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HALDANE AND MODERN BIOLOGY

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Title page photograph of Haldane courtesy of Dr. K. Patau, Univ. of Wisconsin, Madison, Wis.

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XII. SOME TYPES OF POLYMORPHISM IN POPULATIONS

Introduction

In some natural populations of various animal and plant species, a rather long state of polymorphism of this or that character is observed (Ford, 1940). This state is supposed to be due to the maintenance by certain mechanisms of two or more forms in the state of dynamic equilibrium.

In experiments on the relative viability of various mutations and their combinations in *Drosophila funebris* at various temperatures and degrees of overpopulation of cultures (Timoféeff-Ressovsky, 1934), it was found that some mutations which sharply decreased the viability in the homozygous state increased the relative viability of heterozygotes (in comparison with a normal parent homozygote). Based on this, one could suppose that in some cases a state of dynamic equilibrium between normal and mutant forms can be established in the population because of the increased viability of heterozygotes, which constantly segregate a less viable mutant form. These experiments led to a number of special investigations on the relative viability of some mutations in *Drosophila melanogaster* in homo- and heterozygous states and their compatibility with the normal form in stable model populations of this species. The first publications of the results of such experiments were made by Ph. l'Héritier and G. Teissier, who described competitive relations of various mutations of *Drosophila melanogaster* with a normal form, as well as of two *Drosophila* species: *D. melanogaster* and *D. funebris* (l'Héritier, 1936, 1937; l'Héritier and Teissier, 1933, 1934, 1935).

On the other hand, more than ten years of observations of and collections in the same population of the ladybug *Adalia bipunctata* have shown that a more or less permanent ratio of black to red forms of this bug in the population is due to various selection pressures on these forms. This difference is caused by their relative viability in different seasons. Black forms have the advantage (connected apparently with more intensive reproduction) during the vegetative period, and red forms survive winter

better. As a result, the last (fall) population contains more black forms and the first one after winter, the spring population, more red forms. Permanent polymorphism in the population is, thus, maintained by oppositely directed selection pressure on these forms in winter and in summer (Timoféeff-Ressovsky, 1940).

In the cases described above we distinguish two types of polymorphism. We shall refer to the first type as heterozygotic, and the second as adaptational polymorphism. The meaning of these terms will become clear below.

We shall show how the quantitative mathematical model of these two phenomena not only will confirm already known experimental data (which is undoubtedly useful since it, in turn, confirms experimentally the adequacy of the constructed model), but also will allow us to consider the problem of polymorphism in populations from another point of view.

The probabilistic interpretation of the Mendelian rules of heredity, strictly made for the first time by Hardy (1908), helped to construct quantitative models of the influence of selection pressure on genotypic composition of population (Jennings, 1916; Chetverikov, 1926; Wright, 1939). One of the pioneers in this trend in population genetics, the trend based on probabilistic-statistical methods and using an accurate language of numbers, devoid of ambiguous interpretation, was J. B. S. Haldane. At the same time, the works of Haldane usually are based on experimental facts and are never just speculative figures (Haldane, 1932, 1935, 1938, 1957; Haldane and Jayakar, 1963).

Quantitative Model of Genotypic Equilibrium in Populations

In this section a model will be constructed describing the time change of the genotypic composition of population under various selection pressures.

Let there be a sufficiently large, numerically stable, panmictic population of organisms containing only three genotypes: AA, Aa, and aa. This means that heredity in the population is determined only by two allelic genes A and a. Let us assume that all organisms in the population at any moment of time are the same according to all characteristics with the exception of genotypic difference in alleles A and a. Let us take average longevity of one generation for a time unit. Let us assume that at a certain moment of time t, organisms, having appeared at the moment $t - 1$, produce a progeny, after which they leave the population, so that in the time interval from t to $t + 1$ only organisms of the next generation

exist. By index $(-)$ we shall denote such values, meanings of which are taken to the left of point t, by index $(+)$, those to the right of point t.

Let us introduce the following symbols:

$$\begin{aligned} u(t) &= \text{frequency of genotype } AA; \\ 2v(t) &= \text{frequency of genotype } Aa; \\ w(t) &= \text{frequency of genotype } aa; \\ p(t) &= \text{frequency of allele } A; \\ q(t) &= \text{frequency of allele } a. \end{aligned}$$

Normalization conditions are:

$$\begin{aligned} u(t) + 2v(t) + w(t) &= 1; \\ p(t) + q(t) &= 1. \end{aligned}$$

Let frequencies of corresponding genotypes in the population, equal, by the moment t (moment of reproduction), $u_-(t)$; $2v_-(t)$; $w_-(t)$. Then frequencies of alleles A and a correspondingly equal:

$$\begin{aligned} p_-(t) &= u_-(t) + v_-(t) \\ q_-(t) &= v_-(t) + w_-(t). \end{aligned} \tag{1.1}$$

Owing to the assumption of panmixia, frequencies of zygotes in the progeny produced at the moment t will be written as:

$$\begin{aligned} u_+(t) &= p_-^2(t); \\ 2v_+(t) &= 2p_-(t)q_-(t); \\ w_+(t) &= q_-^2(t). \end{aligned} \tag{1.2}$$

It is easy to see that at the moment t, frequencies of zygotes, considered as time functions, undergo a break. Gene frequency however, remains continuous.

Indeed:

$$p_+(t) = u_+(t) + v_+(t);$$

but from (1.2) it follows that:

$$p_+ = u_+ + v_+ = p_-^2 + p_-q_- = p_-^2 + p_-(1 - p_-) = p_-$$

which confirms the above statement.

Since differing selection pressure affects various genotypes, the frequency relation of genotypes must change by the end of the generation.

Let genotype frequencies become as follows as a result of selection effect by the moment $t + 1$ (moment of reproduction of the next generation):

$$u_-(t + 1) = \frac{\alpha u_+(t)}{w};$$

$$2v_-(t + 1) = \frac{2\beta v_+(t)}{w};$$

$$w_-(t + 1) = \frac{\gamma w_+(t)}{w} \tag{1.3}$$

where $1/w = 1/(\alpha u_+(t) + 2\beta v_+(t) + \gamma w_+(t)$ is normalization factor.

Here α, β, γ are certain coefficients, which, in general, may depend on time and the introduction of which allows us to take into account the influence of selection pressure. Indeed, α, β, γ are certain not normalized probabilities of attainability of reproduction age by an individual of corresponding genotype. Values of these probabilities depend on conditions under which the population lives (degree of overpopulation, influence of temperature, humidity, and so on). It is conceivable that these values are determined by the viability of each genotype under given environmental conditions.

Now we shall try to determine these coefficients. Let genotype frequencies be known to us (for instance, from the experiment) at the beginning and the end of life of a certain generation. From (1.3) we shall have

$$\alpha u(u^* - 1) + 2\beta u^* v + \gamma u^* w = 0;$$
$$\alpha u v^* + \beta(2v^* - 1)v + \gamma v^* w = 0;$$
$$\alpha u w^* + 2\beta v w^* + \gamma w(w^* - 1) = 0.$$

Here $u = u_+(t)$; $u^* = u_-(t + 1)$. Similar symbols are introduced for other values.

We obtained a homogeneous set of three linear algebraic equations for the determination of values α, β, γ. A matrix rank of coefficients of this set is less than three. Hence, the set has a non-trivial solution. One of the unknown quantities must be given beforehand. Not interfering with the general pattern, let us assume that the coefficient, corresponding to genotype, viability of which is the highest, is equal to 1. Then other coefficients will be less than 1. In this way we have done the normalization and determined the coefficients α, β, γ as probabilities of corresponding

genotypes to attain the reproduction age, on condition that one of the genotypes always reaches this age (probability unit). The following cases are possible:

1) The homozygote AA is the most viable. Then

$$\alpha = 1; \qquad \beta = \frac{uv^*}{u^*v}; \qquad \gamma = \frac{uw^*}{u^*w}.$$

2) The heterozygote Aa is the most viable. Then

$$\beta = 1; \qquad \alpha = \frac{u^*v}{uv^*}; \qquad \gamma = \frac{vw^*}{v^*w}.$$

3) The homozygote aa is the most viable. Then

$$\gamma = 1; \qquad \alpha = \frac{u^*w}{uw^*}; \qquad \beta = \frac{v^*w}{wv^*}.$$

Let us term factors α, β, γ the relative viability coefficients of genotypes AA, Aa, and aa, correspondingly. In general, α, β, γ can be time functions.

We have determined genotype frequencies in the population by the moment $t + 1$. Correspondingly, for frequency of allele A, we shall have:

$$p_-(t + 1) = u_-(t + 1) + v_-(t + 1).$$

The increase of frequency p during the lifetime of a generation equals:

$$\delta p = p_-(t + 1) - p_+(t) = u_-(t + 1) - u_+(t) + v_-(t + 1) - v_+(t).$$

With a sufficient degree of precision, one can assume that during the lifetime of one generation the increase of gene frequency is linear in time. Thus, the increase of gene frequency for the time $\delta t (\delta t \leq 1)$ equals:

$$p_-(t + \delta t) - p_+(t) = [u_-(t + 1) - u_+(t) + v_-(t + 1) - v_+(t)] \cdot \delta t. \quad (1.4)$$

Substituting in (1.4) the values $u_-(t + 1)$, $v_-(t + 1)$ from (1.3) and keeping in mind that

$$\begin{aligned} u_+(t) + v_+(t) &= p_+(t); \\ u_+(t) &= p_-^2(t); \\ v_+(t) &= p_-(t)[1 - p_-(t)]; \\ p_+(t) &= p_-(t) \end{aligned}$$

we have

$$p_-(t + \delta t) - p_-(t) = \frac{(2\beta-\gamma-\alpha)p_-^3 - (3\beta-2\gamma-\alpha)p_-^2 + (\beta-\gamma)p_-}{\gamma+2(\beta-\gamma)p_- - (2\beta-\gamma-\alpha)p_-^2} \cdot \delta t. \quad (1.5)$$

Since, as shown above, $p(t)$ is a continuous function of t, it is possible to show that $dp_-/dt = \dot{p}_-$ exists and is determined at point t. Passing in (1.5) to the limit at $\delta t \to 0$ we have:

$$\frac{dp}{dt} = \frac{(2\beta - \gamma - \alpha)p^3 - (3\beta - 2\gamma - \alpha)p^2 + (\beta - \gamma)p}{\gamma + 2(\beta - \gamma)p - (2p - \gamma - \alpha)p^2} \tag{1.6}$$

From here on, we shall omit symbol $(-)$ in p_-. In the initial condition: $p(t_0) = p_0$with α, β, γ being constant, the equation (1.6) is integrable and its integral equals:

$$\left\{\frac{p}{p_0}\right\}^{\gamma/\beta-\gamma}\left\{\frac{1-p}{1-p_0}\right\}^{\alpha/\beta-\alpha}\left\{\frac{\epsilon-p}{\epsilon-p_0}\right\}^{\alpha\gamma-\beta^2/(\beta-\gamma)(\beta-\alpha)} = e^t; \tag{1.7}$$

where

$$\epsilon = \frac{\beta - \gamma}{2\beta - \gamma - \alpha}.$$

From (1.7), it is clear that depending on relations between α, β, γ at $t \to \infty$ three states may be reached:

$$p_\infty = 0; \qquad p_\infty = 1; \qquad p_\infty = \epsilon.$$

Let us consider this problem in detail. Equation (1.6) can be rewritten in the form:

$$\dot{p} = \frac{p(1-p)(\epsilon - p)}{\delta + 2\epsilon p - p^2}; \tag{1.8}$$

where

$$\delta = \frac{\gamma}{2\beta - \gamma - \alpha}.$$

We shall investigate phase trajectories of the set described by this equation on the phase plane $(\dot{p}, p; p\epsilon[0,1])$. The following cases are possible:

1) The homozygote AA is the most viable. Then $\alpha = 1; \beta < 1; \gamma < 1$. Let $\beta \geq \gamma$. In this case either $\epsilon > 1$, or $\epsilon \leq 0$. Function $f(p) = \delta + 2\epsilon p - p^2$ is positive at $\epsilon > 1$ and negative at $\epsilon \leq 0$ for any $p\epsilon[0.1]$. Then $\dot{p}$ is always positive. Hence, only one steady state $p^* = 1$ is realized. In Fig. XII-1(a) a phase trajectory at $\beta = 0.9$, $\gamma = 0.5$ is shown.
Let $\beta < \gamma$. Then $0 < \epsilon < 1$ function $f(p)$ is always negative. Therefore, $\dot{p} < 0$ at $p_0 < \epsilon$, $\dot{p} > 0$ at $p_0 > \epsilon$. Hence, there are two steady states $p^* = 0$ and $p^* = 1$. The first one is reached if $p_0 < \epsilon$, the second, if $p_0 > \epsilon$. In Fig. XII-1(b), phase trajectory at $\beta = 0.5$, $\gamma = 0.9$ is shown.

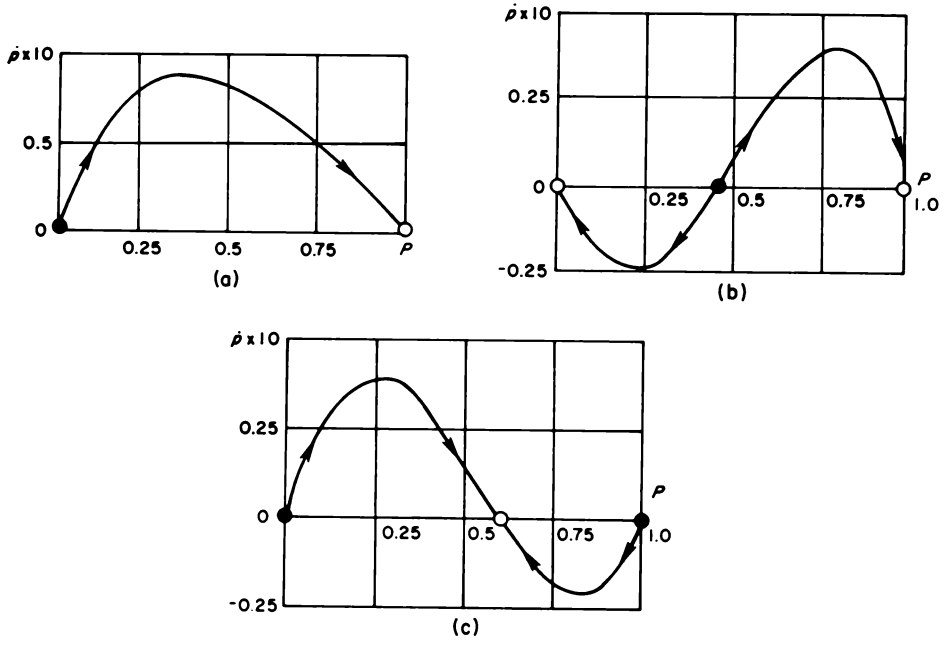

Fig. XII-1. The phase trajectories of a system, described by the equation 1.6. ○ = the stable state, ● = the unstable state. (*a*) $\alpha = 1; \beta = 0.9; \gamma = 0.5$. (*b*) $\alpha = 1; \beta = 0.5; \gamma = 0.9$. (*c*) $\beta = 1; \alpha = 0.8; \gamma = 0.7$.

2) The heterozygote *Aa* is the most viable. Then $\beta = 1; \alpha < 1; \gamma < 1$. At any α and γ less than 1, $0 < \epsilon < 1$, $f(p) > 0$ for $p \epsilon [0.1]$. Therefore $\dot{p} > 0$ at $p_0 < \epsilon$, $\dot{p} < 0$ at $p_0 > \epsilon$. Hence, there is one steady state $p^* = \epsilon$, the so-called polymorphism state. In Fig. XII-1(*c*) a phase trajectory at $\alpha = 0.8$, $\gamma = 0.7$ is shown.

3) The homozygote *aa* is the most viable. In this case, by substituting *A* for *a*, we have again the first case, and it, therefore, will not be considered in detail.

Let us consider the case when $\dot{p} = 0$ for all p. It is clear that for this condition it is necessary and sufficient that the right part in (1.6) equals 0 at any p. This requirement is met if

$$2\beta - \gamma - \alpha = 0;$$
$$3\beta - 2\gamma - \alpha = 0;$$
$$\beta - \gamma = 0.$$

This set has a non-trivial solution: $\alpha = \beta = \gamma$. If we assume that one of the relative viability coefficients equals 1, the rest will also equal 1, which means that selection pressure is absent. Thus, we have proved in a different way Hardy's theorem (Hardy, 1908) which states that in the absence of selection pressure in a panmictic population there is no time change of the frequency ratio of genotypes.

Experimental Heterozygotic Polymorphism in Model Populations; Comparison of Theoretical and Experimental Results

The mutation ebony in *Drosophila melanogaster* (allele e^b) was used for the experiments below. In this allele heterozygotes differ from the parent normal form by a darker color, a clearly pronounced dark strip on the prothorax and a darker ventral side of the abdomen. Because of these indications of partial dominance, it is possible, practically without failure, to distinguish the flies which are heterozygous for ebony from normal ones. As a control, parallel to experiments on ebony mutation, esperiments on plexus mutation were performed, the latter being practically the same in relative viability as normal flies.

Studies on Relative Viability of Ebony Mutation in Homo- and Heterozygous States

Ebony and plexus cultures were crossed repeatedly with the same inbred normal culture for two years. As a result, homozygous ebony, plexus, and normal cultures with little genotypic difference were obtained.

In the first series the ebony flies were crossed with normal ones; then in F_2 the number of homozygous ebony flies was calculated, as well as the heterozygous and homozygous normal ones. In standard tubes with food, about 50, 150, or 300 eggs were placed per tube, laid by heterozygous flies of the first generation. The tubes with 50 eggs were not overpopulated, with 150 eggs, slightly, and with 300 eggs, severely overpopulated. All these F_1- crosses were repeated some hundredfold to obtain enough F_2- flies. The results of these experiments are shown in Table XII-1. It is clear from this table that in tubes not overpopulated the percentage of homozygous normal, heterozygous, and homozygous ebony flies corresponded well with the expected ratio 1:2:1. Accordingly, viabilities of heterozygous and homozygous ebony flies, expressed as percentages of homozygous normal in the table, were practically indistinguishable from 100 per cent.

At slight overpopulation, a positive deviation in the percentage of heterozygous flies and a vegetative deviation in that of the homozygous ebony flies was observed (about 105 and 80 per cent, respectively). At

TABLE XII-1

DETERMINATION OF RELATIVE VIABILITY OF HETEROZYGOUS AND HOMOZYGOUS EBONIES BASED ON DEPARTURES FROM EXPECTED F_2-SEGREGATION (1:2:1) IN CULTURES OVERPOPULATED TO DIFFERENT DEGREES

EGGS PER VIAL	NUMBER AND %	NUMBER AND PERCENTAGE OF FLIES				PERCENTAGE VIABLE	
		+/+	+/e	e/e	Total		
50	No.	3,201	6,407	3,183	12,791	+/e	100.1
	%	25.03	50.10	24.87	100	e/e	99.5
150	No.	5,341	11,183	4,262	20,786	+/e	104.7
	%	25.7	53.8	20.5	100	e/e	79.8
300	No.	3,887	8,423	2,791	15,101	+/e	108.3
	%	25.7	56.4	17.9	100	e/e	71.8

severe overpopulation, these deviations in relative viability were more pronounced: heterozygous flies gave 108 per cent and homozygous ebony, 72 per cent.

Since an error is possible in the classification of heterozygous ebony flies, a second experimental series was performed. In standard tubes with food, the following kinds and numbers of eggs were placed per tube: 100 eggs from the aforementioned plexus culture or 100 eggs of homozygous normal flies, or 100 eggs of heterozygous ebony or 100 eggs of homozygous ebony flies. The results of this experimental series are shown in Table XII-2.

In these experiments the results of the previous series were confirmed: relative viability of heterozygous ebony flies was 108.5 per cent, and homozygous ebony, 77.6 per cent of plexus, while normal and plexus had the same relative viabilities.

TABLE XII-2

RELATIVE VIABILITY OF NORMAL HOMOZYGOTES, HETEROZYGOTES, AND EBONY HOMOZYGOTES CALCULATED AS PERCENTAGE OF VIABILITY OF PLEXUS MUTATION IN OVERPOPULATED CULTURES (200 EGGS PER VIAL)

EGGS PER VIAL	NUMBER AND %	NUMBER AND PERCENTAGE OF FLIES			PERCENTAGE VIABLE (OF PLEXUS)
		px	(e)	Total	
100 px +100 +/+	No.	3,817	3,841	7,658	
	%	49.8	50.2	100	100.7
100 px +100 +/e	No.	4,281	4,537	8,719	
	%	47.3	52.7	100	108.5
100 px +100 e/e	No.	3,453	2,681	6,134	
	%	56.3	43.7	100	77.6

Thus, both experimental series showed that mutation e^b in the heterozygous state had a higher relative viability as compared to its parent normal form, while homozygous e^b flies had a rather decreased relative viability as compared to their parent form.

Experiments with Ebony in Stable Model Populations

Based on the results of the experiments described above, experiments on supplanting of ebony flies by normal ones in stable model populations were carried out.

Model populations of *Drosophila* were obtained in the following way: Twenty pairs of flies were released in boxes with thirty holes made in the bottom to place the standard feeding cups with usual food. Every day a new feeding cup with food was placed in a subsequent hole until all thirty holes were filled. Then, in the same order, an old feeding cup was replaced by a new one with fresh food and so on. This rotation of trophic medium was maintained for several years.

After about six months the number of flies in the box reached the stable level of 14,000–17,000. Later, only insignificant fluctuations from this level were observed. Two of the boxes with quantitatively stabilized populations were "infected" with 50 pairs of normal flies. Every 50 days the number of flies in these boxes was thoroughly calculated, distinguishing normal (including heterozygous ebony) and homozygous ebony flies.

In Tables XII-3 and XII-4, the results of these experiments are shown. In both boxes the supplanting of ebony by normal flies occurred rather

TABLE XII-3

DISPLACEMENT OF EBONY FLIES FROM STABLE MODEL POPULATION WITH 30-DAY FOOD CYCLE (FIRST BOX)

	NUMBERS OF FLIES			PERCENTAGE	
DAYS	e	+	Total	e	+
0	14,380	0	14,380	100	0
50	10,107	6,104	16,211	62.5	37.5
100	7,402	7,925	15,327	48.4	51.6
150	5,883	11,680	17,563	33.4	66.6
200	3,140	12,131	15,271	20.6	79.4
250	1,388	12,354	13,742	10.1	89.9
300	1,118	14,512	15,630	7.2	92.8
350	1,237	13,644	14,881	8.3	91.7
400	1,511	14,641	16,152	9.4	90.6
450	1,126	16,086	17,212	6.5	93.5
500	1,131	14,215	15,346	7.4	92.6
550	1,374	14,496	15,870	8.6	91.4
600	1,113	14,403	14,516	7.6	92.4
650	1,320	14,852	16,172	8.2	91.8

TABLE XII-4

DISPLACEMENTS OF EBONY FLIES FROM STABLE MODEL POPULATION WITH 30-DAY FOOD CYCLE (SECOND BOX)

	NUMBER OF FLIES			PERCENTAGE	
DAYS	e	+	Total	e	+
0	15,281	0	15,281	100	0
50	9,972	6,377	16,349	58.5	41.5
100	7,336	8,374	15,710	48.9	53.1
150	5,329	9,564	14,893	35.8	64.2
200	3,161	12,689	15,850	19.9	80.1
250	1,301	14,331	15,632	8.3	91.7
300	1,601	14,523	16,124	9.9	90.1
350	1,201	13,075	14,276	8.0	92.0
400	1,347	14,067	15,414	8.7	91.3
450	1,591	15,134	16,725	9.5	90.5
500	1,548	13,789	15,337	10.1	89.9
550	1,427	14,753	16,180	8.8	91.2

quickly. After about 250 days the number of ebony flies had fallen to less than 10 per cent of the total number of flies in the box; then it became stabilized, fluctuating insignificantly about a certain mean value (8–9 per cent). In the first box calculations were performed for 650 days, in the second, for 550 days, counting from the moment of release of normal flies into the ebony population. Both populations gave very similar results as far as total number of flies in the boxes was concerned, as well as time changes and changes of stabilization level of percentage of normal and ebony flies. Fig. XII-2 shows the average percentage curve of time change

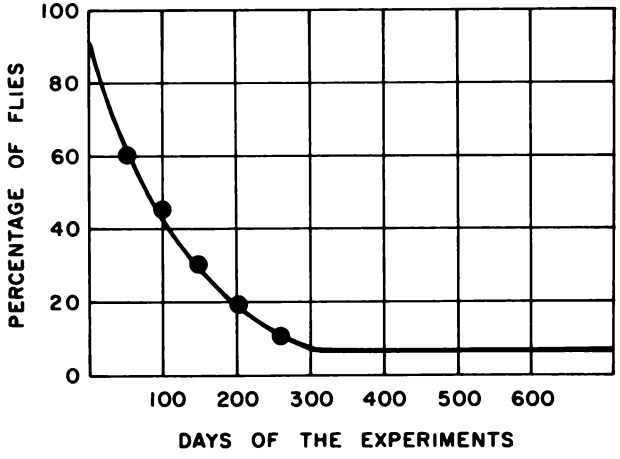

Fig. XII-2. The displacement of ebony flies by normal flies in a stable model population experiment.

of ebony flies for both boxes. Thus, both of the investigated, quantitatively stable fly populations showed that, despite a rather quick supplanting of ebony flies by normal flies at the beginning, ebony flies did not disappear from the population and were stabilized at a certain level, about which only insignificant fluctuations were observed later. It is conceivable to assume that this was due to the interaction of negative selection of homozygous ebony flies (in connection with their lowered relative viability) and positive selection of heterozygotes, which, as was shown above, are of higher relative viability.

Comparison of Theoretical and Experimental Results

In the experiments described above, a steady polymorphism state, connected with the highest viability of heterozygous flies, was observed. In the model constructed by us the following condition corresponds to this case:

$$\beta = 1; \qquad \alpha < 1; \qquad \gamma < 1.$$

Note that all results are preserved if we take that $\alpha = 1$, and, correspondingly, $\beta > 1$. Since in our experiments relative viability was determined in relation to normal form, we shall use the last symbols. Because the dynamics of the substitution of ebony flies was observed in quantitatively stabilized populations, it is only natural to assume the values of relative viability coefficients obtained under the conditions of highly overpopulated cultures. The following values of these coefficients were received:

$\alpha = 1$ for genotype $+/+$
$\beta = 1.083$ for genotype $+/e$
$\gamma = 0.718$ for genotype e/e.

In control experiments with plexus mutation:

$\beta = 1.085$ for genotype $+/e$
$\gamma = 0.776$ for genotype e/e.

Let us assume the mean values of these two as relative viability coefficients for the comparison of theoretical and experimental results:

$$\beta = 1.084; \qquad \gamma = 0.747.$$

The value of the polymorphous level of the wild allele (+) frequency for these values of β and γ equals:

$$p^* = \epsilon = \frac{\beta - \gamma}{2\beta - \gamma - 1} = 0.8.$$

Correspondingly, polymorphous levels for genotype frequencies will be as follows:

$$\begin{aligned}
&\text{frequency of genotype } +/+ = (p^*)^2 = 64\% \\
&\text{frequency of genotype } +/e = p^*(1 - p^*) = 32\% \\
&\text{frequency of genotype } e/e = (1 - p^*)^2 = 4\%.
\end{aligned}$$

In our experiment the polymorphous level of genotype e/e was about 8 per cent. Correspondingly, the polymorphous level of allele (+) was about 72 per cent in contrast to the theoretical level of 80 per cent. In Fig. XII-3 are shown the theoretical and experimental time-dependences of the percentage of allele (+) in population. Mean longevity of one *Drosophila* generation was assumed to be 15 days (720 hours). Experimental frequency p of allele (+) was calculated by formula:

$$p = 1 - \sqrt{w}$$

where w = percentage of ebony flies in population. Theoretical frequency p was calculated by formula (1.7). Since it was rather difficult at the beginning of the experiment to determine the initial frequency p_0, the frequency of allele (+) 50 days (~3.3 generations) after the beginning of the experiment equal to 22.5 per cent was assumed for p_0.

It is seen that at the point where the experimental curve reaches the plateau (20 generations and 300 days after the beginning of the experiment), the theoretical and experimental values of p coincide. Then the theoretical value of p increases, very slowly reaching its asymptotic 80 per cent value. Apparently, the very slow substitution of allele (e) could not be determined experimentally, since it would have demanded about 100 generations to obtain a marked difference between values $p(20)$ and $p(100)$. Besides, at small values of polymorphous level of ebony homozygote (~4%), even rather small absolute errors in the determination

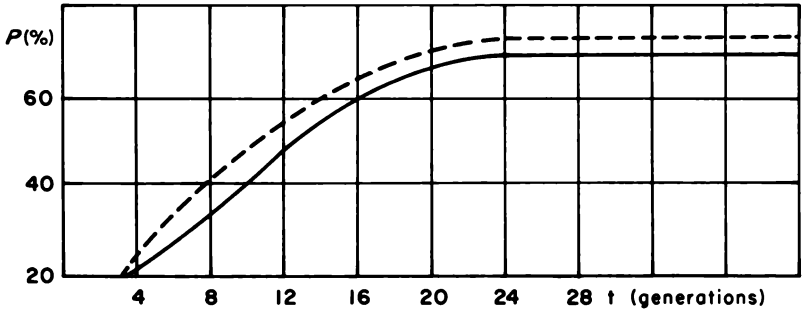

Fig. XII-3. Dynamics of the displacement of e allele from a population and the establishment of polymorphism (- - - - theoretical; —— experimental).

of percentage of homozygous ebony flies lead to greater relative errors. All these factors may somehow explain the discrepancy between theoretical and experimental results.

It is conceivable however, that a quite good correlation was obtained between theoretical and experimental data describing the dynamics of the establishment of polymorphism in population (taking into account difficulties in obtaining similar experimental data and the high probability of error). It indicates that a considerably accurate quantitative description of the real biological system was performed with the help of a mathematical model constructed by us.

Adaptational Polymorphism in Natural Populations of *Adalia bipunctata*; Theoretical Analysis of Adaptational Polymorphism

A population of *Adalia bipunctata* on the Institute territory in the vicinity of Berlin was chosen as material for this investigation. There was a stone building of an old church with deep crevices between stones in the southern wall. These crevices were chosen by *Adalia* and (in less quantities) other ladybug species for mass wintering places. During first two or three sunny warm days (usually in the first days of April) a mass emergence of overwintering ladybugs occurred. In the fall after the last warm period (usually at the end of October), a mass accumulation of ladybugs on the southern wall occurred. Then they crept into crevices for wintering. During these periods it was easy to collect large quantities of *Adalia* on the southern stony wall. The bugs were collected indiscriminately (all specimens) from a certain area of the wall, then divided into two main forms (red and black), scored separately, and released in the same place of wintering. In this simple way for ten years the composition of population which overwintered at a certain place was accurately estimated before and after wintering.

It is known that in many *Adalia bipunctata* populations, eight varying forms are found. Of these, three forms have black spots against brick-red background, the rest, red spots against black background. Under middle European conditions *Adalia*, as a rule, produce three generations during the vegetative period. In especially favorable years (an early spring and a late autumn), a fourth generation may appear in the fall, though such cases must be rare, according to laboratory data. In general, the last generation is most likely to overwinter, creeping into wintering places.

Adalia genetics was studied by Lus (1928, 1932, 1961) who found a simple monohybrid segregation in inheritance of red and black forms. The majority of variations of these forms described by systematists com-

prise a series of multiple alleles, black forms being dominant. In the population investigated by us, more than 97 per cent of all bugs belonged to forms *typica*, 4-*maculata*, 6-*pustulata*; the quantities of the remaining forms were negligible. As stated above, in our work we divided all bugs into two forms: red (*f. typica* and an insignificant number of two variants of *f. annulata*) and black (*f.* 6-*pustulata*, *f.* 4-*maculata* and an insignificant number of forms 2-*maculata*, *lunigera*, and *sublunata*).

After the emergence of all overwintering bugs, a rather large number of individuals which had died during winter remained in crevices, serving as wintering places. One of the large crevices was emptied thoroughly for three years before spring emergence of bugs. All *Adaliae* found were placed in glass containers. Forty-eight hours later all bugs that survived winter revived. The next day the number of live and dead bugs was estimated according to two main forms, which gave direct data on the overwintering of both forms.

Results of Quantitative Estimation of Two Main Forms in Population

The counts of bugs were performed from 1930 to 1940, excluding 1932. Altogether, in spring collections more than 55,000 individuals were registered, in autumn collections, more than 105,000. Yearly results of collections of two forms, red and black, are shown in Table XII-5.

It is clear from this table that in all cases red bugs prevailed in spring collections and black bugs in autumn ones. In spring collections the percentage of red bugs varied, during the ten years, from 57 to 71 per cent and in autumn ones, from 30 to 49 per cent.

The results obtained show that the relative viability of the red form in the winter period is higher than is that of the black one. The picture reverses in the summer period apparently because of increased rates of development and fecundity (in comparison with red form), as well as a higher rate of survival of the black form under summer conditions.

It is possible to assume that constant dimorphism in *Adalia* populations is due to differently directed selection pressure on each of the forms in different seasons. During wintering, the red form is subject to positive selection, whereas the black form is in the breeding period, the warm time of the year.

To confirm this assumption, for three years the live and dead bugs of both forms were counted at a certain wintering place, just before spring emergence. The results are shown in Table XII-6. Data in this table confirm conclusions drawn from the data of Table XII-5. For all three years, among the total number of live and dead bugs in the wintering place, the black form prevailed. Among surviving bugs, however, the red

TABLE XII-5

NUMBER OF BLACK AND RED FORMS OF *Adalia* IN SPRING (APRIL) AND AUTUMN (OCTOBER) COLLECTIONS AT THE WINTERING PLACE DURING TEN YEARS

	SPRING					AUTUMN				
		Black		Red			Black		Red	
YEAR	Total	No.	%	No.	%	Total	No.	%	No.	%
1930	604	176	29.1	428	70.9	1,244	783	70.2	461	29.8
1931	777	334	43.0	443	57.0	1,116	622	55.7	494	44.3
1933	570	213	38.1	357	61.9	1,009	675	66.9	334	33.1
1934	432	149	34.5	283	65.5	1,237	708	66.1	529	33.9
1935	553	199	36.2	354	63.8	981	500	51.0	481	49.0
1936	492	171	34.7	321	65.3	818	435	53.2	383	46.8
1937	397	162	40.8	235	59.2	921	513	55.7	408	44.3
1938	471	192	40.7	279	59.3	880	448	51.0	432	49.0
1939	687	234	34.1	453	65.9	1,223	686	56.1	537	43.9
1940	571	239	41.8	332	58.2	1,142	755	66.1	387	33.9
Total	5,554	2,069	37.3	3,485	62.7	10,571	6,125	58.0	4,446	42.0

form predominated, exceeding the percentage of the black form by two to three times. It is quite clear that the red form has an essential advantage in winter season. In Fig. XII-4 are presented diagrams showing changes in the relative percentages of black and red forms and frequencies of corresponding alleles by years.

TABLE XII-6

WINTER SURVIVAL OF *Adalia*. DATA ON THREE WINTER SEASONS FOR ONE OF THE WINTERING PLACES

		TOTAL		SURVIVORS		
YEAR	FORM	No.	%	No.	%	% of Total Beetles
	Black	1,845	63.9	78	40.2	4.2
1930	Red	1,044	36.1	116	59.8	11.1
	Total	2,889	100.0	194	100.0	6.7
	Black	2,018	58.7	121	41.8	6.0
1931	Red	1,416	41.3	168	58.2	11.9
	Total	3,434	100.0	289	100.0	8.4
	Black	1,983	66.1	63	40.1	3.1
1933	Red	1,018	33.9	94	59.9	9.2
	Total	3,001	100.0	157	100.0	5.2

Theoretical Analysis of Adaptational Polymorphism

Since in the panmictic, rather large *Adalia* population, a simple monohybrid segregation takes place, one can assume that allele *A* determines black form, and allele *a*, the red one, *A* being dominant. Then heterozygotes *Aa* do not differ phenotypically from homozygotes *AA*. Hence, it is possible to assume that the relative viability of homozygote *AA* equals that of heterozygote *Aa*. As was shown above, *Adalia* usually produces three generations during the vegetative period, the third generation generally overwintering. Let us assume that two summer generations are subject to one selection pressure and the wintering generation, to another, each of these pressures being quantitatively constant during the lifetime of two summer and one wintering generations, and, correspondingly, changing abruptly from summer to wintering generations, and vice versa. The same can be said about values quantitatively characterizing these selection pressures—relative viability coefficients.

Let us consider wintering generations. Experimental data in Tables XII-5 and XII-6 allow one to determine the relative frequencies of genotypes at the beginning of the life of the wintering generation (autumn collections) and at the end of it (spring collections). Indeed, if u, $2v$, w are

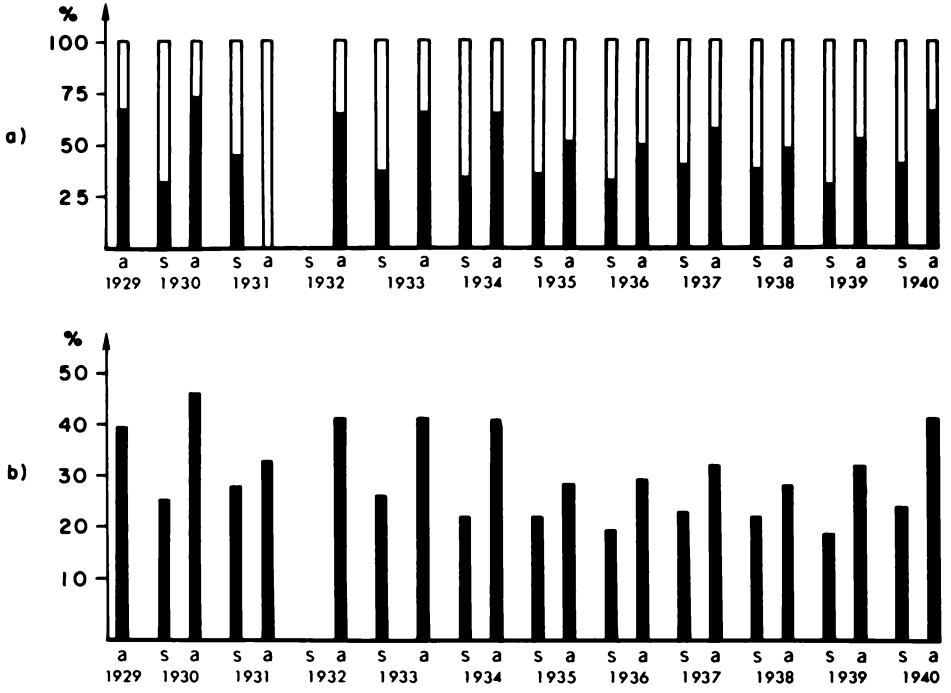

Fig. XII-4. (*a*) The percentage of the black and red forms of *Adalia* in spring (*s*) and autumn (*a*) populations. The dark sections of the columns indicate the black form. (*b*) The frequency of the dominant gene *A* (the black) in the population in spring (*s*) and autumn (*a*) yearly collections.

frequencies of genotypes *AA*, *Aa* (black form), and *aa* (red form) at the beginning of the life of population, and u^*, $2v^*$, w^*— at the end, then values $u + 2v$, w; $u^* + 2v^*$, w^* are the relative percentages of the black and red forms in the population in the autumn collection of the previous year and spring collection of the next year, respectively. It was shown above that the red form has maximum viability in the winter period. It is natural to assume, therefore, that the relative viability coefficient of homozygote *aa* equals 1. As above, let us denote relative viability coefficients of genotypes *AA*, *Aa*, and *aa* by α, β, γ, respectively.
Then $\gamma = 1$; $\alpha = \beta$. If

$$\gamma = 1, \text{ then } \alpha = \beta = \frac{u^*v}{uv^*} = \frac{v^*w}{w^*v}.$$

From this, it is easy to calculate

$$\alpha = \beta = \frac{u^* + 2v^*}{u + 2v} \cdot \frac{w}{w^*}. \tag{3.1}$$

Using the results of Tables XII-5 and XII-6 and employing (3.1), it is possible to calculate the relative viability coefficients $\alpha = \beta$ for the wintering population for almost all winters from 1928 to 1940 (excluding the winter of 1931–32). Values of these coefficients are presented in Table XII-7.

Let us note that for the winter of 1930–31, we obtained two different values $\alpha = \beta$. One value $\alpha = \beta = 0.32$ was calculated according to data of Table XIII-5, when autumn and spring collections were made on the wall before the bugs crept in for wintering and immediately after emergence from wintering places. The second value $\alpha = \beta = 0.506$ was calculated according to data of Table XII-6, when before emergence from one of the crevices a relative percentage of live and dead red and black forms was calculated. However, quantitative discrepancy in the relative viability coefficients, calculated according to two different series of experimental results, is not of major importance. It can be explained by the influence of a large number of non-controlled random factors leading to considerable variations in these values.

Let us consider now the summer generations. In this case, however, we cannot calculate the relative viability coefficients directly on the ground of experimental data, because frequencies of corresponding genotypes at the beginning and end of life of the summer generations are unknown. We shall, therefore, proceed as follows. (Let us first note that since in the summer period black form has the highest relative viability, then $\alpha = \beta = 1$; $\gamma < 1$.)

Let us consider three generations in turn. In the wintering generation we know the frequencies of corresponding genotypes at the beginning of life of the generation. Then p_0 frequency of gene A at the moment equals

$$p_0 = 1 - \sqrt{w_0}\,; \tag{3.2}$$

where w_0 = frequency of zygote aa at the beginning of life of the wintering generation. Since we know the relative viability coefficient $\alpha = \beta$ of genotypes AA and Aa in the winter period, then from formula (1.5) we shall have (at $\alpha = \beta$; $\gamma = 1$)

$$p_1 = \frac{\alpha p_0}{p_0^2(1 - \alpha) - 2p_0(1 - \alpha) + 1}; \tag{3.3}$$

where p_1 = frequency of gene A *at* the end of the life of the wintering generation. Quite similarly (at $\alpha = \beta = 1$) for the frequency of gene A at the end of the first generation, we shall have:

$$p_2 = \frac{p_1}{p_1^2(\gamma - 1) - 2p_1(\gamma - 1) + \gamma}; \tag{3.4}$$

and for the frequency of gene A at the end of the life of the second summer generation:

$$p_3 = \frac{p_2}{p_2^2(\gamma - 1) - 2p_2(\gamma - 1) + \gamma}. \tag{3.5}$$

Here we assume that during the lifetime of two summer generations the relative viability coefficients do not change, and, finally, for the frequency of gene A at the beginning of the life of the next wintering generation we shall have:

$$p_3 = 1 - \sqrt{w_1}. \tag{3.6}$$

Here w_1 = the frequency of genotype aa at the beginning of life of the next wintering generation. Since α is known, values p_1 and p_3 may be estimated easily by formulas (3.2), (3.3), and (3.6) from experimental data in Tables XII-5 and XII-6. Excluding value p_2 from (3.4) and (3.5), we shall have an equation for estimation of

$$(1 - p_1)^4\gamma^3 + 2p_1(1 - p_1)^3\gamma^2 + p_1(1 - p_1)^2(p_1 - \delta)\gamma$$

$$= p_1^2[1 + \delta(2 - p_1)]; \qquad \delta = \frac{1 - 2p_3}{p_3}. \tag{3.7}$$

With the help of data in Tables XII-5, XII-6, and XII-7, let us determine from equation (3.7) the values of the relative viability coefficients γ of genotype *aa* for all summer periods from 1930 to 1940, excluding the summer of 1932. These values are presented in Table XII-8. For the summer of 1931, for the same reasons as for the winter of 1931–32, two values of γ are presented. In addition, calculated according to formulas (3.2), (3.3), and (3.6), the frequencies of gene A in spring and autumn of

TABLE XII-7

COEFFICIENTS OF RELATIVE VIABILITY OF *AA* AND *Aa* ZYGOTES IN WINTER SEASON

YEAR	$\alpha = \beta$
1929–30	0.380
1930–31	0.320 (0.506)
1932–33	0.343
1933–34	0.261
1934–35	0.291
1935–36	0.510
1936–37	0.605
1937–38	0.545
1938–39	0.498
1939–40	0.560

TABLE XII-8

COEFFICIENTS OF RELATIVE VIABILITY OF *aa* ZYGOTES IN SUMMER SEASON

YEAR	γ
1930	0.415
1931	0.780 (0.820)
1933	0.473
1934	0.400
1935	0.775
1936	0.656
1937	0.736
1938	0.850
1939	0.612
1940	0.550

every year (beginning with the autumn of 1929 and ending with the autumn of 1940, excluding the spring of 1932) are presented in Table XII-9.

TABLE XII-9

FREQUENCIES OF GENE *A* (DOMINANT ALLELE) IN STUDIED POPULATION OF *Adalia* IN SPRING (*s*) AND AUTUMN (*a*)

YEAR	SEASON	FREQUENCY OF *A*(p)
1929	a	0.400
1930	s	0.254
1930	a	0.454 (0.400)
1931	s	0.282 (0.300)
1931	a	0.335 (0.357)
1932	s	—
1932	a	0.418
1933	s	0.254
1933	a	0.425
1934	s	0.221
1934	a	0.418
1935	s	0.228
1935	a	0.300
1936	s	0.202
1936	a	0.315
1937	s	0.241
1937	a	0.334
1938	s	0.236
1938	a	0.300
1939	s	0.202
1939	a	0.338
1940	s	0.252
1940	a	0.417

Dynamics of Adaptational Polymorphism in Adalia bipunctata Population

To receive a clearer picture of intra-population polymorphism in *Adalia bipunctata*, let us construct a phase trajectory of the dynamic system describing the change of frequency of gene *A* in the population under the influence of selection pressure.

Since in the summer $\alpha = \beta = 1; \gamma < 1$, and in the winter $-\alpha = \beta < 1; \gamma = 1$, equation (1.8) for summer will be written as follows:

$$\frac{dp}{dt} = \frac{p(1-p)^2}{[\gamma/(1-\gamma)] + 2p - p^2}; \tag{3.8}$$

and for winter as:

$$\frac{dp}{dt} = \frac{p(1-p)^2}{[1/(\alpha-1)] + 2p - p^2}. \tag{3.9}$$

With the help of viability coefficients taken from Tables XII-8 and XII-9, let us construct phase trajectories of the system described by equations (3.8), (3.9), as shown in Fig. XII-5.

It is seen from the considered phase picture that the system fluctuates within a yearly period about a certain slowly drifting center, the deviation of which occurs apparently as a result of changes from year to year in climatic conditions. Since climatic conditions have a certain periodicity, one can assume that the drift of the center also occurs about some equilibrium and that, consequently, such state of polymorphism can be regarded stable.

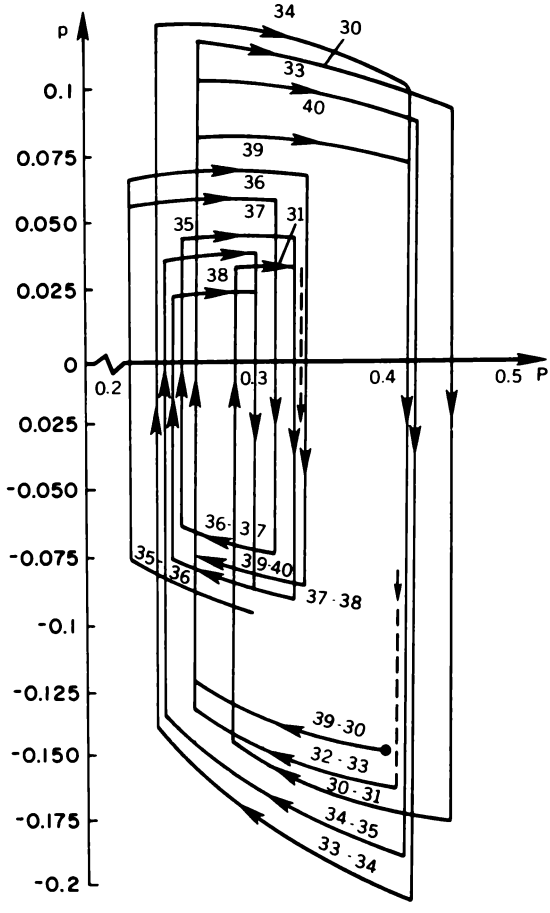

Fig. XII-5. The phase trajectory of a system describing the changes in the frequency of gene *A* in the population under the action of the oppositely directed selection pressures during the different seasons of the year. The phase cycles of the winter season of 1931–32 and the summer season of 1932, for which we have no experimental data, are dotted.

Unlike the previous case of heterozygote polymorphism, where a steady polymorphous state was secured by a higher relative viability of heterozygote and was described by a point on axis p, in this case we deal with a whole area of polymorphism, in which the describing point can not be in the state ($\dot{p} = 0$; $0 < p < 1$). If environmental conditions were constant, the system would be polymorphically unstable (stable states: $p \equiv 0$; $p \equiv 1$), but seasonal changes of environmental conditions ensure the steady polymorphous state. It is conceivable that intra-population polymorphism in the case of *Adalia bipunctata* is ensured by different adaptation of various genotypes to environmental conditions in the winter and summer seasons, and therefore it can be termed the "adaptational polymorphism."

Conclusion

Two essentially different types of polymorphism—heterozygotic and adaptational—were studied. It was shown, both theoretically and experimentally, that in the case of heterozygotic polymorphism the stabilization of mutant homozygotes in a population is due to high relative viability of heterozygotes. Naturally, similar polymorphic conditions may be attained at some other quantitative relations between the relative viabilities under question: a necessary and sufficient requirement for such stable state of polymorphism to exist is higher relative viability of the heterozygote as compared to both the homozygotes.

Unlike the heterozygotic polymorphism, which was attained at constant values of coefficients of relative viability, the adaptational polymorphism in a population of *Adalia bipunctata* was established on the basis of periodic changes in the coefficients, connected with the various degrees of adaptation of the red and the black forms in winter and summer seasons.

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