

The interaction of selection and linkage: Heterotic Model

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In 1960s, we known well how selection of single loci contribute to the genetic change in a population. The study of multiple-gene was just at start point. Most of the multiple-gene formation are simply extensions of single loci models, which ignore the problem of linkage. Then, there were a few of papers which investigated for more or less special cases of selection. The results of these investigations were sufficient to show that even for two loci linkage might have profound effects on the natural selection. Natural selection may major effect on distribution of coupling and repulsion linkage in a population.

Here are the two-locus model from Lewontin and Kojima: 1. If the fitnesses are additive between loci, linkage does not effect the final equilibrium state of the population. 2. If linkage is tighter than the value demanded by the magnitude of the epistasis there may be permanent linkage disequilibrium. 3. The rate of genetic change with time is affected by the tightness of the linkage. 4. In some cases stable gene frequency equilibria are possible only if linkage is tight enough.

Although conclusions were based on two-locus model, they pointed clearly the importance of linkage for understanding the changes of gene frequencies in populations. In fact, some experimental results can be understood only if the interaction of selection and linkage is taken into account.

Here were three main modes of selection in natural and artificial populations. The first is heterotic models, in which heterozygotes at each locus are more fit than homozygotes. The second is the series optimum selection, in which selection against individuals whose phenotypes deviate from some intermediate optimum. The last is unidirectional selection in which an extreme phenotype or genotype is selected against. The linkage of these three modes are different, so I just review the first mode's linkage analysis.

The mathematics of selection and linkage

Let there be two loci with two alleles each denoted by A, a and B, b respectively.

The operation T is really a sequence of operations and the flow from $[g]_0$ to $[g]_1$. M is the mating operator and for the case of random mating it is the row by column multiplication of the vector $[g]_0$ by its transpose $[g]_0'$ to produce the symmetric zygotic matrix $[Z]$.

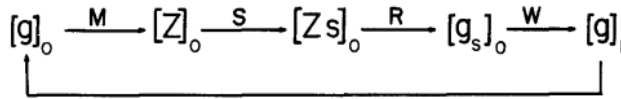


FIGURE 2.—The genetic transformation, T , broken up into its components during a single generation.

Figure 1: Broken up genetic transformation into its components

Heterotic Selection

There is increasing evidence that if heterosis at the locus level is importance in natural populations, the degree of heterosis at each locus is a fuction of the amount of heterozygosity at other loci. In other words, the epistatic interaction determine heterzygote superiority. Then, author assumed that epistasis will cause an ineractino of linkage and selection at gene frequency equilibrium.

This paper examine the results of this interaction for some-locus and five-locus models. The dynamics of two-locus models has been discussed by Lewontin and Kojima. They present paper will examine some two-locus heterotic models in which symmetry of fitness is not assumed, so that numerical solutions are necessary or in which the stability of equilibria is not obvious and considerable numerical calculation was necessary to test the stability of the equilibria.

Two-locus models:

It is a simple heterotic model with epistatic interation. Each locus shows heterosis in every combination with other locus, but the heterosis is not additive between loci. Thus, the degree of heterosis at locus A is greater when in the presence of Bb than in the presence of BB or bb . A similar inequality holds for the B locus, where heterosis is also more pronounced when A is heterozygous than when it is homozygous. This is then a cumulative heterotic model, fitness increasing more rapidly the mroe loci that are made heterozygous.

- Frist, the stable equilibrium of gametic frequencies does not correspond to linkage equilibrium even with free recombination although the degree of linkage disequilibrium is small. That is, there is s significant excess of coupling or repulsion at equilibrium no matter how much recombination goes on.
- Second, there are pairs of soolutions for each recombination value, one corresponding to an excess of coupling and one to an excess of repulsion. Gene frequencies change with recombination.
- Third, the mean adptive value of the population is highest when there is close linkage and it is higher for repulsion equilibrium than for coupling equilibria. The most profound chagne in the population due to linkage is

in the genotypic distribution at equilibrium which is turn a reflection of the very large differences in gametic frequency from one value of linkage to another.

Model 2 It is slightly different from Model 1. The results represents a considerable change for the first locus.

Model 3 This is a symmetrical model of the kind considered by L and K, but has certain peculiarities which require careful investigation. This model is not presented as representing a particular natural linkage and natural selection.

Five-locus models:

Simplifying assumptions: - (1).The loci are interchangeable in their effect - (2).There is some heterosis for each locus, irrespective of whether the other four loci are heterozygous or homozygous. This assure that all gene frequencies will come to a stable equilibrium of gene frequencies at an intermediate value. - (3).In view of (2), there is no loss of generality by further specifying that 0/0 and 1/1 homozygotes have equal fitness so that the gene frequencies at each locus come to equilibrium at $p=q=0.50$.

Model 1 was chosen to have decreasing epistatic interaction with added heterozygosity, so that the increase from four to five loci heterozygous is accompanied by an increase in fitness nearly equal to that found in the increase from 3 to 4 loci heterozygous. However, model 2 shows a constant epistatic interaction from level to level of heterozygosity.

Here are three features.

Correspondence to Experiments

Any extra comparison of prediction to experiment is virtually impossible with five loci, since the fitnesses of all the genotype would be virtually impossible to measure. However, the qualitative aspects of these prediction can be tested in experimental populations in which five loci are segregating.

General Implications of the Results

Five-locus models add an important observation not seen in the two locus model