of inheritance in Virginia pine, cannot be accepted or rejected without further experimentation.

The presence of lethal and semi-lethal recessive alleles has long been hypothesized to partially explain the large percentage of empty seed in the seed crop of pines (e.g. SARVAS, 1962). JOHNSSON (1967) was able to demonstrate that empty seed does have a strong, though unspecified, genetic component by using controlled crosses of the tester, partial diallele and complete diallele designs. Based on results from the reciprocal crosses he postulated the presence of lethal alleles affecting the development of both the female gametophyte and the embryo.

The GOT system described here is a potential example of a specific semi-lethal allelic system in which specific, as yet nonpredictable, genotypes have reduced viability in the development of a mature megagametophyte from a megaspore.

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Simulation of populations with fluctuating fitness values. Two-locus case

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Summary

The effect of fluctuating fitness values on the genotypic composition of two-locus populations is investigated in this paper. A comparison to the results of one-locus populations is attempted. The interaction of epistasis and recombination is studied in more detail. Selection pressures are assumed to fluctuate independently, neither with autocorrelation between genotypes nor between generations. Whereas the expectation of fitnesses follow simple additive or multiplicative selection schemes, actual values of genotypic fitness in any generation do not exhibit a simple relationship. This is due to independent fluctuations of selection intensities. The following results are obtained.

1) Fluctuating fitness values introduce less amounts of fluctuations of zygote frequencies in two-locus populations as compared to one-locus populations.

2) Recombination fractions may be assigned in their effect to three regions. In the first region with no or loose linkage, gene frequencies fluctuate independently and account completely for the fluctuations of gamete frequencies. In the second region with intermediate recombination, there are additional fluctuations of linkage disequilibrium resulting in increased fluctuations of gamete frequencies. In the third region with tight linkage, only fluctuations of gene frequencies are left. Fluctuations of gamete frequencies are consequently reduced again. It is not possible to demonstrate a systematic effect of recombination on gene frequency fluctuations. Range and location of the different regions of recombination fractions are determined by the amount of conditional epistasis present in the selection scheme applied.

The results are discussed with respect to the evolutionary advantage of recombination.

Key words: Simulation, fluctuating fitness, two-locus model, linkage disequilibrium, recombination, epistasis.

Zusammenfassung

In der vorliegenden Arbeit wurde der Einfluß fluktuierender Fitnesswerte auf die genotypische Zusammensetzung digener Populationen untersucht. Ein Vergleich mit den Ergebnissen monogener Populationen wurde angestrebt, Wechselwirkungen zwischen Epistasie und Rekombination näher untersucht. Die Fluktuationen der Selektionskräfte wurden als unabhängig angesehen, d. h. ohne Autokorrelation zwischen Genotypen und zwischen Generationen. Während die Erwartungswerte der Fitness einfachen additiven oder multiplikativen Selektionsmustern folgen, sind die aktuellen Werte der genotypischen Fitness als Folge der unabhängigen Fluktuationen der Selektionswerte in keiner Generation nach einer einfachen Beziehung zusammengesetzt. Im einzelnen wurden die folgenden Ergebnisse erhalten.

1) In digenen Populationen sind die Fluktuationen der Zygotenfrequenzen, die durch variable Fitnesswerte induziert werden, kleiner als in monogenen Populationen.

2) Die Rekombinationsfrequenzen können ihrem Einfluß nach drei Regionen zugeordnet werden. In der ersten Re-

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gion mit keiner oder geringer Kopplung fluktuieren die Genfrequenzen unabhängig voneinander und können die Fluktuationen der Gametenfrequenzen vollständig erklären. In der zweiten Region mit mittleren Rekombinationsfrequenzen sind zusätzlich Fluktuationen des Kopplungsungleichgewichts vorhanden, die zu größeren Fluktuationen der Gametenfrequenzen führen. In der dritten Region mit enger Kopplung bleiben nur die Fluktuationen der Genfrequenzen erhalten. Die Fluktuationen der Gametenfrequenzen sind also wieder geringer. Ein systematischer Einfluß von Rekombination auf die Fluktuationen der Genfrequenzen konnte nicht nachgewiesen werden. Bereich und Lage der unterschiedlichen Regionen der Rekombinationsfrequenzen werden durch das Maß an Epistasie bestimmt, das in dem angewendeten Selektionsmuster der Erwartungswerte enthalten ist.

Die Ergebnisse werden im Zusammenhang mit Fragen des Vorteils der Rekombination im Rahmen der Evolution diskutiert.

Introduction

One of the most impressing results of investigations on natural populations is the high amount of polymorphisms found in structural genes coding for soluble enzymatic proteins. Consequently the question arose as to if and how these polymorphisms are maintained by natural selection, resulting in a central problem of population genetics. Many theoretical studies considered initially one-locus populations with deterministic conditions. In this case, a lot of mechanisms are demonstrated yielding stable nontrivial equilibria with respect to this aspect (cf. Karlin and McGregor 1972). Selective superiority of heterozygotes, however, is assumed by a great number of authors to play a prominent role.

Two main features of natural populations are not taken into account in these models. First, natural populations do not live in constant environments and second, they consist of more than one locus. Many components of natural selection are exposed to random fluctuations. In a first paper, we considered the influence of random fluctuations of fitness values on the genotypic composition of one-locus populations (Schumacher and Wöhrmann 1974, cf. Eggers-Schumacher 1975). In this work, we were able to demonstrate that equilibria maintained under deterministic conditions with large mean selection coefficients are retained also under stochastic conditions, whereas with small mean selection coefficients and large variances, the fluctuation patterns of different selection schemes overlap.

In one-locus models, important parameters for the composition of natural populations remain unconsidered. Linkage and epistasis are essential in this respect. Even in two-locus populations, little is known about the characteristics of models with general selection schemes (Karlin 1975). On the other hand in some special classes of models, as additive and multiplicative models, conditions for equilibria are well known (Bodmer and Felsenstein 1967). Another class known as symmetric viability models was extensively studied by Karlin and Feldman (1970). Besides such analytical approaches numerical methods, especially computer simulations, have yielded useful results (see e.g. Karlin and Carmelli 1975). They are particularly helpful for studies of complex multilocus models (Lewontin 1964, Franklin and Lewontin 1970).

Beginning with simple deterministic selection schemes (additive and multiplicative), the effect of random fluctuations of selection intensities on the composition of two-locus populations is studied in the present investigation. For each of the nine genotypes in each generation, it is assumed that random fitnesses are generated independently. In no generation do the actual fitness values follow a simple selection scheme. Two main aspects of problems associated with multilocus systems are studied in more detail. First, a comparison of the results to one-locus models is attempted, and second, the interaction of epistasis and recombination on fluctuation patterns of the genotypic composition of populations is demonstrated.

The model

Consider a two-locus (A, B), two-allele (A,a and B,b, resp.) infinite diploid population reproducing in discrete generations by random mating. Ten genotypes are considered including both double heterozygotes (AB/ab and Ab/aB). The population dynamics are described by relative variances of gamete frequencies (RV_{xi}) and gene frequencies (RV_{pi}).

Further parameters of populations considered are, mean fitness of populations ($\bar{\bar{w}}$) and its relative variance over generations ($RV_{\bar{w}}$). The relative variances are defined by the ratio of variance and mean. The zygote frequencies for each locus are summarized for comparison with the corresponding one-locus model.

Let D be the linkage disequilibrium function — gametic phase unbalance as called by Jain and Allard (1966) — x_1 the frequency of gamete AB, p_1 and p_2 the frequencies of the alleles A and B, resp., then the following relation holds:

$$D = x_1 - p_1 p_2.$$

The linkage disequilibrium function D is taken as a measure referring to the departure of a gamete frequency from being in a state of random association of its genes. The characteristics of this measure are investigated as a function of the number of generations.

The following fitness array has been used.

	BB	Bb	bb
AA	w_{11}	w_{12}	w_{13}
Aa	w_{21}	w_{22}	w_{23}
aa	w_{31}	w_{32}	w_{33}

The fitness values of the nine genotypes are generated by a program for random variables with rectangular distribution in each generation. The values obtained are transformed to normal distribution and assigned to the genotypes.

The simulation work has been done on a Control Data 3300 of the "Zentrum für Datenverarbeitung der Universität Tübingen". The figures have been drawn by an incremental-plotter Calcomp.

1. Comparison of two-locus and one-locus populations.

In two-locus populations, the fitnesses of the genotypes of one locus depend not only on the contribution of this locus alone, but are determined also by the contributions of the second locus, the kind of relationship between the contributions of both loci, and the genetic composition of the population as well. These further characteristics disallow a direct comparision to one-locus populations. They can be avoided if one locus is conditionally selectively neutral. Only in this case is a comparison meaningful.

The expectations of fitness values $E(w_{ij})$ of genotypes Z_{ij} formally can be considered as to be composed of the contributions of locus A $E(a_i)$ and locus B $E(b_j)$ giving e.g. $E(w_{ij}) = E(a_i)xE(b_j)$. In the following, the expectations of the contributions of the three genotypes of locus A are $E(a_i) = 1$, and of locus B are $E(b_1) = E(b_3) = 1 - s$, and $E(b_2) = 1$. Thus the results for locus B can be compared to the one-locus case.

Figure 1 shows the zygote frequencies as a function of the number of generations for each locus separately with the conditions: selection coefficient $s = 0.5$, relative variance of fitnesses $RV_{wi} = 0.04$, and recombination fraction $r = 0.5$. The fluctuations in the genotypic composition of locus A lead to its quasifixation after 600—700 generations, after

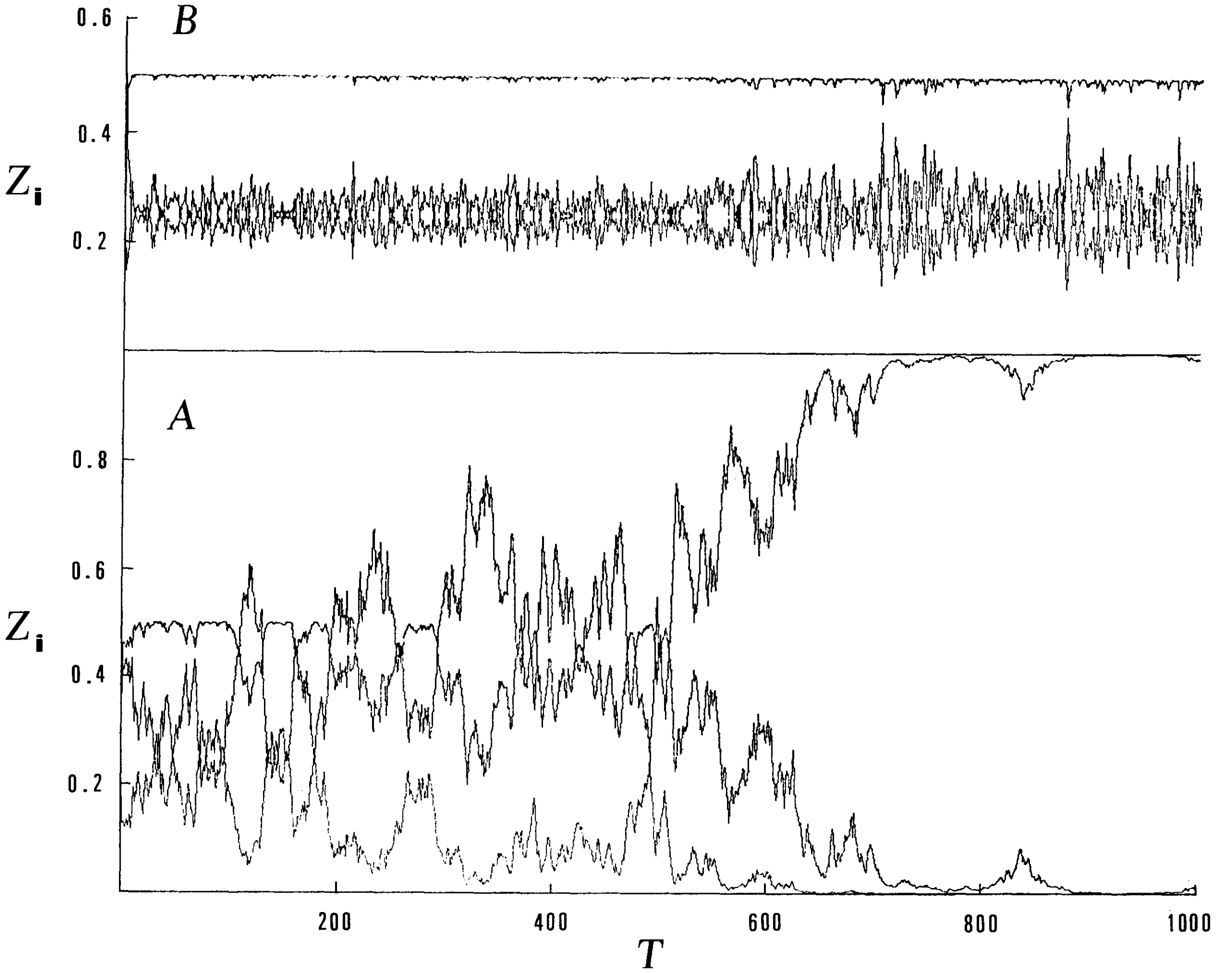

Figure 1. — Zygote frequencies (Z_i) of locus A (below) and locus B (above) as a function of the number of generations (T) of a population with conditions, s = 0.5, RV_{wi} = 0.04, r = 0.5.

which there are only fluctuations in the genotypic composition of locus B. The two-locus population is reduced effectively to an one-locus population. Consequently, it is possible to compare directly the fluctuations of two-locus and one-locus systems in this computer run. There is a striking increase in the amplitude of the fluctuations of locus B when locus A is near quasifixation, i.e. in the last 300 generations, indicating less sensitivity of genotype to environmental variation in a two-locus system when both loci are polymorphic.

Table 1 reports similar facts for populations having various combinations of selection coefficients and relative variances of fitness values. The relative variance of the gene frequency RV_{p2} of locus B in the two-locus populations, for instance, is about a factor of 2 to 3 smaller than in the one-locus case 1L). This factor is actually underestimated because of some quasifixation of locus A, as shown in *figure 1*, resulting in overestimated relative variances of gene and zygote frequencies of locus B. A specific influence of the recombination fraction on the fluctuations is not apparent.

The reduction of the fluctuations of locus B in the two-locus case appears to be reasonable due to the following arguments. In one-locus populations, selection operates by three independent random variables. Combinations of the variables with large opposite effects in successive generations, therefore, are generated frequently enough to produce large fluctuations of the zygote frequencies. In two-locus populations, on the contrary, the fitness value of one geno-

Table 1. — Means of gene frequency p_2, and frequency of heterozygotes $\overline{Z}_2$, and the relative variances of gene and zygote frequencies RV_{p2} and RV_{Z_i} in comparison of two-locus and one-locus (1L) populations (RV_{wi} = relative variance of fitness, s_{bi} = selection coefficient, r = recombination fraction)

r	$\bar{p}_2$	$\bar{Z}_2$	RV_{p2}	RV_{Z1}	RV_{Z2}	RV_{Z3}
			s_{bi} = 0.05, RV_{wi} = 0.04			
.001	.500	.4769	.0322	.0629	.0136	.0687
.010	.502	.4651	.0327	.0572	.00777	.0658
.500	.503	.4728	.0256	.0496	.00293	.0482
1L	.479	.4464	.0531	.0882	.0140	.101
			s_{bi} = 0.05, RV_{wi} = 0.0025			
.001	.498	.4989	.00095	.00189	.0000048	.00189
.010	.500	.4988	.00108	.00218	.0000053	.00216
.500	.499	.4987	.00120	.00238	.0000063	.00240
1L	.504	.4960	.00349	.00696	.0000610	.00698
			s_{bi} = 0.5, RV_{wi} = 0.04			
.001	.500	.4972	.00283	.00564	.000040	.00564
.010	.500	.4975	.00249	.00496	.000030	.00497
.500	.499	.4973	.00273	.00539	.000039	.00546
1L	.500	.4954	.00452	.00899	.000091	.00903
			s_{bi} = 0.5, RV_{wi} = 0.0025			
.001	.500	.4999	.00011	.000212	.00000005	.000212
.010	.500	.4999	.00011	.000224	.00000005	.000223
.500	.500	.4999	.00010	.000209	.00000004	.000209
1L	.501	.4997	.00025	.000500	.00000030	.000499

Table 2. — Means and relative variances of gamete frequencies $\bar{x}_i$ and RV_{xi} of populations with the multiplicative or additive viability pattern and mean selection coefficients s_{ai}, s_{bi}, recombination fraction r and relative variance of fitnesses $RV_{wi} = 0.04$

r	x_1	x_2	x_3	x_4	RV_{x1}	RV_{x2}	RV_{x3}	RV_{x4}
				$s_{ai} = s_{bi} = 0.05$ multipl.				
.500	.234	.255	.244	.266	.0201	.0190	.0189	.0200
.010	.251	.237	.260	.252	.0346	.0290	.0346	.0354
.001	.260	.246	.238	.255	.0366	.0479	.0440	.0461
				$s_{ai} = 0.5$, $s_{bi} = 0.05$ multipl.				
.500	.245	.256	.244	.255	.0170	.0167	.0174	.0168
.010	.271	.229	.239	.261	.0210	.0254	.0259	.0238
.001	.293	.206	.220	.281	.0300	.0432	.0548	.0393
				$s_{ai} = s_{bi} = 0.05$ additive				
.500	.248	.241	.260	.251	.0177	.0193	.0182	.0168
.010	.245	.245	.263	.248	.0300	.0282	.0277	.0269
.001	.226	.284	.267	.223	.0415	.0382	.0326	.0551
				$s_{ai} = 0.5$, $s_{bi} = 0.05$ additive				
.500	.248	.253	.252	.247	.0102	.0105	.0107	.0103
.010	.265	.243	.237	.255	.0145	.0168	.0160	.0168
.001	.248	.252	.251	.248	.0269	.0234	.0265	.0240
				$s_{ai} = s_{bi} = 0.25$ additive				
.500	.253	.250	.250	.247	.0043	.0042	.0041	.0043
.010	.253	.248	.246	.252	.0092	.0095	.0093	.0092
.001	.211	.290	.289	.211	.0299	.0202	.0192	.0344

Table 3. — Means and relative variances of gene frequencies $\bar{p}_i$, RV_{pi} and population mean fitness $\bar{\bar{w}}$, $RV_{\bar{w}}$ of populations with the multiplicative or additive viability pattern and mean selection coefficients s_{ai}, s_{bi}, recombination fraction r and relative variance of fitnesses $RV_{wi} = 0.04$

r	p_1	p_2	RV_{p1}	RV_{p2}	$\bar{w}$	$RV_{\bar{w}}$
			$s_{ai} = s_{bi} = 0.05$ multipl.			
.500	.490	.478	.01950	.01950	.950	.00611
.010	.488	.511	.02610	.01800	.950	.00666
.001	.507	.498	.02060	.02530	.949	.00756
			$s_{ai} = 0.5$, $s_{bi} = 0.05$ multipl.			
.500	.500	.489	.00176	.03220	.729	.00695
.010	.501	.510	.00188	.02340	.731	.00727
.001	.499	.513	.00241	.01630	.731	.00961
			$s_{ai} = s_{bi} = 0.05$ additive			
.500	.489	.508	.01900	.01630	.949	.00628
.010	.490	.507	.02060	.02050	.948	.00623
.001	.510	.493	.01760	.01940	.947	.00694
			$s_{ai} = 0.5$, $s_{bi} = 0.05$ additive			
.500	.500	.495	.00161	.01900	.724	.00672
.010	.498	.492	.00173	.01990	.723	.00677
.001	.500	.499	.00172	.01840	.722	.00743
			$s_{ai} = s_{bi} = 0.25$ additive			
.500	.503	.503	.00397	.00407	.747	.00655
.010	.502	.500	.00361	.00399	.748	.00642
.001	.500	.499	.00377	.00390	.749	.00811

type of a specific locus is formed by the weighted sum of the generated values of three combinations with the different genotypes at the other locus. In this case, the genotypes are exposed to the mean of three random variables. Thus, extreme differences in the selective values of the genotypes and consequently large fluctuations in the genetic composition are less likely in two-locus populations as compared to one-locus populations.

2. *Influence of the recombination fraction on the fluctuation of the genotypic composition.*

In this investigation the additive and multiplicative viability pattern for the mean fitnesses are taken into consideration. For each locus, overdominant expectations of the fitness contributions are assumed ($E(a_1) = 1 - s_{a1}$, $E(a_2) = 1$, $E(a_3) = 1 - s_{a3}$ of **locus** A, and $E(b_1) = 1 - s_{b1}$, $E(b_2) = 1$, $E(b_3) = 1 - s_{b3}$ of locus B, resp.). The results can be classified by the amount of epistasis (deviation from additivity) being present in the deterministic viability pattern. This will be referred to as conditional epistasis.

2.1 *Little or no conditional epistasis in the deterministic viability pattern.*

In this case, in each generation much or little epistasis can be built up by randomly generated fitness values. *Table 2* reports the influence of the recombination fraction on the means and relative variances of the gamete frequencies $\bar{x}_i$ and RV_{xi}, respectively, for a series of fitness systems. For each combination of fitness parameters, there is a clear increase in the RV_{xi}-values with tight linkage, i.e. little recombination. This increase may be caused by two different mechanisms. The fluctuations of the gene frequencies may be more extensive with tight linkage, or there may be additional fluctuations in the distribution of the alleles forming the different gamete types.

Table 3, however, shows that there is no clear influence of the recombination fraction on the relative variance of the gene frequencies RV_{pi} only. In the second system ($s_{ai} = 0.5$, $s_{bi} = 0.05$ multiplicative pattern), there is an approximation of the RV_{pi}-values of both loci with tight linkage caused by linkage disequilibria then present. The results indicate that the enhanced fluctuations of the gamete frequencies cannot account for the enhanced fluctuations of the gene frequencies.

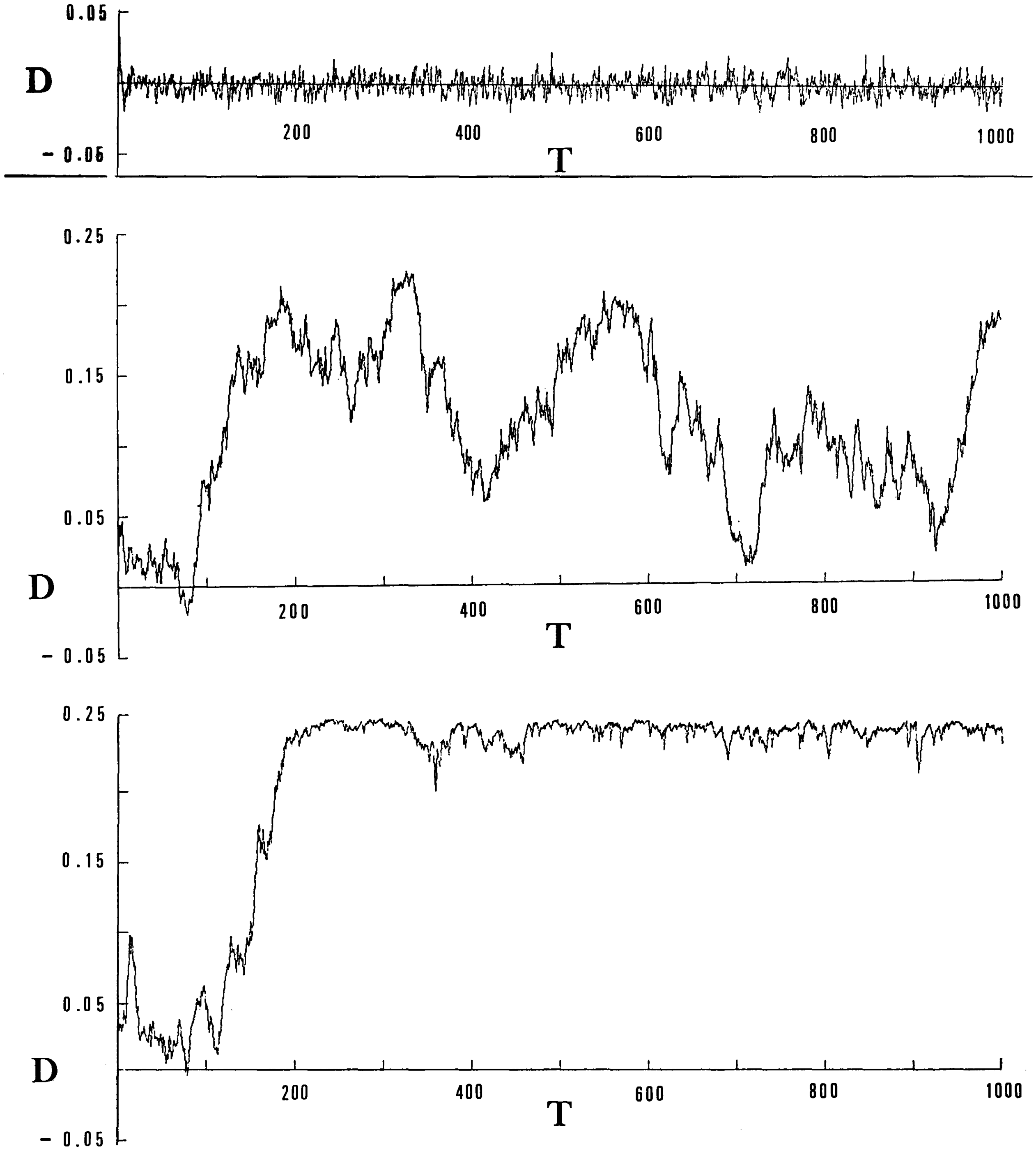

Figure 2 a—c. — Linkage disequilibrium (D) as a function of the number of generations (T) of populations with the 1. viability pattern in table 4 and conditions: $RV_{wi} = 0.04$ and $r = 0.5$ (above), $r = 0.01$ (middle), $r = 0.001$ (below).

The deviation of the distribution of the alleles in the gametes from random association is measured by the linkage disequilibrium function D. Populations having viability patterns with little or no conditional epistasis (examples introduced in *table 3)* show large fluctuations of D with tight linkage as demonstrated in *figure 2 b*. There may be substantial changes in the amount of linkage disequilibrium within a short time (50—100 generations) as well as constantly high amounts for a longer period (e.g. 400 generations). A change from positive to negative D-values and vice versa is possible as well. A comparison to populations with free recombination and corresponding viability patterns reports that high amounts of D and thereby large fluctuations are only possible with sufficiently tight linkage. Fluctuations of D found under these conditions are of the same magnitude as illustrated in *figure 2 a*. Thus, the increase in the RV_{ix}-values can be traced back to additonal fluctuations in the distribution of the associated alleles forming the gametes.

High amounts of linkage disequilibrium indicate large deviations from random association of the alleles. In this case, the populations are composed mainly of few genotypes with special allele arangements well adapted to the conditions present. Large fluctuations of the gamete frequencies due to fluctuations of D allow rapid adaptation of the populations to changed environmental conditions

Table 4. — Means and relative variances of gamete frequencies $\bar{x}_i$ and RV_{xi} of populations with the multiplicative viability pattern and mean selection coefficients s_{ai}, s_{bi}, recombination fraction r and relative variance of fitnesses $RV_{wi} = 0.04$

r	x_1	x_2	x_3	x_4	RV_{x1}	RV_{x2}	RV_{x3}	RV_{x4}
1. $s_{a1} = s_{b1} = 0.293$								
.500	.250	.251	.249	.251	.0042	.0040	.0041	.0043
.010	.287	.211	.213	.289	.0239	.0268	.0267	.0243
.001	.492	.010	.009	.490	.0042	.0064	.0070	.0043
2. $s_{a1} = s_{b1} = 0.5$								
.500	.250	.250	.250	.250	.0026	.0025	.0024	.0026
.010	.477	.023	.023	.477	.0020	.0035	.0035	.0020
.001	.497	.002	.002	.498	.0020	.0040	.0044	.0021
3. $s_{a1} = 0.5$, $s_{a3} = 0.25$, $s_{b1} = 0.5$								
.500	.166	.167	.333	.334	.0040	.0041	.0034	.0031
.010	.380	.021	.099	.500	.0059	.0034	.0240	.0030
.001	.353	.091	.121	.435	.0026	.0008	.0115	.0041
4. $s_{a1} = s_{b1} = 0.5$, $s_{a3} = s_{b3} = 0.25$								
.500	.111	.222	.222	.445	.0044	.0058	.0057	.0047
.010	.220	.133	.131	.515	.0143	.0165	.0185	.0091
.001	.219	.150	.147	.484	.0040	.0040	.0047	.0130

without loss of genetic variability. Populations having strongly linked genes and these fitness systems therefore, are able to adapt to special selective conditions and nevertheless retain the requirements for a new adaptation to changed conditions.

The influence of the recombination fraction on the dynamics of the populations is exemplified by one example of the multiplicative pattern with selection coefficients. In the case of free recombination, i.e. $r = 0.5$ the population dynamics have characteristics analogous to the one-locus system. The fluctuations in the genotypic composition of locus B with large selection coefficients ($s_{bi} = 0.5$) are homogenous but have slightly smaller amplitudes than in the one-locus case corresponding to those of locus B in *figure 1* with $s_{bi} = 0.5$, $s_{ai} = 0$ and the same conditions otherwise. The fluctuations of locus A with small selection coefficients $s_{ai} = 0.05$ are of a more complex pattern. Analogous to the one-locus model, different periods can be distinguished. There are periods in which the frequencies of both homozygote genotypes oscillate around a common value and others in which the frequencies of one homozygote and the heterozygote genotype fluctuate around a value near 0.05. The amplitudes are of less intensity as compared to the one-locus case for locus A (cf. SCHUMACHER and WÖHRMANN, 1974).

There is only a slight influence of little recombination on the population dynamics under these conditions. The fluctuation patterns of both loci have hardly changed. Only the amplitudes, are slightly less for locus A and slightly greater for locus B. These alterations are in agreement with the results for the relative variances of gene and zygote frequencies with similar conditions as discussed above (vis. 2nd system of *table 3*).

The small influence of the recombination fraction on the population dynamics of separately considered loci could be proved for the other fitness combinations of *tables 2* and *3*, too.

Summarizing the results of these fitness systems it is apparent that there is an increase in the relative variances of the gamete frequencies with little recombination. Such a phenomenon is not observed if both loci are investigated separately. There is no clear-cut relation between the relative variances of gene resp. zygote frequencies and the recombination fraction. This outcome is confirmed by the results on population dynamics. Fluctuations of the linkage disequilibrium have to be taken into account to get a complete picture of the dynamics of two-locus populations.

2.2 *Conditional epistasis in the deterministic viability pattern.*

Under deterministic conditions, two-locus populations with sufficiently little recombination contain high amounts of linkage disequilibrium in equilibrium. The reduction of epistasis emerging from randomly generated fitness values does not suffice to destroy appreciably the high amounts of disequilibrium. This requirement is met e.g., by populations

Table 5. — Means and relative variances of gene frequencies $\bar{p}_i$, RV_{pi} and population mean fitness $\bar{\bar{w}}$, $RV_{\bar{w}}$ of populations with the multiplicative viability pattern and mean selection coefficients s_{ai}, s_{bi}, recombination fraction r and relative variance of fitnesses $RV_{wi} = 0.04$

r	p_1	p_2	RV_{p1}	RV_{p2}	$\bar{\bar{w}}$	$RV_{\bar{w}}$
1. $s_{a1} = s_{b1} = 0.293$						
.500	.501	.498	.0038	.0041	.727	.00640
.010	.498	.500	.0038	.0038	.734	.00937
.001	.502	.500	.0041	.0041	.747	.01570
2. $s_{a1} = s_{b1} = 0.5$						
.500	.500	.500	.0024	.0024	.561	.00695
.010	.500	.500	.0018	.0018	.614	.01550
.001	.499	.499	.0021	.0021	.624	.01720
3. $s_{a1} = 0.5$, $s_{a3} = 0.25$, $s_{b1} = 0.5$						
.500	.333	.499	.0063	.0021	.623	.00730
.010	.401	.478	.0051	.0028	.647	.01250
.001	.443	.474	.0032	.0028	.657	.01660
4. $s_{a1} = s_{b1} = 0.5$, $s_{a3} = s_{b3} = 0.25$						
.500	.332	.333	.0065	.0063	.692	.00742
.010	.353	.351	.0064	.0065	.706	.01120
.001	.369	.366	.0069	.0071	.713	.01400

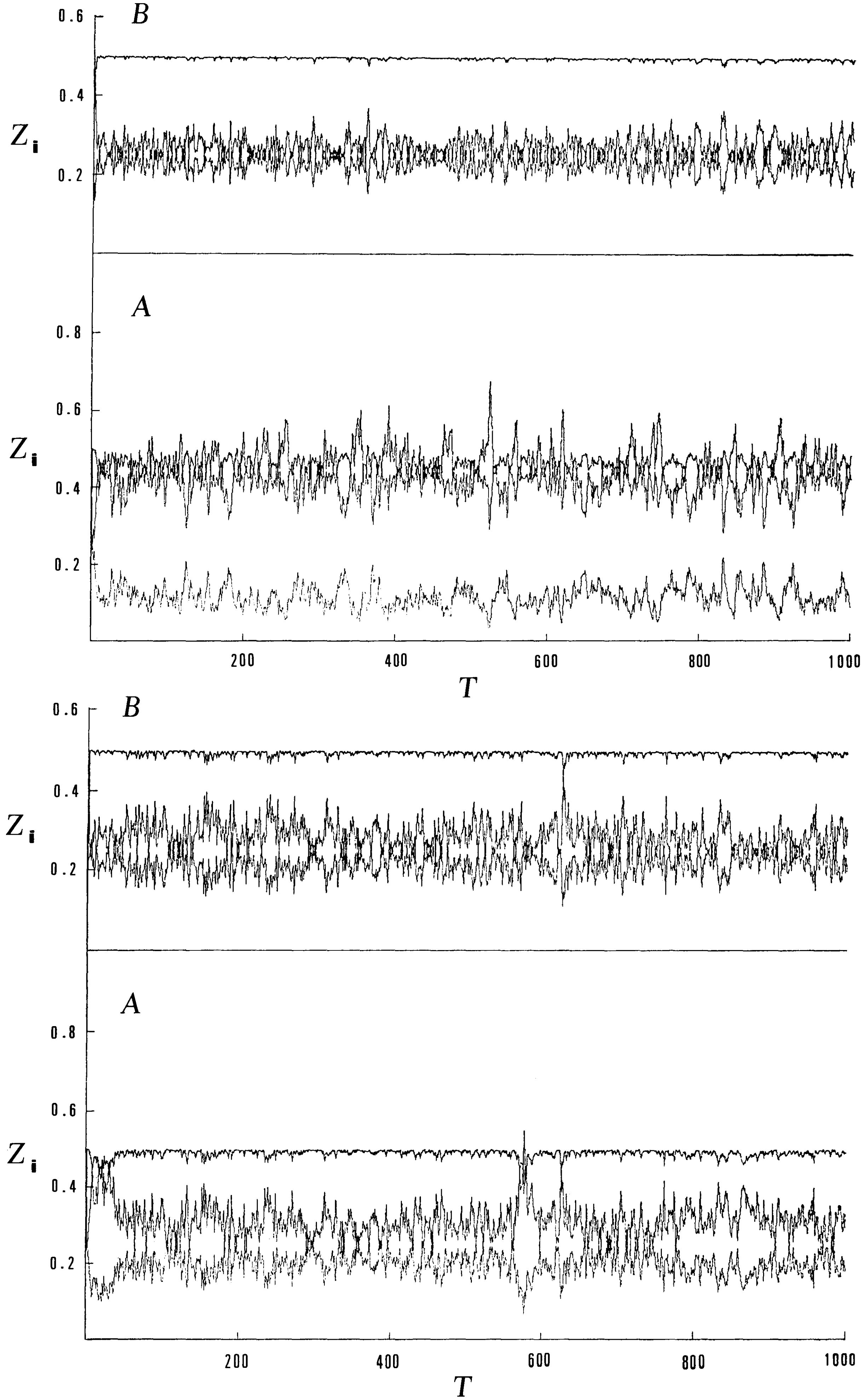

Figure 3 a—b. — Zygote frequencies (Z_i) of locus A and locus B as a function of the number of generations (T) of populations with the 3rd viability pattern in table 4 and conditions: $RV_{wi} = 0.04$ and $r = 0.5$ (above), $r = 0.001$ (below).

with multiplicative viability pattern and large selection coefficients. With intermediate recombination, the disequilibrium become susceptible to random fitness fluctuations, too.

This transition is shown by an example of the multiplicative viability pattern with the selection coefficients $s_{ai} = s_{bi} = 0.293$. *Figures 2 a — c* report the linkage disequilibrium D as a function of the number of generations for three different recombination fractions r. *Figure 2 a* ($r = 0.5$) and *figure 2 c* ($r = 0.001$) demonstrate only small fluctuations of D. In the first case, the mean of D is near 0, in the second case near to the maximum value 0.25. *Figure 2 b* ($r = 0.01$), in contrast, exhibits large fluctuations.

Tables 4 and 5 give a survey of relative variances of gamete (RV_{xi} in *table 4)* and gene frequencies (RV_p in *table 5)* for a number of model systems. In all systems there is no longer a clear-cut increase in the RV_{xi}-values with reduced recombination in contrast to the fitness array with little deterministic epistasis (Section 2.1). In the first system, for instance ($s_{ai} = s_{bi} = 0.293$), an increase of RV_{xi} by about a factor of 5 is noticed with $r = 0.01$, then, however, with $r = 0.001$ a decrease to the initial values at $r = 0.5$ is observed. These changes correspond to the reported fluctuations of the linkage disequilibrium at different recombination fractions. The first observed increase of RV_{xi} at $r = 0.01$ is due to large fluctuations of D present under these conditions. At $r = 0.001$, however, there are only slight fluctuations of D left. Consequently, the RV_{xi}-values are mainly determined by the fluctuations of the gene frequencies, i.e. the size of RV_{pi}, just as for free recombination. A relation between RV_{pi} and the recombination fraction is not observed ordinarily (cf. *table 5).* In the third system ($s_{a1} = 0.5$, $s_{a3} = 0.25$, $s_{bi} = 0.5$ and multiplicative interaction), however, there is an approximation of the RV_{pi} of both loci with tight linkage due to high amounts of linkage disequilibrium then present.

High amounts of linkage disequilibrium D have additional effects on the population parameters. They result in populations consisting mainly of two complementary gametes *(table 4).* Under the initial conditions chosen, these are the gametes AB and ab with frequencies x_1 and x_4, resp. If the expectations of the equilibrium gene frequencies $\hat{p}_i$ are different for both loci, there is an approximation of the mean frequencies p_i to an intermediate value (p_1 and p_2 in *table 5* for second fitness system). If the equilibrium gene frequencies of both loci expected from the corresponding fitness systems deviate from $\hat{p}_i = 0.5$ with tight linkage, both mean gene frequencies approximate to $p_i = 0.5$. There is a concomitant increase of the mean fitness.

These consequences of high amounts of D are not due to fluctuations in the selection parameters. They are present already under deterministic conditions and are retained in the stochastic systems only if D is not appreciably diminished by the influence of fluctuating parameters.

The reduction of the number of gametes to two predominant types results in gene complexes operating as one-locus systems. In the first fitness system at $r = 0.001$, for instance, the populations consist mainly of three genotypes (AB/AB, AB/ab, ab/ab) with the expectations of fitnesses $E(w_1) = 0.5$, $E(w_5) = 1$, $E(w_9) = 0.5$. Thereby, the populations are subject to similar conditions as one-locus systems with $s = 0.5$. The gamete frequencies correspond to the gene frequencies p and q. Consequently, the relative variances of gene frequencies RV_{pi} and gamete frequencies RV_{x1} and RV_{x4} have equal values and, in addition, are in good agreement with the relative variance of gene frequencies RV_{p2} of the one-locus model (cf. *table 1).*

High amounts of D with little recombination have further a large influence on the fluctuations of the zygote frequencies considering each locus separately as shown by the dynamics of both loci for a population with the first fitness system ($s_{ai} = s_{bi} = 0.293$) with free recombination ($r = 0.5$) and tight linkage ($r = 0.001$), resp. There are no striking differences apparent in the size of the fluctuations (amplitude and frequency of oscillations of zygote frequencies around their mean) by an comparison of populations with $r = 0.5$ and $r = 0.001$. Whereas the fluctuations of the zygote frequencies of both loci with $r = 0.5$ are unsynchronized, there is a good agreement of their pattern with $r = 0.001$. Both loci are exposed to nearly identical fluctuations in their genotypical composition.

The effects of high amounts of D are even more obvious by a comparison of *figure 3 a* ($r = 0.5$) and *figure 3 b* ($r = 0.001$) for the third fitness system ($s_{a1} = 0.5$, $s_{a3} = 0.25$, $s_{bi} = 0.5$ and multiplicative interaction). The dynamics of the population in *figure 3 a* ($r = 0.5$) correspond completely for each locus to the pattern expected by their fitness contributions, i.e. oscillations of the zygote frequencies of genotypes AA and Aa around a common value for locus A and analogous oscillations of the zygote frequencies of both homozygotes for locus B. The reduction to a one-locus system at $r = 0.001$ *(fig. 3 b)* leads to not only partly synchronized fluctuations but also to an approximation of the means of the frequencies of corresponding genotypes of the loci (e.g. AA and BB). This is in agreement with an adjustment of the mean gene frequencies (cf. *table 4).* Thus, the zygote frequencies get a new fluctuation pattern common to both loci.

As a result of the findings discussed above, there is an interesting relationship between the fluctuations of the gamete frequencies and the recombination fraction for populations with multiplicative viability pattern. The relative variances RV_{xi} at free recombination and sufficiently tight linkage are determined almost completely by the fluctuations of the gene frequencies. In between, there is a range of recombination fractions where an additional factor contributes to RV_{xi}. This is a frequent alteration of the distribution of the associated alleles, i.e. fluctuations in D. In this case, the populations are able to build up high amounts of D within a relatively short time. Hence, they consist of a few well adapted genotypes. This process can be reversed rapidly. The populations, thereby, remain adaptable to changing environments in spite of being well adapted to a special one.

Discussion

Two main aspects of investigations on two-locus problems are considered in this paper. One purpose is to compare results on one-locus and two-locus models, the second to study the effect of recombination. In two-locus models, it is suggestive to look at the influence of varying selection pressures on one locus with another conditionally selective neutral one segregating in the background. As soon as this locus is fixed, the system is similar to a one-locus model. This investigation has been done in the first part of the paper.

Conditionally selective neutrality in this contect means, the locus behaves strictly neutral with respect to expectations of fitnesses. In stochastic environments, however, there is some random but no systematic interaction with the second locus resulting in noncorrelated fitness values for different allele arrangements. Whereas these values belong to the same distribution, they are assumed to differ randomly between any arrangement of alleles in any generation. What biological mechanism can account for this random interaction? First it is possible that the neutral locus is neutral only on the average, but in a fluctuating environment varying responses due to special genotype-environment interactions take place. Second, even in the case of strict neutrality, the locus could be taken as a marker of genetic background. Different genotypes are associated with random samples of other loci not selectively neutral. Thus, the array of genotypes at the selected locus is subdivided into classes of genotypes marked by the neutral locus and exposed to different selection pressures. In this case, some autocorrelation of fitnesses of genotypes belonging to the same genotypes of the selected locus could be expected. Complete autocorrelation corresponds to the one-locus system, irrespective of whether the neutral locus is polymorphic or not. The fitness of the genotype is exclusively determined by the genotypic constellation at the selected locus. Three different fitness values are operating in the population.

As the amount of autocorrelation decreases random interactions are introduced by the stochastic process. This effect is most drastically expressed with independent fitness values. This case has been studied in more detail. The main conclusion is that the fluctuations of the selected locus are buffered in the two-locus case as long as the neutral locus is polymorphic to an appreciable amount. In one-locus systems, extreme environments in a given distribution of fitness values favouring one homozygous genotype will occur and lead to drastic changes in gene frequencies resulting in large fluctuations of the population's composition. These environments will be experienced in two-locus systems with equal frequencies but this condition will affect mainly one class of genotypes in the genotypic array of the locus in view, and is compensated for to some extent by less favoured classes of the same genotype. This buffering should tend to disappear with increasing amounts of autocorrelation, but this suggestion clearly remains to be demonstrated.

The second problem to be investigated is the effect of recombination in multilocus populations. Many studies of multilocus systems lead to coadapted gene complexes being favoured by epistatic interactions. These gene complexes are stable with no recombination and thus selection should tend to produce genetic systems without recombination. Although some evidence for coadapted gene blocks has been found (ALLARD *et al.* 1972), the question arises as to why recombination exists. TURNER (1967) put it the following way: "Why does the genotype not congeal?" The search for conditions favouring recombination was intensified. Advantage of no recombination implies that favourable gene arrangements exist in the population and are selected for. This advantage is mainly expressed by some form of positive epistasis. The consequence is linkage disequilibrium or gametic unbalance. Linkage disequilibrium is favoured if nonalleles which interact functionally in an beneficial way are held together. So it is an advantage in a static sense. For populations already in an equilibrium with linkage disequilibrium, recombination is disavantagous. This statement coresponds to the conjecture of FISHER (1930) that there is a selective advantage to reducing recombination rates in populations segregating for interacting genes.

In contrast, in populations having loci linked in a way that some recombination is needed to get favourable gene arrangements, recombination will be selected for as long as this condition is met. Some special cases have been described. FELSENSTEIN (1974) discussed the case of random linkage disequilibrium generated by genetic drift which causes linked loci to interfere with each other's response to selection even when there was no gene interaction between the loci. The advantage of recombination in this situation is to break down such random linkage disequilibrium. Such an advantage is expressed even more if detrimental mutations are held in the population by linkage to a locus polymorphic due to some form of balancing selection. The effect of recombination on the fate of selectively favoured alleles has been investigated by STROBECK *et al.* (1976). In this case recombination may be favoured by the increase of production of selectively advantageous types of gametes with which they tend to remain associated. The spread of advantageous alleles in the population is accelerated. A more general approach to the advantage of random assortment under different selection regimes has been given by WILLS and MILLER (1976). They claim that linkage disequilibrium may hinder the movement of alleles to their selective equilibria, thus leading to the advantage of random assortment.

These considerations reflect situations where populations are exposed to dynamic processes of some form. These may be responses to random effects of genetic drift, spread of selectively favoured or detrimental mutants or the movement of alleles to their selective equilibria. Conditions where such dynamic processes are continuously involved may be generated by environments fluctuating in time and space. An example is presented by CHARLESWORTH (1976) in terms of selection on neutral genes modifiying recombination. He shows that temporal variation in linkage disequilibrium between the pair of selected loci can give rise to selection in favour of recombination. The temporal variation of linkage disequilibrium is assumed to be due to fluctuations in selection intensities.

The results obtained in this paper demonstrate variation of linkage disequilibrium in response to environmental fluctuations and are, thus, related to the work of Charlesworth. Linkage disequilibrium emerges as the result of interaction of epistasis and linkage. The effect of recombination, particularly on population dynamics, has been investigated taking into account fluctuations of linkage disequilibrium. Different amounts of conditional epistasis, epistasis generated by the expectations of fitness values, are considered. As a result, fluctuations in the composition of the population, expressed by variances of gamete resp. zygote frequencies, can be assigned to different regions of recombination fractions. In the first region with random assortment, gene frequencies fluctuate independently and determine completely the fluctuations of gamete frequencies. According by only a small amount of fluctuations of linkage disequilibrium is found.

In the second region of recombination fractions, large fluctuations of linkage disequilibrium are present indicating occasionally correlated fluctuations of gene frequencies. The populations respond to changed environmental conditions by rapid alterations of gene arrangements. Recombination is frequent enough to produce new adapted gene arrangements, but these arrangements are not necessarily destroyed by recombination in the next generation. The populations having recombination fractions in this region, thus, are capable to adapt highly to special environments without loss of genetic variability, and nevertheless retain the capacity of rapid adaptation to changed conditions.

In a third region of recombination fractions, highly adapted gene arrangements are selected as well, but new gene arrangements can no longer rapidly evolve. High amounts of linkage disequilibrium arise and are hardly susceptible to random environmental fluctuations. Range and location of these recombination regions are determined by the amount of conditional epistasis present in the selection regime. Selection regimes generating little or no epistasis have a second region of recombination fractions which extends to thight linkage. Selection schemes with high amounts of conditional epistasis, on the other hand, exhibit an extended third region at the expense of the second.

The results discussed above have some implications for the evolutionary advantage of recombination. Two types of interaction between loci are operating. First, there is a functional relation expressed by epistasis and second, physical linkage expressed by the amount of recombination. Both are tied together determining the fate of gene arrangements. In environments favouring special gene arrangements, recombination has an advantage if environmental conditions favouring different arrangements are generated and alternate in some way. Moderate alternations are expected to be most favourable for recombination. The populations are exposed long enough to environments — long environmental period — so adaptation can nearly be accomplished, but environmental changes are experienced to an extent that populations have to respond with rapid adaptation. Rates of recombination in the second region of recombination fractions would be most appropriate for this purpose.

Frequent alternations of environments should give rise to tight linkage. The populations need some time to reach the state of equilibrium. With frequent changes — short environmental period — and recombination, the populations are only randomly in equilibrium spending most of the time in aproaching it. In this case, may be, it more favourable for a population to stay in a genotypic composition well adapted to a frequently generated environment with no recombination. In situations with no change in environments, recombination is obviously not necessary and will result in segregational load. Tight linkage is selected for as well.

Random fluctuations of selection intensities with no autocorrelation between generations as applied in this investigation produce very different kinds of selection schemes from generation to generation including situations of moderate alternations in environmental conditions. The second region of recombination fractions, as defined by the results of population dynamics, is appropriate to allow high adaptation — high mean fitness — and retain adaptability of populations. This advantage is not expressed by the mean of the mean fitness in systems with fluctuating fitnesses without autocorrelation of environments.

Conditions favouring one type of arrangement are generated frequently enough to produce an increase of the mean fitness with tighter linkage (cf. *table 5*). An advantage of some recombination, however, should be expressed in terms of mean fitness, too, with some autocorrelation or cyclically varying environments according to the results of Charlesworth (1976).

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