilaterally. The ocelli in some of the flies were slightly displaced from their normal positions, and sometimes their sizes were also affected. Since a positive correlation was found between the presence of bristles and of ocelli, the degree of expression of the mutant was measured by giving a unit "score" for the presence of each of the structures studied. Earlier work (1-3) had shown that by selective breeding for higher score it was possible to obtain a population which, although carrying the mutant, contained a high proportion of wild-type individuals. Continued selection, after the wild-type phenotype had been reached, increased the frequency of (i) repeated bristles, (ii) repeated ocelli, (iii) neomorphs, a novel pair of bristles which is normally absent in *Drosophilidae* but is present in a family closely related to it, Aulacigasteridae, (iv) additional central bristles at irregular sites, and (v) of additional ocelli at irregular sites. These repeated

and additional structures at both specific and irregular sites were found to be highly correlated with genes for higher score.

In the other direction, selection for lower score eliminated the central structures (three ocelli, ocellar and post-vertical setae) after which little progress was made. In the later generations of selection, however, flies showed depressions on the margins of the head, on one side or both sides, which varied in the degree of expression. Such depressions were highly correlated with genes for lower score.

In these experiments (1-4), the three pairs of orbital setae were not included in the scoring system, and, in later experiments (2-4), the pair of vertical setae II was also not scored, as they were not much affected by the mutant. With the elimination of central structures in the downward selected line, however, a curious phenomenon was observed. In some of the flies in which central structures were absent, additional marginal bristles at irregular

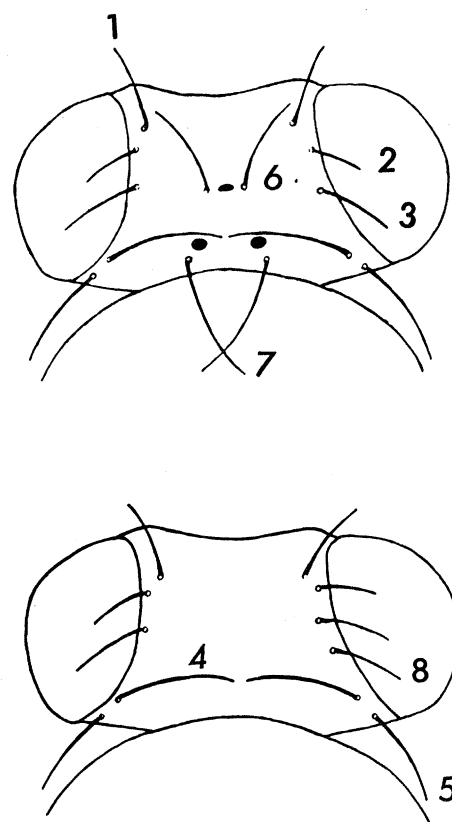


Fig. 1. (Top) The wild-type pattern of macrochaetae and ocelli in *Drosophila subobscura*. (Bottom) The pattern of macrochaetae in the *ocelli-less* population selected for lower number of structures; 1-3, orbital setae; 4, vertical seta I; 5, vertical seta II; 6, ocellar seta; 7, post-vertical seta; 8, additional bristle; •, ocelli.

sites were seen. They were either interpolated between normal bristles, or in positions involving respacing (Fig. 1, bottom) of associated bristles. In order to study this effect another foundation population was constructed by crossing together different *ocelli-less* populations selected for various patterns in which the mean score was low. Starting from this heterogeneous population, flies were selected for lower score. The system of scoring was similar except that the three pairs of orbital setae were taken into account. A unit score was given for the presence of each of the twelve bristles and three ocelli, and also for each repeated bristle, bristle at an irregular site, repeated ocellus, and ocellus at an irregular site. The effect of selection was manifold. With progressive response to selection, central structures were gradually eliminated. Elimination of central bristles and the three ocelli was associated with an increase in the frequency of additional marginal bristles, which rose to 13.39 percent in population S-6, compared with a frequency of 0.3 percent in the control population selected for higher score. In the last generation of selection nearly all flies had dorsoventral depressions in the head. These depressions were not restricted to the margins of the head alone, but in a high proportion of flies were spread over the entire surface of the head, giving it a hollow appearance. These deformations of the head affected the orientation of bristles. In such cases the bristles were directed outward.

The major interest of these findings is that the frequency of additional marginal bristles at irregular sites increases with an increase in the frequency of genes for lower score. This relationship is confirmed by the almost complete absence of additional bristles in the flies of the population selected for a higher score, in which all the normal structures were present. Only one fly out of the total of 328 recorded in population S-43 showed the presence of one additional marginal bristle on one side.

Figure 2 shows the mechanisms of the origin of structures in terms of primarily an unvarying "prepattern" determining the positions of bristles and ocelli, and of an ocelli-bristle-forming substance, or "precursor," which is variable in amount and which must be present in the required amount if structures are to be formed. This model is an extension of that suggested by Stern (5) in the light of mathematical

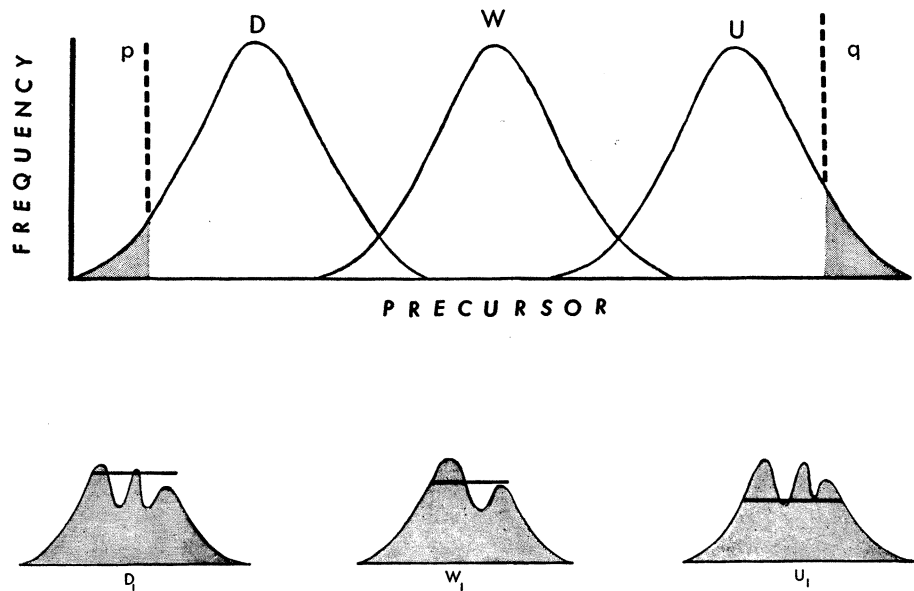


Fig. 2. Model to explain the nonhomeomorphic distortion of structures in the two-way selected populations of the *ocelli-less* mutant in *Drosophila subobscura*.

considerations of Turing (6). The mechanisms by which various arrangements of structures can arise are described in detail elsewhere (3, 7).

It is supposed that there are a number of pairs of alleles which alter the expression of flies by altering the amount and distribution of precursor, which is distributed in the required amount in the wild-type flies. The reasons for postulating a common precursor of bristles and ocelli are mainly two. First, there exists a genetic correlation between the presence of bristles and of ocelli; second, both are derivatives of hypodermis. The prepattern is shown as peaks of concentration of some inducing substance with regions of high and low concentration, the regions of high concentration occurring at sites where structures later form.

The frequency of flies with the amounts of precursor in the three *ocelli-less* populations, D, W and U, is shown in Fig. 2, top. D represents the downward-selected population in which additional marginal bristles at irregular sites are present, W an upward-selected population in which most of the individuals have a wild-type phenotype, and U an upward-selected population in which neomorphs and additional structures at irregular sites are present. Since structures at irregular sites distorting the positions of associated structures were observed only at the two extremes of the mutant expression, it is argued that a particular amount of precursor is required for their expression. It is supposed that only

the flies having the amounts of precursor outside the range from p to q produce phenotypes involving changes in the positions of associated structures. For W_1 only two peaks of the prepattern are shown, one of which is typical of the peaks that induce structures in the wild-type flies. A submerged peak of the prepattern indicates the possibility that there can also exist peaks to which wild-type tissue does not respond. Horizontal lines represent the level of the precursor. It is suggested that the flies having the amounts of precursor within the range p to q increase or decrease the number of structures only by varying that amount. But the flies with the amounts of precursor less than p and greater than q produce nonhomeomorphic distortion of structures by changing the prepattern, that is, by changing the number and shapes of the peaks of the prepattern (Fig. 2, bottom).

The distinction between precursor and prepattern is necessary because of the nature of phenotypes observed in the selected populations. The reason for considering changes in the prepattern is simply this: in terms of Turing's reaction-diffusion model, the actual pattern of peaks and valleys of concentration of inducing substance depends on the size and shape of the field, and the "chemical wave length," that is, the preferred spacing between peaks, which in turn depends on the rates of reaction and diffusion of chemical substances. The ratio between the chemical wave length and the size of the field in which

waves are developing can vary to a certain extent without producing any change in the actual pattern formed. However, a threshold would be reached, involving the appearance of an additional peak or peaks and respacing of other peaks in the field. The respacing of bristles in the present experiments cannot be explained easily without considering changes in the number and shapes of the peaks of the prepattern. Since such phenotypes were seen only at the two extremes of the mutant expression, it is reasonable to suggest that the primary effect of the *ocelli-less* gene is to alter the amount and distribution of precursor, and that this alteration in turn may change the prepattern.

K. C. SONDHI

Division of Genetics, New England
Institute for Medical Research,
Ridgefield, Connecticut

References

1. K. C. Sondhi, *J. Genet.* **57**, 193 (1960-61).
2. ———, *Nature* **189**, 249 (1961).
3. ———, *Evolution* **16**, 186 (1962).
4. J. Maynard Smith and K. C. Sondhi, *Genetics* **45**, 1039 (1960).
5. C. Stern, *Caryologia* **6**, 355 (1954); *Arch. Entwicklungsmech. Organ.* **149**, 1 (1956).
6. A. M. Turing, *Phil. Trans. Roy. Soc. London, Ser. B* **237**, 37 (1952).
7. J. Maynard Smith and K. C. Sondhi, *J. Embryol. Exptl. Morphol.* **9**, 661 (1961); K. C. Sondhi and J. Maynard Smith, *Sci. Am.*, in press.

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Theory of Homologous Sublattices and Intracrystalline Equilibria

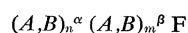
Abstract. A method is presented by which the isothermal-isobaric distribution of certain atomic or ionic species among two sublattices of a crystal may be calculated from the heterogeneous exchange equilibria of the species between two coexisting crystalline phases, one of which is the crystal under investigation. The method depends on structural homologies between the crystals. Quantitative data on the distribution of Mg^{2+} and Fe^{2+} in the mineral cummingtonite are found to agree with the theory.

Although a quantitative concept of order-disorder for alloys dates to the work of Gorsky (1) and of Bragg and Williams (2), few methods based upon easily measurable parameters have been proposed to treat the distribution of atomic or ionic species within complex phases. The purpose of this paper is to present a simple, essentially thermodynamic approach to certain types of distribution equilibria in crystals.

In order to illustrate the method it is convenient to discuss a particular type of crystal structure which has been in-

vestigated. It should, however, be apparent from this illustration how the method may be extended to certain other types of structures.

Consider two stably coexisting crystals with the formulas

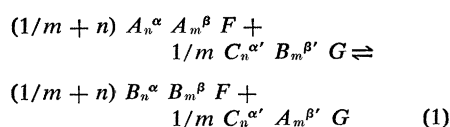


and



In these formulas A , B , and C represent three different species which are distributed among the sublattices α , β , α' , and β' of the two crystals. F and G represent essentially nonparticipating framework structures, and n and m are small whole numbers. The species A and B are somewhat similar in properties such as electronegativity and atomic or ionic radii, whereas C must differ from A and B in one or more of these fundamental properties. This difference causes C to be nearly confined to the α' sublattice. Although this model may appear somewhat narrowly restricted in properties it does in fact describe several important groups of compounds which exhibit broad miscibility gaps.

In the heterogeneous system consisting of at least these two crystals the exchange equilibrium between the coexisting crystals may be represented by the reaction



The compositions of the coexisting phases may be determined by chemical analyses. These analyses are expressed as activities which involve the mole fractions of the total A - B content of each phase. For example, the activities of the components of the F phases are

$$a_A^F = X_A^F f_A^F$$

and

$$a_B^F = (1 - X_A^F) f_B^F \quad (2)$$

where $X_A^F = A/(A + B)$ in $\alpha + \beta$ and f_A^F and f_B^F are the corresponding activity coefficients. Similarly for the G phase:

$$a_A^G = X_A^G f_A^G$$

and

$$a_B^G = (1 - X_A^G) f_B^G \quad (3)$$

But $X_A^G = A/(A + B)$ in β' only since α' is filled with C .

However, our interest here is in the homogeneous intracrystalline equilibrium:

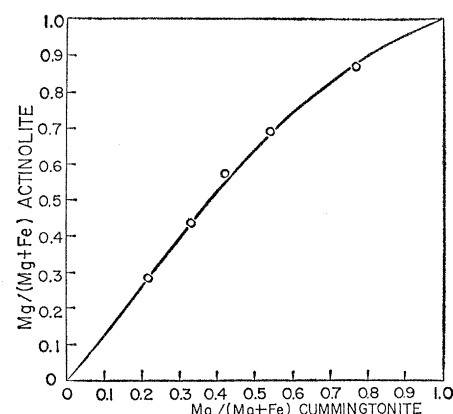
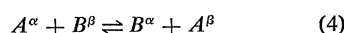


Fig. 1. Distribution of Mg^{2+} and Fe^{2+} among coexisting cummingtonites and actinolites expressed as atomic fractions.

which governs the distribution of A and B among the α and β sublattices of the F crystal. Consequently it is necessary to find alternative expressions for the activities which are functions of the mole fractions of the sublattices. For A in the F -crystal we have, for example:

$$a_A^F = f(X_A^\alpha, X_A^\beta) \quad (5)$$

which is equivalent to the first relation of Eq. 2. One type of expression is given directly by the stoichiometric relations of the total A - B lattice ($\alpha + \beta$) to the sublattices. Thus

$$X_A^F = (1 - p) X_A^\alpha + p X_A^\beta$$

and

$$X_B^F = (1 - p)(1 - X_A^\alpha) + p(1 - X_A^\beta) \quad (6)$$

where $p = m/(m + n)$. These expressions may be substituted into the activi-

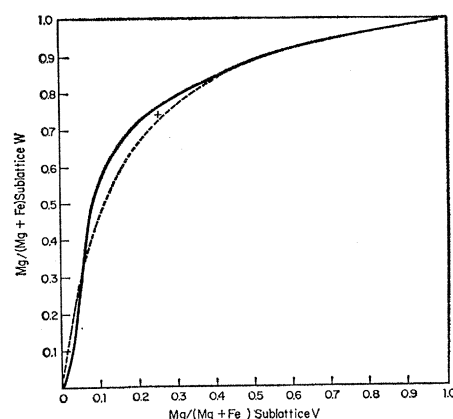


Fig. 2. Theoretical and observed distributions of Mg^{2+} and Fe^{2+} among the V and W sublattices of cummingtonite expressed as atomic fractions. The full curve is the more exact theoretical relation, whereas the dashed curve is the simplified approximation (see text). The cross is a value observed by Ghose with x-ray diffraction.