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Probability of Ultimate Survival of a Newly Occurred Inversion in Natural Populations

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Summary. An expression was derived that gave necessary and sufficient conditions for the ultimate probability of survival of a newly occurred inversion to be positive. The assumptions included a large population with a Poisson progeny distribution per parent and a time-heterogeneous average number of inversion heterozygote progeny (λ_t) for one inversion heterozygote parent. It was shown that an inversion, not possessing a unique or constant selective advantage, could have a positive ultimate probability of survival.

Introduction

Inversion polymorphisms exist widely in natural populations, particularly those of *Drosophila.* There are many experimental studies on the fitness of inversion polymorphisms in natural populations. Little has been done, however, by way of investigating the genetic mechanisms with which an inversion might be established in a population. As Nei, Kojima and Schaffer (1967) pointed out, there are three stages in the establishment of an inversion. The first stage consists of the survival of an inversion, which has occurred in an individual in the population. The second stage is its increase in frequency; and the third stage is the way it is brought to a balanced polymorphism. In large populations the first stage is stochastic, while the second and third stages are deterministic. Using a deterministic model, Nei, Kojima and Schaffer (1967) have investigated ways by which an inversion can increase in frequency in a population. Haldane (1957) studied, also, some of the genetic mechanisms by which an inversion may be brought to a stable equilibrium. Ohta and Kojima (1968) investigated the first stage in the evolutionary process of an inversion. Assuming a large population and a Poisson progeny distribution per individual, they derived approximate expressions for the ultimate probability of survival of an inversion under a simple genetic model. Of interest was their conclusion, in part, that the ultimate probability of survival of an inversion is zero if the inversion does not possess a unique effect (an effect located only on the inverted segment) which gives it a permanent and constant selective superiority at all times.

Our purpose in this note is to provide necessary and sufficient conditions for the ultimate probability of survival of an inversion to be positive. We will also show that it is possible to have a positive probability that the inversion is ultimately retained in the population when it does not have a unique selective advantage.

Probability of Ultimate Survival

We shall assume, as Ohta and Kojima (1968), a single inversion in a large population and let λ_t denote the mean number of inversion heterozygote progeny for one inversion heterozygote parent in generation t. Assuming a Poisson progeny distribution, the probability generating function of the number of inversion heterozygote progeny per heterozygote parent is

$$P_t(z) = \exp \lambda_t (z - 1) .$$

Let $G_t(z)$ denote the probability generating function of the number of progeny of an original inversion heterozygote in generation t. Then

$$\begin{aligned} G_1(z) &= \exp \lambda_0 (z - 1) , \\ G_2(z) &= G_1(P_1(z)) = \exp \lambda_0 \left(\exp \lambda_1 (z - 1) - 1\right) , \\ &\vdots \\ G_t(z) &= G_{t-1}\left(P_{t-1}(z)\right) \\ &= \exp [\lambda_0, \ldots , \\ &\qquad \lambda_{t-2} (\exp \{\lambda_{t-1} (z - 1)\} - 1) \ldots)] . \qquad (1) \end{aligned}$$

The probability that there are no inversions in the population in generation t is $G_t(0)$ and, therefore, the probability that there is at least one in generation t is

$$U_t = 1 - G_t(0) .$$

U_t is the survival probability of the inversion at time t and is dependent on the entire set of fitness values (λ_t) prior to generation t. From (1) U_t can be expressed as

$$\begin{aligned} U_t = 1 - \\ \exp \left(- \lambda_0 (1 - \exp - \lambda_1 (\ldots \lambda_{t-2} (1 - \exp - \lambda_{t-1})))\right) \end{aligned} \qquad (2)$$

If we let

$$V_{t+1,1} = 1 - \exp - \lambda_t$$

and define recursively

$$V_{t+1,n} = 1 - \exp - \lambda_t(V_{t+2,n-1}); \qquad n = 2, 3, \ldots, \tag{3}$$

we see that

$V_{t+1,n} = U_{t+n} =$ the survival probability at time $t+n$

and for $t = 0$

$$V_{1,n} = U_n\,.$$

In the limit (3) is

$$V_{t+1,\infty} = 1 - \exp - \lambda_t(V_{t+2,\infty})\,, \tag{4}$$

using (3) we now show that if $\lambda_t \geq 1 + \varepsilon$ for all t larger than some t_0 and any $\varepsilon > 0$, then $\lim\limits_{t} U_t = U_\infty > 0$, where U_∞ is the ultimate survival probability of a new inversion. Because of (4) we can, without loss of generality, assume $t_0 = 0$.

It is easily seen that

$$(1 - e^{-x}) > \frac{x}{1+x} \tag{5}$$

for $x > 0$. Thus,

$$V_{t+1,1} = 1 - \exp - \lambda_t >$$
$$1 - \exp - (1+\varepsilon) > \frac{1+\varepsilon}{1+(1+\varepsilon)}\,.$$

Repeatedly utilizing (5), it can be shown by induction that

$$V_{t+1,n} > (1+\varepsilon)^n \Big/ \sum_{i=0}^{n} (1+\varepsilon)^i\,.$$

Setting $t = 0$, and taking the limit on both sides of this expression gives

$$U_\infty \geq \frac{\varepsilon}{1+\varepsilon} > 0 \tag{6}$$

which is the desired conclusion. This case is that of the inverted segment having a unique selective advantage, ε. Notice also that (6) provides a lower bound for U_∞ when the unique advantage is initially present.

We now establish necessary and sufficient conditions for the loss of a newly induced inversion to occur with probability one. Because of the previous result and expression (4), we can assume $0 < \lambda_t < 2$ for all t.

It is easily seen that

$$\frac{x}{1+x} < 1 - e^{-x} < \frac{2x}{2+x} \tag{7}$$

for $0 < x < 2$ and, therefore,

$$\frac{\lambda_t}{1+\lambda_t} < V_{t+1,1} < \frac{2\lambda_t}{2+\lambda_t}$$

for all t. Repeatedly using (7) and by induction, it can be shown that

$$\frac{\prod\limits_{j=t}^{t+n-1} \lambda_j}{1 + \sum\limits_{j=t}^{t+n-1} \prod\limits_{v=j}^{t+n-1} \lambda_v} < V_{t+1,n} < \frac{2\left[\prod\limits_{j=t}^{t+n-1} \lambda_j\right]}{2 + \sum\limits_{j=t}^{t+n-1} \prod\limits_{v=j}^{t+n-1} \lambda_v}\,.$$

Setting $t = 0$ and simplifying, we have

$$\left[1 + \sum_{j=0}^{n-1} \prod_{v=0}^{j} \frac{1}{\lambda_v}\right]^{-1} < U_n <$$
$$2\left[1 + \prod_{j=0}^{n-1} \frac{1}{\lambda_v} + \sum_{j=0}^{n-1} \prod_{v=0}^{j} \frac{1}{\lambda_v}\right]^{-1}. \tag{8}$$

Clearly, a necessary and sufficient condition for loss to occur with probability one is

$$\sum_{j=0}^{\infty} \prod_{v=0}^{j} \frac{1}{\lambda_v} = \infty\,. \tag{9}$$

Expression (9) indicates that for the ultimate probability of survival to be positive, the expected number of inversion descendants must be infinite at time infinity. Ohta and Kojima reached the same conclusion by a different approach.

If $\lambda_t < 1$ for $t \geq t_0$, in which case the fitness of the inversion has a selective disadvantage, expression (9) is satisfied and the inversion is lost with probability one as expected. If $\lambda_t = 1 + \delta_t$, but $\lim \lambda_t = 1$, then (9) might or might not be satisfied depending on the rate of convergence of λ_t to 1; and, therefore, U_∞ might be zero or might be greater than zero.

Discussion

It is seen that, when the inverted segment has a constant or unique selective advantage (i.e., $\lambda_t \geq 1 + \varepsilon$) for all t, expression (6) gives a lower bound $\left(\frac{\varepsilon}{1+\varepsilon}\right)$ for the ultimate probability of survival. If ε is small the ultimate probability of survival is equal or greater than ε. If the inversion heterozygote has a non-unique selective advantage, it might still be possible for the ultimate probability of survival to be positive. To see that, let us assume that $\lambda_t = 1 + 2/t$; $t \geq 1$. Direct calculation yields

$$\sum_{j=0}^{\infty} \prod_{t=0}^{j} \frac{1}{\lambda_t} = \frac{1}{\lambda_0}\left[1 + \sum_{j=1}^{\infty} \frac{2}{(j+1)(j+2)}\right] < \infty$$

thus condition (9) is not satisfied and from (8) $U_\infty > 0$. What is happening here is that the process by which the inversion heterozygote loses its superiority with time to become selectively neutral ($\lambda_t = 1$) is rather slow that the inversion becomes established before it loses all of its selective advantage.

Ohta and Kojima reached the opposite conclusion when they stated that an inversion that does not have a unique advantage will become extinct with probability one ($U_\infty = 0$). Their conclusion turns out to be correct for the simple genetic model that they considered, but what we should emphasize here is that this need not be true under more complicated models.

The model considered by Ohta and Kojima is the following: Assume that there are n loci in the inverted segment and let the fitness of the ith locus be

$A_i\,A_i$	$A_i\,a_i$	$a_i\,a_i$
1	$1 - h_i\,s_i$	$1 - s_i$

with the frequencies of A_i and a_i at time t being P_{it} and q_{it}. If the ith locus of the inversion carries the A_i allele, then the difference in average fitness over n loci, between the inversion heterozygote and non-inversion zygotes is

$$\delta_t = \frac{\sum_{i=1}^{n} s\, q_{it}\,(2\, h_i\, P_{it} - h_i + q_{it})}{1 - \sum_{i=1}^{n} s_i\, q_{it}\,(2\, h_i\, P_{it} + q_{it})}\,.$$

For this model $\lambda_t = 1 + \delta_t$ and

$$\lim_t \lambda_t = 1\ ,$$

the rate at which $\lambda_t \to 1$ is proportional to the rate at which $q_t \to 0$ or $q_t \to \hat{q}$ where $\hat{q}$ is the equilibrium gene frequency in case of overdominance. It can be shown that this rate is proportional to e^{-t} and hence the convergence of $\lambda_t \to 1$ is "fairly fast" such that expression (9) is satisfied and $U_\infty = 0$ or the ultimate probability of survival of the inversion is zero.

For the same model, Ohta and Kojima considered the case where at one locus (i) the a_i allele is fixed in the non-inversion portion of the population in which case the inversion heterozygote has a constant selective advantage $s\,(1 - h)$ at that locus. (This was termed a unique advantage for the inversion.) For s small, $h = 1/2$ and all loci having the same effect, δ_t becomes

$$\delta_t = 1/2\, s + \frac{n\, s}{2}\, q_t$$

and

$$\lambda_t = 1 + \delta_t = 1 + 1/2\, s + \frac{n\, s}{2}\, q_t\,. \qquad (10)$$

Here the ultimate probability of survival is positive and was shown by Ohta and Kojima to be

$$s \leq U_\infty \leq (n+1)\, s\,. \qquad (11)$$

In (10) λ_t is of the form

$$\lim \lambda_t = 1 + \varepsilon\,,$$

hence from (6) $\frac{\varepsilon}{1+\varepsilon} \leq U_\infty$ which conforms to the inequality in (11). Furthermore, if we choose the fitness of the ith locus to be time dependent, $s = \frac{4}{t}$, then there is a positive probability of ultimate survival without requiring that the inversion has a unique or constant advantage $1/2\, s$. That is so, since

$$\lambda_t = 1 + \frac{2}{t} + 2\, n\, q_t/t > 1 + 2/t$$

hence condition (9) is not satisfied and from (8) the ultimate probability of survival is positive ($U_\infty > 0$). The assumption that $s = 4/t$ is small compared to unity does not hold for the initial generations. This, however, does not affect the conclusion $U_\infty > 0$.

It occurred to us that any genetic model, of the sort investigated by Ohta and Kojima, where fitness is constant over time will give a zero ultimate probability of survival, since the rate at which the non-unique selective advantage δ_t converges to zero is proportional to the rate gene frequencies converge to one, zero or the equilibrium values. This rate is deterministic and is seen to be "fast" such that $U_\infty = 0$.

It is when we take into account non-constant fitness values that the rate of convergence δ_t to zero may become slow enough for U_∞ to be positive.

The assumption in the above argument that $s = \frac{4}{t}$ is of course arbitrary; and we do not know of any specific situation where this might be the case. It is not unrealistic, however, to suppose that the selective advantage of a gene or gene complex might be a function of time. This can be understood when we consider that the selective advantage of a gene is conditioned by the environment and genetic background of that gene. Environment and genetic background change with time. This makes it plausible for a gene to lose its advantage with time. The rate at which this happens can be very slow and possibly slower than $\frac{1}{t}$, the required rate of convergence in our model.

Zusammenfassung

Es wurde ein Ausdruck abgeleitet, der notwendige und hinreichende Bedingungen dafür ergab, daß die endgültige Überlebenswahrscheinlichkeit einer neu aufgetretenen Inversion positiv ist. Die Annahmen schließen eine große Population mit einer Poisson-Verteilung der Nachkommen je Elter und eine zeitheterogene durchschnittliche Anzahl von inversionsheterozygoten Nachkommen (λ_t) eines inversionsheterozygoten Elters ein. Es wird gezeigt, daß eine Inversion, die keinen konstanten oder einzigartigen Selektionsvorteil hat, eine positive endgültige Überlebenswahrscheinlichkeit haben kann.

References

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