MATHEMATICAL MODELLING AND ANALYSIS OF THE FIXATION PROCESS OF DISCRETE GENETIC STRUCTURES IN A MENDELIAN ONE-LOCUS POPULATION OF DIPLOID ORGANISMS

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Summary

Motivation: An explaining the mechanisms of formation of discrete biological taxa is one of the main problems of evolutionary theory.

Results: An integral model of the evolution of a Mendelian one-locus population of diploid organisms with continual allele diversity developing under density-limiting conditions or without density limitation has been proposed and analyzed. The model was used to study the mechanism of the appearance of discrete genetic structures, i.e., the fixation of a limited number of alleles. Local resistance of the resultant genetic distributions to homogeneous equiprobable mutations has been demonstrated.

Introduction

To explain the mechanisms of formation of discrete biological taxa is one of the main problems of evolutionary theory. The genetic diversity within a species is often discrete and strictly limited. The reason is hardly the discreteness of the “heredity carrier” itself, i.e., DNA, consisting of monomers. A protein consists of several hundred aminoacids. Mutational variation may yield a vast diversity of molecules of a given protein, with most of these molecules functioning normally (Altukhov, 2003). However, only one form of a given protein is usually fixed in the populations. Two forms of a protein are seldom fixed; three forms, even more seldom; etc. What is the mechanism of fixation of some alleles and loss of others? There are two main hypothesis answering this question: (1) random loss of alleles because of gene drift and (2) balanced polymorphism determined by the selective advantage of heterozygotes. Both of them have supporters and opponents (Crow, Kimura, 1971; Lewontin, 1974; Altukhov, 2003), but neither provides a definite solution to the problem. Our study is one more attempt to analyze this issue.

Model

Let us consider a large Mendelian panmictic sexless population in which the inheritance of a certain character is determined by one with gene infinite number alleles. The genetic-structure and population dynamics in this population can be described by the following system of equations:
Here, \( n \) is the ordinal number of the generation, \( x_n \) is the population number, the function \( q_n(\tau) \) is the frequency density of allele \( \tau \) in the population in the \( n \)-th generation, \( W(\xi, \tau) \) is the adaptation function of the genotype \((\xi, \tau)\), \( W_n \) – is the population mean adaptation in the \( n \)-th generation, each of \( \xi \) and \( \tau \) being the allele markers and may be any real number within the interval \([0, 1]\). In fact, we approximate a finite-dimensional situation by an infinite-dimensional one (Gorban, Khlebopros, 1988) in order to use all the possibilities of continuous functions analysis.

If density-dependent selection takes place in the population, then fitnesses are decreasing functions of the population size. The exponential dependence of fitness on population size is suitable for analysis. This dependence can be written as follows:

\[
W(\xi, \tau, x_n) = \exp \left( R(\xi, \tau) (1 - x_n/K(\xi, \tau)) \right).
\] (2)

In this case, each genotype is characterized by two parameters, \( R(\xi, \tau) \) and \( K(\xi, \tau) \) (the Malthusian and the resource parameters, respectively) (Evdokimov, 1999).

The special case of the integral dynamic model of a one-locus diallelic population with adaptations independent of the population number, i.e., in the absence of density control, is of special interest. This model is a logical generalization of the classical model of the dynamics of a one-locus diallelic population with constant adaptations of genotypes (Ratner, 1977; Frisman, 1986) extending it to the case when there is a continual number of alleles of one locus.

In the absence of density limitation, the population number dynamics is of no interest, because it will either infinitely grow (if \( W_n > 1 \)) or constantly decrease (if \( W_n < 1 \)). Therefore, let us consider separately the dynamics of allele-frequency density in case of unlimited population:

\[
q_{n+1}(\tau) = q_n(\tau) \left( \int_0^1 W(\xi, \tau) q_n(\xi) d\xi \right) \left/ \int_0^1 W(\xi, \tau) q_n(\xi) d\xi d\tau \right.
\] (3)

Here the adaptation function \( W(\xi, \tau) \) is also a function of the Malthusian and the resource parameters of \((\xi, \tau)\)-genotype.

Then we studied the effect of mutations on the dynamics of the integral model of unlimited population. Let mutations occur before selection; then, the allele-frequency density in the \( n \)-th generation after mutation takes the form

\[
\tilde{q}_n(\tau) = \int_0^1 q_n(\xi) \mu(\xi, \tau) d\xi,
\] (4)

where \( \mu(\xi, \tau) \) is the probability density of the mutation from \( \xi \) to \( \tau \).

After this, selection takes place:

\[
q_{n+1}(\tau) = \tilde{q}_n(\tau) \left( \int_0^1 W(\xi, \tau) \tilde{q}_n(\xi) d\xi \right) \left/ \int_0^1 W(\xi, \tau) \tilde{q}_n(\xi) d\xi d\tau \right.
\] (5)

Stationary solutions of Eq. (5) are continuous functions explicitly depending on mutations described by the function \( \mu(\xi, \tau) \). It may be expected that, if selection “aims” at creating a discrete distribution of allele “frequencies” in the population, mutations will “smear” the almost discrete peaks.

We assume also that mutations are homogeneous and equiprobable (6) and then Eq. (6) may be rewritten as (7).
\[ \mu(\xi, \tau) = \begin{cases} \delta, & \forall \xi \neq \tau \\ [1-\delta, & \forall \xi = \tau, \xi, \tau \in [0,1]. \end{cases} \] (6)

\[ \tilde{q}_n(\tau) = (1-\delta)q_n(\tau) + \delta. \] (7)

**Results**

It has been analytically demonstrated that both of the evolution described by system of equations (1) and those described by equation (3) transforms correct genetic distributions into correct ones (Frisman, Zhdanova, 2003). Furthermore, we have found that, if there is fitness heterogeneity in the space of genotypic classes (in mathematical terms, this means that \( \{1\), 0\( (,, ) (, ) ( ))\ Wd x d xf x \xi \tau \xi \neq \Psi \int , \) where \( f(x_n) \) is the function of population number alone and does not depend on \( \tau \) – in case of density-dependent natural selection\) and \( \{\int_0^\infty W(\xi, \tau, x_n)d\xi = \Psi(\tau, x_n) = f(x_n), \) where \( f(x_n) \) is the function of population number alone and does not depend on \( \tau \) – in case of unlimited population\), then the proposed model has no continuous, stationary distributions of allele frequencies (Frisman, Zhdanova, 2003). Therefore, it can be expected that the evolution of (1) (and (3)) will result in the transformation of continuous density distributions of allele frequencies into vastly inhomogeneous ones provided that there is diversity of fitness values.

The dynamics of the proposed model was studied numerically. We have analyzed the population number dynamics and changes in population genetic structure with time for different variants of the initial distributions of allele “frequencies” and adaptation functions. The stationary genetic distributions being vastly inhomogeneous were obtained really in case of adaptations heterogeneity presence. Moreover, the stationary genetic distributions obtained have a few peaks number. Then we have performed numerical analysis of the dynamic behavior of the system with mutations of (7, 5) at a fixed value \( \delta = 0.1 \). It has been shown that mutations can slightly smear the “discrete” distribution and, in addition, increase the size of the peak and considerably change the distribution pattern. Note, however, that markedly heterogeneous distributions with small numbers of peaks are still observed, the mutation rate that we set in the model \( \delta = 0.1 \) is substantially exaggerated compared to the actual value in natural populations \( (10^{-5}) \). Note that mutations have increased genetic diversity in some model cases.

**Discussion**

Thus, the results of our study demonstrate that, “in the general case,” even an infinitely (continually) large diversity of alleles is reduced to a small number of discrete alleles in the course of evolution under strictly determined conditions. Even introduction of some equiprobable mutations into the model does not result in stable homogeneous distributions. The mutations process somewhat “smears” the resultant distributions; however, a few almost discrete peaks are preserved, although both their number and heights may increase. Apparently, this situation will not change even in the case of a large (but finite) number of original alleles. The dynamic equations are such that evolution does not lead to homogeneous distributions of large numbers of alleles. Typically, distributions with small numbers of forms appear. Apparently, this explains why the allelic diversities of many genes are substantially limited in natural populations.

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References