the normal dose (Table 2). It seems more likely to us that the difference between the two sets of tumors is an all-or-none difference: tumors either have the agent or they have not.

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Sign of Taxis as a Property of the Genotype

Abstract. Previous studies have assumed *Drosophila* to be negatively geotactic and found this to be the case. New methods of observation now yield a spectrum of geotactic behavior both positive and negative. Two-way selection produces races of animals performing in diametrically opposite fashion to the same stimulus conditions.

In the study of behavior it is usually assumed that for a given species there is a characteristic way of responding which defines a behavioral process under analysis. Though individuals may differ somewhat in the way they respond, the assumption is made that individual differences represent minor variations around the normal (*1*). In particular, taxes have been considered an invariant property of a species under a given set of conditions—for example, moths are positively phototactic, cockroaches negatively phototactic, and flies negatively geotactic (*2*).

In previous behavior genetic studies of *Drosophila melanogaster*, it was assumed that certain tactic orientations were normal, and individual differences were measured as deviations from the assumed normal orientation. Furthermore, these assumptions were often incorporated into the methods of observation and analysis, effectively guaranteeing that the results would accord with the preconception of the normal. In the study of geotaxis (*3*), individuals were scored on the strength of their negative geotaxis. The alternatives on every trial were those of responding or not responding, that is, ascending the walls of a test tube or failing to do so. In studies of phototaxis, individual (*4*) and population (*5*) differences were measured in terms of the strength of positive phototaxis. The alternatives in these studies were effectively those of approaching a light source or not.

Recently, Lewontin (*6*) has shown how the sign of phototaxis can depend on the conditions of observation. *Drosophila pseudoobscura* that were agitated while responding were predominantly photopositive while those that were not agitated were predominantly photonegative.

The present study places no restrictions on the sign of the taxis. Apparatus has been developed which affords objective and automatic measurement of both positive and negative geotactic behavior in populations under a single set of stimulus conditions as well as reliable mass screening measurements of individual differences in the expression of each. The observations have been made in a 15-trial modification of the multiple unit classification maze (Fig. 1), which has been described elsewhere (*7*). The alternatives at each choice point in the maze require diametrically opposite responses, namely, going against the pull of gravity by climbing up (negative geotaxis) or going toward the pull of gravity by climbing down (positive geotaxis).

With the maze, geotaxis has been studied in an unselected wild-type population of *Drosophila melanogaster* developed by mixing in a population cage the Formosa stock from Berkeley, Calif., with freshly trapped Capetown and Syosset stock from Cold Spring Harbor, N.Y. The middle ogive in Fig. 2 shows that observation of the performance in the maze of large numbers of individuals from the unselected population reveals a response distribution which contains a spectrum of geotactic scores. The expression of geotaxis in this population ranges from a score of −7.5, which represents the extreme of negative geotaxis, through 0, a score indicating a neutral response to gravity, to +7.5, the extreme of positive geotaxis. The distribution is slightly skewed; 47 percent receive positive scores and 53 percent negative scores.

With a system of assortative mating, two-way selection pressure is applied. The maximum separation so far obtained was reached at the 48th generation of selection and is shown by the outer ogives in Fig. 2. The curve near the ordinate shows that 96 percent of the individuals in the strain selected for negative geotaxis receive a negative score in the maze, with 50 percent receiving the extreme negative score of −7.5. The curve farthest from the ordinate shows that 95 percent of the individuals in the other strain receive positive scores in the maze, with 16 percent receiving the extreme positive score of +7.5.

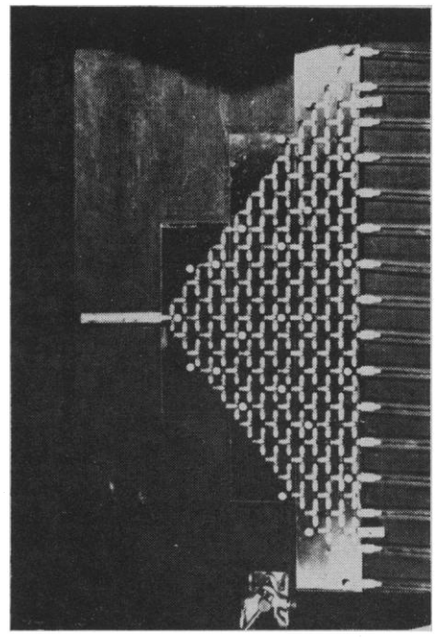

Fig. 1 Photograph of a 15-unit vertically placed maze. Large groups of flies are introduced into the vial at left and collected from vials at right. The flies are attracted by food in the vials at right and by a fluorescent light in a vertical position at the right. Small trap-like funnels discourage backward movement in the maze.

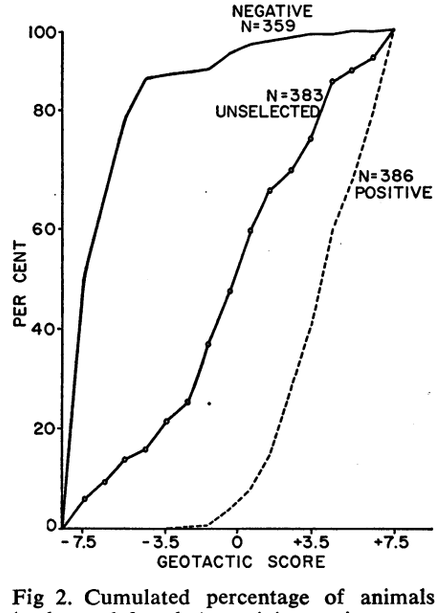

Fig 2. Cumulated percentage of animals (males and females) receiving various geotactic scores in the maze in the unselected foundation population (middle ogive) and in the two selected strains (outer ogives).

These experiments show that, when the conditions of observation permit, the members of a population may display a spectrum of geotactic reactions. Some individuals give a negative response, others a positive response, and there are varying degrees in the extent to which individuals respond positively or negatively to gravity. Furthermore, it is possible to breed races of animals which perform in diametrically opposite fashion to the same physically specified stimulus conditions (*8*).

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8. A more extensive report of these findings is being prepared for submission to the *Journal of Comparative and Physiological Psychology*. Complete data on the behavior of the foundation population and all selected generations are available in the two doctoral dissertations on which this report is based: J. M. Weiss, Columbia Univ. (1959), and L. Erlenmeyer-Kimling, Columbia Univ. (1961). Grateful acknowledgment is expressed to T. Dobzhansky and F. J. Ryan for generously providing laboratory space and many research facilities. This research was supported by grants G-3846, G-8998, and G-13595 from the National Science Foundation.

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Mechanism of Inactivation of Enzyme Proteins by Ultraviolet Light

Abstract. Some quantum yields for the destruction of amino acids have been determined. The inactivation of the enzymes chymotrypsin, lysozyme, ribonuclease, and trypsin by ultraviolet light can be accounted for quantitatively by summing the products of (i) the probability that light is absorbed by a given amino acid residue, ϵ_i, and (ii) the probability that absorbed light induces a chemical change, with a quantum efficiency ϕ_i, in the residue. The principal residues involved are cystyl and tryptophanyl. Peptide bond rupture is not important. Analysis of inactivated enzymes verifies the assumption of the existence of several inactivation mechanisms.

It has been suggested that the inactivation of enzymes by ultraviolet light involves, as the primary chemical reaction, photolysis of disulfide and aromatic residues (*1*), and Setlow has had some success in calculating quantum yields for enzyme inactivation based on this assumption (*2*). For small degrees of enzyme (E) inactivation, giving rise to inactive products P, we have for the rate (*3*)

$$-\mathrm{d}(E)/\mathrm{d}t = \Phi I_{\mathrm{abs}}\epsilon_e(E)/[\epsilon_e(E) + \epsilon_p(P)] \cong \Phi I_{\mathrm{abs}}\epsilon_e(E)/\epsilon_e(E_o) \quad (1)$$

where ϵ_e is the molecular extinction coefficient of the enzyme and ϵ_p that of the products in time t, I_{abs} is the absorbed intensity, for unit path length, and Φ is the quantum yield for enzyme inactivation. If we make the assumption that an enzyme molecule can undergo inactivation by loss of identity of any one of the aromatic residues, –SS– bonds or –CONH– bonds (the other moieties do not absorb appreciably at this wavelength), we can write

$$-\mathrm{d}(E)/\mathrm{d}t \cong [I_{\mathrm{abs}}/\epsilon_e(\mathrm{E}_o)] \sum^{I} n_i\varepsilon_i(E)\phi_i \quad (2)$$

where n_i is the number of residues per molecule of enzyme of molar concentration (E), ε_i is the extinction coefficient of each residue, and ϕ_i is the quantum yield for destruction (loss of chemical identity) of each residue. Equating the rates we find that

$$\Phi_{enz} = \sum^{I} n_i\varepsilon_i\phi_i/\varepsilon_e \quad (3)$$

First we have determined the quantum yields, ϕ = reactant molecules chemically changed per quanta absorbed by reactant, for the total destruction of amino acids with appreciable absorption at 2537 A (irrespective of the multiplicity of products). These values, for acid media and under nitrogen, are listed in Table 1. For analysis, ion exchange or paper chromatography was generally used; the details are recorded elsewhere (*4*). Second, we assume that the quantum yields, ϕ_i, and extinction coefficients, ε_i, also apply to the intact protein. Although we have no way of knowing, a priori, whether ϕ_i for the amino acid side chain is the same whether free or combined, ε_i for these residues are only approximately the same for free and combined amino acids (*5*). From this information, quantum yields for enzyme inactivation, Φ, calculated from Eq. 3, are compared with the known values for chymotrypsin, lysozyme, ribonuclease, and trypsin: agreement is obtained within a factor of two to three, which is surprisingly good in view of the number of factors upon which Φ depends (*1*).

Table 1. Estimation of quantum yields for enzyme inactivation from quantum yields for amino acid destruction (2537 A).

Amino acid, ϕ	Enzyme							
	Chymotrypsin ϵ_e = 23,000		Lysozyme ϵ_e = 18,000		Ribonuclease ϵ_e = 4,400		Trypsin ϵ_e = 15,500	
	n_i	$n_i\epsilon_i\phi_i$	n_i	$n_i\epsilon_i\phi_i$	n_i	$n_i\epsilon_i\phi_i$	n_i	$n_i\epsilon_i\phi_i$
Cystine, 0.13	5	175	5	175	4	140	6	210
Histidine, <0.03	2	<0.015	1	0.007	4	<0.03	1	0.007
Phenylalanine, 0.013	6	11	3	5	3	5	3	5
Tryptophan, 0.004	7	80	8	92	0		4	46
Tyrosine, 0.0020	4	3	3	2	6	4	4	3
—CONH— as in acetylalanine, 0.05	~200	~1	~130	~1	~130	~1	~200	~1
	Φ *for enzymes*							
Calculated	0.01		0.01		0.30		0.01	
Known	0.005		0.024		0.027		0.105	

By chemical analysis of hydrolyzates of ultraviolet-inactivated enzymes, it was also found that about one tryptophan residue per enzyme molecule is destroyed in chymotrypsin and trypsin and that two to three disulfide linkages are broken in trypsin, 1.7 in ribonuclease, and none in chymotrypsin. No phenylalanine, tyrosine, lysine, and/or histidine or arginine residues were changed; with a calculated inactivation well over 99.999 percent, some of these were altered, however. No titratable amino groups appeared during inactivation of the nonproteolytic enzymes, which indicates no ruptured –CONH– (compare *6*). Histidine does not appear to be the vulnerable group with ultraviolet light; this residue is primarily involved in photosensitized inactivation with visible light, incidentally (*7*).

That breakage of hydrogen bonds is also involved in the inactivation-denaturation of enzymes has been demonstrated elsewhere and involved a study of the influence of temperature on Φ (*1*).

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