A MATHEMATICAL MODEL FOR THE CO-EVOLUTION OF OBLIGATE PARASITES AND THEIR HOSTS[1]

CHARLES J. MODE[2]
Department of Mathematics, Montana State College
Received September 9, 1957

INTRODUCTION

The genetics of disease resistance in plants has been studied by numerous investigators since Biffen first reported in 1905 that host resistance to plant pathogens was a Mendelian character. Although a considerable literature on the genetics of disease resistance has accumulated through the years, the work of Flor, Briggs, and his associates is particularly notable in that a concerted effort has been made to explore the genetic structure of a species in terms of disease resistance. In the present paper, the genetic systems uncovered by the work of Flor, Briggs, and his associates will be briefly reviewed and their evolutionary significance will be interpreted from the standpoint of population genetics.

REVIEW OF LITERATURE

The genetics of pathogenicity and host resistance to flax rust, *Melampsora lini* (Pers) Lev., has been reported by Flor (1955 and 1956). Through a series of genetic studies, Flor has shown that the host and parasite possess complementary genetic systems. That is to say, any gene in the host for resistance acts if and only if there is a corresponding gene in the pathogen for avirulence.

The genes for host resistance exist as a series of multiple alleles at five loci, designated as the K, L, M, N, and P. There is one gene at the K locus, 11 at the L, six at the M, three at the N, and four at the P, making a total of twenty-five genes identified thus far (Flor, 1956). The K, L, and M loci are inherited independently, but the N and P loci are linked with about 26 percent recombination. Unlike the genes for host resistance, the genes for pathogenicity in the pathogen exist at twenty-five separate loci.

Resistance of a host genotype to a particular pathogen genotype occurs whenever any allele in the host (at any one of the five multiple allelic loci) and its complementary gene for avirulence in the pathogen (at any one of the twenty-five diallelic loci) are present simultaneously. The alleles for host resistance are all dominant or semi-dominant so that the heterozygote as well as the homozygote is resistant. The genes for avirulence in the pathogen are also dominant, with the exception of one locus where the homozygous recessive in combination with one or two doses in the host is necessary for resistance. These complementary genetic systems of the host and parasite can best be understood by inspection of the model set forth in table 1. In this model the host has three alleles at one

TABLE 1. *A triallelic-digenic model illustrating the complementary genetic systems of flax and flax rust*

Pathogen Rust phenotype	Host Flax genotype					
	R_1R_1	R_2R_2	R_1R_2	R_1r	R_2r	rr
A_1–A_2–	R	R	R	R	R	S
A_1–a_2a_2	R	S	R	R	S	S
$a_1a_1A_2$–	S	R	R	S	R	S
$a_1a_1a_2a_2$	S	S	S	S	S	S

R—Host resistance and avirulence of the pathogen.

S—Host susceptibility and virulence of the pathogen.

[1] A portion of a thesis submitted to the Graduate Division, Univ. of Calif., Davis, in partial fulfillment of the requirements for the Ph.D. degree.

[2] Statistical Geneticist, Department of Mathematics, Montana State College, Bozeman.

locus and the pathogen a pair of alleles at each of two loci. The notation has been adopted from that of Flor (1955), and for the sake of simplicity complete dominance is assumed.

From inspection of table 1 it will be noted that only those host genotypes possessing the R_1 gene are resistant to the pathogen phenotype, A_1–a_2a_2, due to the interaction of gene R_1 in the host and gene A_1 in the pathogen. The recessive host genotype rr, on the other hand, is susceptible to all phenotypes of the pathogen due to the absence of dominant genes for resistance. Likewise, the pathogen genotype, $a_1a_1a_2a_2$, is virulent on all host genotypes due to the absence of dominant genes for avirulence.

An additional feature to be noted from the table is that host genotype, R_1R_2, is resistant to three phenotypes of the pathogen, whereas the other host genotypes possessing dominant genes are resistant to only two. In other words, the presence of two different alleles for host resistance produces an overdominant effect, a necessary condition for the maintenance of stable polymorphism under random mating.

In contrast to the work of Flor, in which both the genetics of the host and parasite were studied, Briggs and his associates have confined their efforts to the genetics of host resistance. Schaller and Briggs (1955a), summarizing the results of long-term investigations on the inheritance of resistance to stinking smut (*Tillitia caries* (DC.) of wheat, report that four genes for disease resistance—H, M, R, and T—belong to the same linkage group. Extensive investigations on the inheritance of resistance to powdery mildew of barley, *Erysiphe graminis hordie* (DC.), have produced similar results. Out of a total of ten genes for mildew resistance identified thus far, five have been found to belong to linkage group II (Schaller and Briggs, 1955b). At one of the five linked loci, at least two alleles for resistance occurs. The genes for resistance to stinking smut of wheat are rather loosely linked, ranging from about a minimum of 15 to a maximum of 37 per cent recombination between two adjacent genes. The genes for resistance to mildew of barley, however, are more tightly linked, the minimum and maximum recombination between two adjacent genes being about 10 and 18 per cent respectively.

From the evolutionary standpoint, at least three questions arise in connection with genetic systems uncovered by the work of Briggs and Flor: (1) What are the consequences of the complementary genetic systems of host and parasite when both the host and parasite mate at random over long periods of time? (2) What is the significance of linkage of genes for disease resistance? (3) What relationship does the genetic systems uncovered by the work of Briggs and Flor bear to the co-evolution of obligate parasites and their hosts? These questions will be considered in turn, but first it is necessary to digress for a moment and discuss some biology of the organisms in question, since a biological understanding of the situation is essential to mathematical arguments that follow.

Biological Considerations

Flax rust is an obligate parasite and cannot survive apart from its host. It is autoecious, i.e., all spore forms are produced on a single host. In mild climates the rust may live from year to year in the uredial or repeating stage, but in more rigorous climates it overwinters as telia on flax straw from the previous season.

The dikaryotic teliospores germinate in the spring and ultimately give rise to haploid sporidia. Sporidial infection of the host plants results in the formation of pycnia of two complementary mating types, plus and minus. Unless a pycnium is fertilized by a pycniospore of the opposite mating type, it is incapable of further development, making the flax rust fungus on obligate outbreeder. A

fertilized pycnium gives a rise to dikaryotic aeciospores, and the aeciospores in turn give rise to the uredial stage which produces a new generation about every ten days. When the fungus is unable to maintain itself in the uredial stage, then, the initiation of each year's infection is concomitant with a sexual-like process. In light of the biology of the flax rust fungus, therefore, it may be treated mathematically as an ordinary diploid organism.

When we consider the evolution of a species from the standpoint of population genetics, the mating system is of prime importance. Since all the host plants in question reproduce by self-fertilization, it is necessary to consider briefly the evolution of selfing systems. There is general agreement among most evolutionists that selfing systems have evolved from previously existing outcrossing systems. Stebbins (1950) states that there is little doubt that the genetic system promoting greater flexibility is the ancestral one; and that self-fertilized types, such as certain annual grasses and herbs, have arisen repeatedly in various phyla and classes in response to selection pressures presumably for immediate fitness.

Throughout this paper we shall assume that such self-fertilized, cultivated annuals as wheat, barley, and flax, like their counterparts in nature, have evolved from open-pollinated ancestors. If this is the case, the genetic structure of these species has evolved for the most part under a system of random mating. Furthermore, it seems reasonable to assume, as suggested by Flor (1955), that such obligate parasites as the rust, smut, and mildew fungi have evolved in association with their hosts. The genetic system of the host and parasite, therefore, have very likely been established in response to two types of opposing selection pressures, namely, the selection pressure exerted on the host by the parasite, and the selection pressure exerted on the parasite by the host. Such selection pressures, acting from remotest antiquity, have very likely resulted in the establishment of genetic systems uncovered by present-day genetic studies. Having disposed of some preliminary biological considerations, we are now ready for a mathematical model of a host-pathogen system.

A Mathematical Model of a Host-Pathogen System

Consider a host-pathogen system in which both the host and parasite mate at random with respect to a single locus in the host and two independent loci in the pathogen. Assume that Flor's complementary genetic systems hold. Let x_1 and x_2 ($x_1 + x_2 = 1$) be the frequencies of genes R_1 and R_2 respectively in the host population, and let y_1, y_2, y_3, and y_4 ($y_1 + y_2 + y_3 + y_4 = 1$) be the frequencies of the gametes A_1A_2, A_1a_2, a_1A_2, and a_1a_2 respectively in the pathogen population.

We shall measure the two opposing selection pressures of the host and parasite in terms of constants analogous to Fisher's (1930) Malthusian parameters. It is assumed that the fitness of the host in a particular host-parasite combination varies inversely as the fitness of the pathogen. That is, if s is the fitness of the pathogen in a particular combination the fitness of the host is a $-$ks. To put it another way, the contributions of offspring of the host and parasite to the next generation are proportional to e^{s} and e^{-ks} respectively. The fitness of the various pathogen genotypes in the vari-

Table 2

Pathogen		Host		
		x_1^2 R_1R_1	$2x_1x_2$ R_1R_2	x_2^2 R_2R_2
y_1^2	$A_1A_1A_2A_2$	s_1	s_1	s_1
$2y_1y_3$	$A_1a_1A_2A_2$	s_2	s_1	s_1
$2y_1y_2$	$A_1A_1A_2a_2$	s_1	s_1	s_2
$2(y_1y_4 + y_2y_3)$	$A_1a_1A_2a_2$	s_2	s_2	s_2
y_2^2	$A_1A_1a_2a_2$	s_1	s_1	s_3
$2y_2y_4$	$A_1a_1a_2a_2$	s_2	s_2	s_3
y_3^2	$a_1a_1A_2A_2$	s_3	s_1	s_1
$2y_3y_4$	$a_1a_1A_2a_2$	s_3	s_2	s_2
y_4^2	$a_1a_1a_1a_1$	s_4	s_4	s_4

ous host-parasite combinations in the proposed system are given in table 2. The fitness of the various host genotypes in a particular combination is obtained by multiplying by $-k$.

The over-all fitness of a particular pathogen genotype is obtained by weighting the fitness of the parasite in each host-pathogen combination by the frequency of the host genotype. Thus the over-all fitness of the pathogen genotype $A_1A_1A_2A_2$ is $s_1(x_1^2 + 2x_1x_2 + x_2^2) = s_1$. Proceeding in the same way, we find the over-all fitness of the host genotype R_1R_1 is $-k[s_1(y_1 + y_2)^2 + 2s_2(y_1 + y_2)(y_3 + y_4) + s_3(y_3^2 + 2y_3y_4) + s_4y_4^2]$.

Continuing in this manner, the two opposing selection pressures of the host and parasite may be presented in tabular form. The selection pressure exerted on the host by the pathogen population is given in table 3; while the selection pressure exerted on the pathogen by the host population is given in table 4.

Under the assumption of continuous generation time, and proceeding in a manner similar to that of Crow and Kimura (1955) and Kimura (1956), the rate of change in the gene and gametic frequencies of the system may be expressed by the set of differential equations:

$$\dot{x}_i = x_i(m_{i.} - \bar{m}) \quad (\text{for } i = 1, 2) \qquad (1)$$
$$\dot{y}_i = y_i(\mu_{i.} - \bar{\mu}) \quad (\text{for } i = 1, 2, 3, 4)$$

TABLE 3

	x_1 R_1	x_2 R_2
x_1R_1	m_{11}	m_{12}
x_2R_2	m_{21}	m_{22}

where

$$m_{11} = -k\{s_1(y_1+y_2)^2+2s_2(y_1+y_2)(y_3+y_2)+s_3(y_3^2+2y_3y_4)+s_4y_4^2\}$$
$$m_{12}=m_{21} = -k\{s_1[(y_1+y_2)^2+2y_1y_3+y_3^2]+2s_2[y_4(y_1+y_2)+y_3(y_2+y_4)]+s_4y_4^2\}$$
$$m_{22} = -k\{s_1(y_1+y_3)^2+2s_2(y_1+y_3)(y_2+y_4)+s_3(y_2^2+2y_2y_4)+s_4y_4^2\}$$

TABLE 4

	y_1 A_1A_2	y_2 A_1a_2	y_3 a_1A_2	y_4 a_1a_2
$y_1A_1A_2$	μ_{11}	μ_{12}	μ_{13}	μ_{14}
$y_2A_1a_2$	μ_{21}	μ_{22}	μ_{23}	μ_{24}
$y_3a_1A_2$	μ_{31}	μ_{32}	μ_{33}	μ_{34}
$y_4a_1a_2$	μ_{41}	μ_{42}	μ_{43}	μ_{44}

where

$\mu_{11}=s_1$; $\mu_{12}=\mu_{21}=(1-x_2^2)s_1+s_2x_2^2$;
$\mu_{13}=\mu_{31}=s_2x_1^2+(1-x_1^2)s_1$;
$\mu_{14}=\mu_{41}=\mu_{32}=\mu_{23}=s_2$;
$\mu_{22}=(1-x_2^2)s_1+x_2^2s_3$;
$\mu_{24}=\mu_{42}=(1-x_2^2)s_2+s_3x_2^2$;
$\mu_{33}=x_1^2s_3+(1-x_1^2)s_1$;
$\mu_{34}=\mu_{43}=x_1^2s_3+(1-x_1^2)s_2$, and $\mu_{44}=s_4$

where

$$m_{i.} = \sum_{j=1}^{2} x_jm_{ij}, \quad \bar{m} = \sum_{i=1}^{2}\sum_{j=1}^{2} x_ix_jm_{ij},$$

$$\mu_{i.} = \sum_{j=1}^{4} y_j\mu_{ij}, \quad \bar{\mu} = \sum_{i=1}^{4}\sum_{j=1}^{4} y_iy_j\mu_{ij},$$

and

$$\dot{x}_i = \frac{dx_i}{dt}.$$

At equilibrium the conditions, $\dot{x}_i = 0$ $(i = 1, 2)$ and $\dot{y}_i = 0$ $(i = 1, 2, 3, 4)$, must be satisfied, or equivalently

$$m_{i.} - \bar{m} = 0 \quad (\text{for } i = 1, 2) \qquad (2)$$
$$\mu_{i.} - \bar{\mu} = 0 \quad (\text{for } i = 1, 2, 3, 4)$$

To solve for the gene and gametic frequencies in terms of the parameters of the system is not only difficult but leads to very cumbersome algebraic expressions. A simpler approach is to specify the gene frequencies at equilibrium and then place conditions on the parameters, s_1, s_2, s_3, and s_4. For instance, suppose

the opposing selection pressures are such that the equilibrium $x_1 = x_2 = 1/2$ and $y_1 = y_2 = y_3 = y_4 = 1/4$. Then the parameters of the system must satisfy the equations

$$\begin{aligned} 2s_1 - s_2 - s_3 &= 0 \\ 5s_1 - 2s_2 - s_3 &= 2s_4 \\ 3s_1 - s_2 &= 2s_4 \end{aligned} \tag{3}$$

These equations are not linearly independent, i.e., the first equation is the difference of the latter two and so on. By choosing arbitrary values of two parameters, however, the other two may be determined uniquely by solving any two of the above equations simultaneously.

The next and crucial part of the problem is to obtain the stability conditions for this equilibrium. The methodology for obtaining these conditions has been set forth in detail by Bellman (1953) and has also been used by Kimura (1956). To simplify the argument let x_3 and x_4 be the frequencies of genes A_1 and A_2 respectively in the pathogen population. Then the gametic frequencies become $y_1 = x_3x_4$, $y_2 = x_3(1 - x_4)$, $y_3 = (1 - x_3)x_4$, and $y_4 = (1 - x_3)(1 - x_4)$, and differential equations (1) reduce to the following set of differential equations:

$$\begin{aligned} \dot{x}_1 &= x_1(m_{1.} - \bar{m}) \\ \dot{x}_3 &= \dot{y}_1 + \dot{y}_2 = x_3[x_4\mu_{1.} + (1 - x_4)\mu_{2.} - \bar{\mu}] \\ \dot{x}_4 &= \dot{y}_1 + \dot{y}_3 = x_4[x_3\mu_{1.} + (1 - x_3)\mu_{3.} - \bar{\mu}] \end{aligned} \tag{4}$$

To derive the stability conditions for this equilibrium we begin by evaluating the second differentials of the above equations at equilibrium. Thus in matrix form we have

$$\begin{bmatrix} \delta\dot{x}_1 \\ \delta\dot{x}_3 \\ \delta\dot{x}_4 \end{bmatrix} = \begin{bmatrix} \left(\frac{\partial\dot{x}_1}{\partial x_1}\right)_e & \left(\frac{\partial\dot{x}_1}{\partial x_3}\right)_e & \left(\frac{\partial\dot{x}_1}{\partial x_4}\right)_e \\ \left(\frac{\partial\dot{x}_3}{\partial x_1}\right)_e & \left(\frac{\partial\dot{x}_3}{\partial\dot{x}_3}\right)_e & \left(\frac{\partial\dot{x}_3}{\partial x_4}\right)_e \\ \left(\frac{\partial\dot{x}_4}{\partial x_1}\right)_e & \left(\frac{\partial\dot{x}_4}{\partial x_3}\right)_e & \left(\frac{\partial\dot{x}_4}{\partial x_4}\right)_e \end{bmatrix} \begin{bmatrix} \delta x_1 \\ \delta x_3 \\ \delta x_4 \end{bmatrix}$$

where $(\partial\dot{x}_1/\partial x_1)_e$ means $\partial\dot{x}_1/\partial x_1$ evaluated at equilibrium and so on.

In terms of the parameters of the system, the above equation becomes

$$\begin{bmatrix} \delta\dot{x}_1 \\ \delta\dot{x}_3 \\ \delta\dot{x}_4 \end{bmatrix} = \begin{bmatrix} (\frac{7}{16}s_1 + \frac{1}{2}s_2 + \frac{1}{16}s_4) & -\frac{1}{8}(s_1 - s_3) & \frac{1}{8}(s_1 - s_3) \\ (\frac{1}{8}(s_1 - s_3)) & \frac{5}{16}(s_1 - s_2) & \frac{1}{16}(\frac{3}{2}s_1 - s_2 - \frac{3}{2}s_3 + s_4) \\ -\frac{1}{8}(s_1 - s_3) & \frac{1}{16}(\frac{3}{2}s_1 - s_2 - \frac{3}{2}s_3 + s_4) & \frac{1}{8}(s_1 - \frac{1}{2}s_2 - \frac{1}{4}s_3) \end{bmatrix} \begin{bmatrix} \delta x_1 \\ \delta x_3 \\ \delta x_4 \end{bmatrix}$$

The necessary and sufficient conditions that the equilibrium be stable is that all solutions of the above equations tend to zero as $t \to \infty$, or that the characteristic roots of the above matrix be negative and real. By straight forward calculations we get the characteristic equation in the following form:

$$\lambda^3 - A\lambda^2 - B\lambda - c = 0$$

where

$$\begin{aligned} A &= a_{11} + a_{22} + a_{33}, \\ B &= a_{12}a_{21} + a_{13}a_{31} + a_{23}a_{32} \\ &\quad - (a_{11}a_{22} + a_{11}a_{33} + a_{22}a_{33}), \\ C &= a_{11}(a_{23}a_{32} - a_{22}a_{23}) \\ &\quad - a_{12}(a_{21}a_{33} - a_{31}a_{23}) \\ &\quad - a_{13}(a_{31}a_{22} - a_{21}a_{32}) \end{aligned}$$

and the a's are the elements of the above matrix, i.e., $a_{11} = \frac{7}{16}s_1 + \frac{1}{2}s_2 + \frac{1}{16}s_4$, $a_{12} = -\frac{1}{8}(s_1 - s_3)$ and so on. The roots of the above cubic equation will be negative and real if and only if $A < 0$, $B < 0$, $C < 0$, and $AB - C > 0$. By specifying values of s_1, s_2, s_3, and s_4, we are in a position to determine the stability of the equilibrium.

For example, suppose we set $s_3 = 0$ and $s_4 = -0.05$, then the simultaneous solution of equations (3) yields $s_1 = -0.10$ and $s_2 = -0.20$. Evaluating the above matrix for these values of s_1, s_2, s_3, and s_4 we find $A = -13/8 < 0$, $B = -67/256 < 0$, $C = -5/2048 < 0$; therefore $AB - C > 0$. Hence, $x_1 = x_2 = x_4 = \frac{1}{2}$ in a stable equilibrium point.

From the mathematical model we see that a host-pathogen system operating under complementary genetic systems of the host and parasite will eventually reach a state of stable equilibrium, providing the above conditions are met. A state of stable equilibrium is advantageous to both the host and parasite. In the first place, a stable pathogen population solves the host's problem of maintenance of resistance to disease, and secondly the pathogen is able to survive without eliminating its host. For, if the genotypes in the pathogen population are not held constant by selection pressure, they will shift in frequency and the more virulent genotypes will finally predominate, resulting in complete susceptibility of the host population. A completely susceptible host population is actually disadvantageous to the pathogen population in the long run. For, under such circumstances, the pathogen tends to eliminate the host and thus eliminates itself in the process. On the other hand, when the opposing selection pressures are such that genes for host resistance and genes for avirulence are held in the system in constant frequency, it is possible for the host and parasite to co-exist over long periods of time. Thus, the problem of the pathogen, existence without eliminating its host, and the problem of the host, the maintenance of resistance to the pathogen, have been solved simultaneously by the complementary genetic systems of the host and parasite.

Linkage of Genes for Disease Resistance

In some situations, linkage of genes for host resistance may also lead to a stable state in a host-pathogen system. For instance, suppose we have a system consisting of three races of the pathogen and two genes for host resistance. Assume the pathogen reproduces asexually, the host reproduces by random mating, and that dominant gene A confers resistance to race α of the pathogen, while gene B confers resistance to race β. Assume further the host population is susceptible to race γ, the third race of the pathogen, but that races α and β predominate race γ by virtue of their superior fitness on susceptible host genotypes.

Now if genes A and B are inherited independently, continued selection against the susceptible genotypes would bring the host population to near homozygosity with respect to genes A and B. This would result in the disappearance of races α and β of the pathogen. But, just as in the case of the complementary genetic systems, the host's problem of maintaining resistance is not solved. For as the frequencies of races α and β diminish, race γ predominates and the host population is completely susceptible to the pathogen.

Next, suppose the dominant genes for resistance are tightly linked in repulsion phase, simulating a single locus system. One of the composite alleles would be of type Ab, the other aB. Two features now become clear. Both homozygotes, Ab/Ab and aB/aB, are susceptible to at least two of the three races; the heterozygote Ab/aB, carrying two genes for resistance, is susceptible to only race γ, the race of low frequency. Under the assumption that the frequencies of the

host genotypes and the fitnesses of races α and β are such that any loss in racial frequency incurred on resistant genotypes is equally balanced by a gain in frequency on susceptible genotypes, it can be shown that such a host-pathogen system would reach a state of stable equilibrium. It should be emphasized, however, that such a state is possible only if a cross-over suppressor, such as a chomosomal inversion, completely inhibits recombination between genes A and B; otherwise the system would be identical to that described above.

It should also be noted that the presence of inversion systems would not necessarily restrict the argument to tight linkage. In fact, two genes may be a considerable distance apart on the chomosome, but as long as they are contained in the inversion they would function as a unit in a population heterozygous for the inversion. If the system of linked genes found in wheat and barley, then, are inversions which have become homozygous when these species evolved from outbreeding to selfing systems, the fact that genes for resistance are separated by several crossover units does not present any serious difficulty to the theory.

Thus we see when the system reaches a state of equilibrium, a host population of intermediate resistance, capable of being maintained over long periods of time, has been substituted for a population of high resistance but of short duration. Under such circumstances, the host population would be better off, in the long run, than if only race γ were present in the system. For the presence of races α and β, by virtue of their superior fitness on susceptible genotypes, would tend to keep new races which arise by mutation in check, since another race would gain ascendency in the system only if its fitness were greater than that of α and β. Hence, the host would not have to cope with rapid race shifts in the pathogen. If a highly virulent race did arise through mutation, however, it would eventually supplant the existing races and the system would degenerate and again the host would have to evolve another defensive mechanism for its survival.

Evolutionary Significance

If the arguments which have just been advanced approximate reality, the evolutionary significance of the genetic systems uncovered by the work of Briggs and Flor becomes clear. They are the relics of ancient systems of balanced polymorphism, stemming from the time wheat, barley and flax reproduced by outbreeding. In the final analysis, it seems quite plausible that these dual systems of balanced polymorphism, one in the host population the other in the pathogen population and due either to complementary genetic systems of the host and parasite or to linked genes for host resistance, have provided the mechanism for the co-evolution of obligate parasites and their hosts. Indeed, it seems quite likely that some such state of balance and equilibrium was a necessary condition for this co-evolution.

Summary

A mathematical model of a host-pathogen system was presented and a theory of the evolutionary significance of the genetic systems uncovered by the work of Briggs and Flor was proposed. It was suggested that these genetic systems uncovered by present day genetic studies are the relics of ancient systems of balanced polymorphism, stemming from the time wheat, barley, and flax reproduced by outbreeding. It was further suggested that a state of dual balanced polymorphism was a necessary condition for the co-evolution of obligate parasites and their hosts.

Acknowledgment

The writer wishes to express his thanks to Dr. F. N. Briggs, Dean of the School of Agriculture, University of California,

Davis, for calling his attention to the problem. Thanks are also due to Dr. G. L. Stebbins for his helpful suggestions concerning the biological aspects of the paper.

Literature Cited

BELLMAN, R. 1953. Stability Theory of Differential Equations. McGraw-Hill, New York.

BIFFEN, R. H. 1905. Mendel's laws of inheritance and wheat breeding. J. Agr. Sci. **1**: 4–48.

CROW, J., AND M. KIMURA. 1955. Some genetic problems in natural populations. Proceedings of the Third Berkeley Symposium on Mathematical Statistics and Probability. Univ. of Calif. Press.

FISHER, R. A. 1930. The Genetical Theory of Natural Selection. Oxford, Clarendon Press.

FLOR, H. H. 1955. Host-parasite interaction in flax rust—its genetics and other implications. Phytopath., **45**: 680–685.

——. 1956. The complementary genic systems in flax and flax rust. In Advances in Genetics, New York: Academic Press, Inc., **VIII**: 29–59.

KIMURA, M. A model of a genetic system which leads to closer linkage by natural selection. EVOLUTION, **10**: 278–287.

SCHALLER, C. W., AND F. N. BRIGGS. 1955a. Linkage relations of Martin, Hussar, Turkey, and Rio genes for bunt resistance in wheat. Agron. Jour., **47**: 181–185.

————. 1955b. Inheritance of resistance to mildew, *Erysiphe graminis hordei;* in the barley variety, Black Russian. Genetics, **41**: 421–428.

STEBBINS, G. L. 1950. Variation and Evolution in Plants. New York, Columbia Univ. Press.