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THEORETICAL AND APPLIED GENETICS

The Effect of Positive Assortative Mating at One Locus on a Second Linked Locus

Part 1: The Genotypic Structure of the Offspring Generation

H.-R. Gregorius
Lehrstuhl für Forstgenetik und Forstpflanzenzüchtung, Universität Göttingen (Federal Republic of Germany)

Summary. A model for positive assortative mating based on genotype for one locus is employed to investigate the effect of this mating system on the genotypic structure of a second linked locus as well as on the joint genotypic structure of these two loci. It is shown that the second locus does not attain a precise positive assortative mating structure, but yet it shares a property that is characteristic of positive assortative mating, namely an increase in the frequency of homozygotes over that typically found in panmictic structures. Given any arbitrary genotypic structure for the parental population, the resulting offspring generation possesses a structure at the second locus that does not depend on the recombination frequency, while the joint structure of course does. In case assortative mating as well as linkage are not complete, there exists a unique joint equilibrium state for the two loci, which is characterized by complete stochastic independence between the two loci as well as by Hardy-Weinberg proportions at the second locus. For the second locus alone, Hardy-Weinberg equilibrium is realized if and only if gametic linkage equilibrium and an additionally specified condition are realized.

Key words: Equilibria – Hitchhiking – Linkage disequilibrium – Stochastic independence

Introduction

Systems of mating may be grouped according to two points of view:
a) the system is defined with respect to criteria that do not refer to individuals' genetic properties (such as systems of inbreeding or random-mating),
b) the system is defined with reference to characters that are subject to genetic control (such as assortative mating based on genotype or phenotype).

Since a system of type a) does not take into consideration genotypes present at any of the gene loci, all of them are affected in a like manner as far as allelic structures (allele frequencies) and genotypic structures (genotype frequencies) are concerned.

This certainly does not hold true for a system of type b), since here a particular section of an individual's genome is explicitly responsible for this individual's mating behavior, while for all remaining loci no laws are specified. Nevertheless, in view of linkage or, more generally speaking, any kind of stochastic dependence (e.g. linkage disequilibrium) between the different loci, one expects some of the implications of the mating system to be carried over to those loci that are not explicitly affected by the system's rules.

This supposition, of course, does not apply to mating systems only, but is also of importance for any system involving forces that act upon a specific section of the genome.

For example, the consequences of selection in this context have been investigated thoroughly by several authors, and the main results have been reviewed by Kojima and Lewontin (1970) under the viewpoint of their evolutionary significance. Applying the Wrightian fitness model to one locus, selection results in an alteration of allele frequencies; and it was shown that at a second, selectively neutral locus, a change in allele frequencies is induced that is related to the allelic change at the locus subject to selection, and to the amount of linkage disequilibrium (hitch-hiking effect). The above statement describes, in a comparatively simple manner, the mode of action of one of the mechanisms responsible for transmitting the laws from one locus to another within the frame of basic selection theory.

Whereas selection is an evolutionary component affecting the genic variability of a population, mating systems predominantly influence the organization of the gene pool, that is, mating systems affect the way in which pairs of alleles (for diploid organisms) are assigned to individuals and thus affect the genotypic structure. Recalling the definition of mating systems of type b), given in the beginning, one now has to clarify the effects of such a system on the genotypic structures at loci that are 'neutral', in the sense that the mating behavior of individuals is not influenced by these loci.

A considerable number of publications deal with various kinds of assortative mating at one locus (for a résumé see for example Karlin 1969), but to the present author's knowledge no attempts has yet been made to extend these results to the above-mentioned supposition, with the exception of the paper by Vinogradova and Zhivotovsky (1974). These authors investigated a model of positive assortative mating under a number of restrictions. The aim of the present paper is to describe, in general, the effect of positive assortative mating that is based on genotype with regard to one locus on the genotypic structure of a second linked locus. In the present treatment, I have excluded all other forces, such as drift, selection, mutation and migration, which also act upon the genetic structure of the population.

Experimental data about frequency distributions of genotypes (e.g. referring to isozyme phenotypes), recorded with the intention of investigating mating systems, must rely on the information obtainable from the parental population and the resulting offspring generation as close to the zygotic stage as possible (for instance, from adult plants and their seeds). It is therefore of interest to investigate the way in which assortative mating affects transformation of the parental genotypic structure into that of the progeny.

The Model

Considerations are based on two diploid autosomal loci, with arbitrary numbers of alleles each, and recombination frequency 1-c. The alleles at the one locus (the A-locus) are denoted by A_i and at the other locus (the B-locus) by B_j. The two-locus genotype

$$\begin{matrix} A_i A_k \\ B_j B_l \end{matrix}$$

is assumed to be the result of the fusion of two gametes carrying the genes A_i, B_j and A_k, B_l respectively. No attention is paid to which of these two gametes is the male or the female.

If P^{ik}_{jl}, P^{ik}, P_{jl} and P^i_j are the frequencies of the genotypes $\begin{matrix} A_iA_k \\ B_jB_l \end{matrix}$, A_iA_k, B_jB_l and the gamete $\begin{matrix} A_i \\ B_j \end{matrix}$ in the gametic production, respectively, this implies

$P^{ik}_{jl} = P^{ki}_{lj}$, $P^{ik} = P^{ki}$, $P_{jl} = P_{lj}$, $P^{ik} = \sum\limits_{j,l} P^{ik}_{jl}$ for $i \neq k$,

$P^{ii} = \sum\limits_{\substack{j,l \\ j \leqslant l}} P^{ii}_{jl}$, P_{jl} attains an analogous representation,

$$\sum_{\substack{i,k,j,l \\ i<k}} P^{ik}_{jl} + \sum_{\substack{i,j,l \\ j \leqslant l}} P^{ii}_{jl} = \sum_{\substack{i,k \\ i \leqslant k}} P^{ik} = \sum_{\substack{j,l \\ j \leqslant l}} P_{jl} = \sum_{\substack{i,k,j,l \\ j<l}} P^{ik}_{jl} + \sum_{\substack{i,k,j \\ i \leqslant k}} P^{ik}_{jj} = 1,$$

$P^i_j = \frac{1}{2} \cdot \sum\limits_{k,l} (c \cdot P^{ik}_{jl} + (1-c) \cdot P^{ik}_{lj}) + \frac{1}{2} \cdot P^{ii}_{jj}$. Furthermore,

$p^i = \sum\limits_j P^i_j$ is the frequency of A_i at the A-locus and $p_j = \sum\limits_i P^i_j$

is the frequency of B_j at the B-locus. The P^i_j refer to the gamete production of a population whose genotypic structure is given by the above set of genotype frequencies, and these are assumed to be the same among the males and among the females within the population.

The mating system now shall be defined with regard to the A-locus as follows: Each individual possessing genotype A_iA_k has the probability α of selectively (i.e. assortatively) mating with an A_iA_k type, while with probability $1\text{-}\alpha$ it mates at random from the whole population; for simplicity the probability α is assumed to be the same for all genotypes with regard to the A-locus. As a consequence of the absence of differential reproductive selection, all individuals are equally likely to take part in the process of reproduction. This condition can be realized, for instance, if the assortative choosing of mates is restricted to one sex, while all members of the other sex fertilize or are fertilized.

The basic idea is to consider the population to be subdivided into parts, each of which corresponds to the set of all individuals possessing a genotype A_iA_k at the A-locus. According to the above specifications, a fraction α of such a group practices assortative mating with a like A-locus group but mates randomly with regard to the B-locus, and a fraction $1\text{-}\alpha$ mates at random with the whole population. In order to arrive at numerical results, the following definitions will be applied:

$P^{i|ik}_j$:= frequency of the gamete $\begin{matrix} A_i \\ B_j \end{matrix}$ within the gametic production of the group of A_iA_k-individuals,

$p_{j|ik}$:= frequency of the allele B_j at the B-locus within the group of A_iA_k-individuals,

$P^{i;ik}_j$:= $P^{i|ik}_j . P^{ik}$ and $p_{j;ik} := p_{j|ik} . P^{ik}$ are the corresponding unconditional probabilities (frequencies).

It follows that $P_j^{i;ik} = \frac{1}{2} \cdot \sum_l (c \cdot P_{jl}^{ik} + (1-c) \cdot P_{lj}^{ik})$

for $i \neq k$ and $P_j^{i;ii} = \frac{1}{2} \cdot \sum_l P_{jl}^{ii} + \frac{1\frac{1}{2}}{2} \cdot P_{jj}^{ii}$,

$p_{j;ik} = \frac{1}{2} \cdot \sum_l (P_{jl}^{ik} + P_{lj}^{ik}) = P_j^{i;ik} + P_j^{k;ik}$ $(i \neq k)$ and

$p_{j;ii} = P_j^{i;ii}$.

From this, some elementary properties may be deduced:

$$\left.\begin{array}{l}
\sum\limits_j P_j^{i;ik} = \frac{1}{2} \cdot P^{ik}, \ \sum\limits_j P_j^{i;ii} = P^{ii}, \ \sum\limits_{j,i} P_j^{i;ik} = p^k, \\[2ex]
\sum\limits_k P_j^{i;ik} = P_j^i, \ \sum\limits_{i,k} P_j^{i;ik} = p_j, \ \sum\limits_{\substack{i \\ i \neq k}} P_j^{i;ik} = \sum\limits_i p_{j;ik} - P_j^k, \\[2ex]
\sum\limits_j p_{j;ik} = P^{ik} \text{ for all i,k and } \sum\limits_{\substack{i,k \\ i \leqslant k}} p_{j;ik} = p_j.
\end{array}\right\} \quad (1)$$

In the following sections it will be shown that, without such detailed description of the association of genes at two loci, it is impossible to investigate the effects on the B-locus produced by the mating system of and linkage to the A-locus.

The Genotypic Structure of the Resulting Offspring Generation

The basic equations specifying the transition from the parental genotypic structure to that of their progeny are given in the Appendix. This section, therefore, concentrates only on reformulations that are appropriate for demonstrating immediately the type of dependence of the B-locus on the A-locus. Summation over j and l in Eqs. (2) in the Appendix leads to the structure of the A-locus:

$$\begin{aligned}
P'^{ik} &= \frac{1}{2} \cdot \alpha \cdot P^{ik} + 2(1-\alpha) \cdot p^i \cdot p^k = 2 \cdot p^i \cdot p^k - \\
&\quad - 2 \cdot \alpha \cdot (p^i \cdot p^k - \frac{1}{4} \cdot P^{ik}) \text{ for } i \neq k \\
P'^{ii} &= \frac{1}{2} \cdot \alpha \cdot (p^i + P^{ii}) + (1-\alpha) \cdot (p^i)^2 = \\
&= (p^i)^2 + \alpha \cdot (\frac{1}{2}(p^i + P^{ii}) - (p^i)^2)
\end{aligned} \quad (3)$$

Equations (3) represent the well-known results for positive assortative mating based on genotype for one locus (see e.g. Jaquard 1974, p. 250). In these formulae, $\frac{1}{2} \cdot (p^i + P^{ii}) - (p^i)^2$ is always non-negative and therefore the homozygote frequencies exceed those of the corresponding Hardy-Weinberg structure. On the other hand, the expression for two different alleles, $p^i \cdot p^k - \frac{1}{4} \cdot P^{ik}$ may sometimes be negative, indicating that heterozygote frequencies must not always be smaller than the corresponding Hardy-Weinberg frequencies.

Equations (2) and (4) in the Appendix can be rewritten in an intuitively more appealing way if we consider that the allele and gamete frequencies within each group of A_iA_k-individuals may vary from group to group.

With this idea in mind

$V_j^i := \sum_k (P_j^{i|ik})^2 \cdot P^{ik} - (P_j^i)^2$ is the variance of the frequency of the gamete $\genfrac{}{}{0pt}{}{A_i}{B_j}$ between the groups,

$C_{jl}^{ik} := P_j^{i|ik} \cdot P_l^{k|ik} \cdot P^{ik} - P_j^i \cdot P_l^k$ for $i \neq k$ and

$C_{jl}^{ii} := \sum_k P_j^{i|ik} \cdot P_l^{i|ik} \cdot P^{ik} - P_j^i \cdot P_l^i$ for $l \neq j$ is the covariance of the frequencies of the gametes $\genfrac{}{}{0pt}{}{A_i}{B_j}$ and $\genfrac{}{}{0pt}{}{A_k}{B_l}$ with respect to the groups,

$V_j := \sum_{\substack{i,k \\ i \leqslant k}} (p_{j|ik})^2 \cdot P^{ik} - (p_j)^2$ is the variance of the frequency of the allele B_j at the B-locus between the groups, and

$C_{jl} := \sum_{\substack{i,k \\ i \leqslant k}} p_{j|ik} \cdot p_{l|ik} \cdot P^{ik} - p_j \cdot p_l$ is the covariance of the frequencies of the alleles B_j and B_l at the B-locus with respect to the groups. Thus

$$P'^{ik}_{jl} = 2\alpha \cdot C_{jl}^{ik} + 2 \cdot P_j^i \cdot P_l^k \text{ for } i \neq k \text{ or } j \neq l \text{ and}$$

$$P'^{ii}_{jj} = \alpha \cdot V_j^i + (P_j^i)^2 \quad (2a)$$

$$P'_{jl} = 2\alpha \cdot C_{jl} + 2 \cdot p_j \cdot p_l \text{ and } P'_{jj} = \alpha \cdot V_j + (p_j)^2 \quad (4a)$$

These highly condensed representations contain all the relevant information desired in a lucid form. First, a well-known characteristic result from the theory of positive assortative mating at one locus is maintained for the joint structure of the A and B loci as well as for the B-locus separately, namely that the double and single (B-locus) homozygote frequencies exceed the corresponding random-mating frequencies. This excess is proportional to the degree of assortment, α, and the variance of the appropriate gamete and allele frequencies between the groups, each one of which is defined by the set of all individuals having the same genotype at the A-locus. On the other hand the B-locus structure is not precisely a positive assortative mating structure of the kind stated in equations (3), since, in general,

$$V_i \neq \frac{1}{2}\,(p_i + P_{ii}) - (p_i)^2 \quad \text{and} \quad C_{jl} \neq \frac{1}{4} \cdot P_{jl} - p_j \cdot p_l\,.$$

Furthermore, given the genotypic structure of the parental generation, the structure of the offspring at the B-locus does not depend on the recombination frequency, since c is not involved in the computation of the variances V_j and covariances C_{jl}, as can be taken from their definitions. A dependence on c can be realized only if the parental structure already is expressed in terms of c, which certainly will be the case if the above results are extended to several generations.

Some short remarks about the effect and meaning of linkage disequilibrium within the present context shall close this section.

Coefficients of linkage disequilibrium for the two-locus multi-allelic case can be defined properly, according to Cockerham and Weir (1973), with reference to gametes drawn from the whole population. This idea does not apply to our representations, since we need more detailed information concerning the kind of stochastic dependence of genes located on gametes which belong to special groups in the above sense. Therefore, whether or not there is an association between the B_j alleles at the B-locus and the group of A_iA_k-individuals shall be explored. In case there is none, then they are stochastically independent and

$$P_j^{i|ik} = P_j^{k|ik} = \frac{1}{2} \cdot p_{j|ik} = \frac{1}{2} \cdot p_j \ \text{for } i \neq k \text{ and}$$

$P_j^{i|ii} = p_{j|ii} = p_j$. If this independence holds for all groups of A_iA_k-individuals, B_j is completely independent of the A-locus and consequently

$$P_j^i = p^i \cdot p_j \ \text{(from formulae (1))},$$

$$V_j^i = (p_j)^2 \left(\frac{1}{2}\,(p^i + P^{ii}) - (p^i)^2\right),$$

$V_j = 0$ for all i. Finally, extending these assumptions to all alleles at the B-locus, i.e. to all j, it is easily verified that, as a result, the offspring generation has Hardy-Weinberg proportions at the B-locus. Equations (5) together with (3) show that complete stochastic independence between the two loci is preserved in the offspring-generation, which thus implies genetic equilibrium for the B-locus.

The Genetic Equilibrium

As shown above, complete stochastic independence between the two loci in general is sufficient for the genotypic structure at the B-locus to attain a stationary state. Thus one can conclude that a joint equilibrium state for the two loci is realized if, in addition, the population has reached genetic equilibrium at the A-locus. Intuition might indicate that this is the only possible equilibrium state. Whether or not this is true can be proved with the help of Eqs. (5) in the Appendix if one equates the primed and non-primed quantities, and designates these equilibrium values by an upper bar. This leads to the following system of equations:

$$\bar{p}_{j;ik} = 2 \cdot \frac{1-\alpha}{2-\alpha}\,(\bar{P}_j^i \cdot p^k + \bar{P}_j^k \cdot p^i),$$

$$\bar{p}_{j;ii} = \frac{\alpha + 2(1-\alpha)p^i}{2-\alpha} \cdot \bar{P}_j^i = \bar{P}_j^{i;ii},$$

$$\bar{P}_j^{i;ik} = \frac{2(1-\alpha)c}{2-\alpha \cdot c} \cdot \bar{P}_j^i \cdot p^k + \frac{\alpha(1-c)}{2-\alpha \cdot c} \cdot \bar{P}_j^{k;ik} + \frac{2(1-\alpha)(1-c)}{2-\alpha \cdot c} \cdot \bar{P}_j^k \cdot p^i,$$

$$\bar{P}_j^i = \sum_{\substack{k \\ k \neq i}} \bar{P}_j^{i;ik} + \bar{p}_{j;ii}$$

The solutions to this system for $\alpha \neq 1$ and $c \neq 1$ are obtained by applying formulae (1) repeatedly:

$$\bar{P}_j^i = p^i \cdot p_j,\ \bar{P}_j^{i;ik} = \frac{2(1-\alpha)}{2-\alpha} \cdot p^i \cdot p^k \cdot p_j,\ \bar{P}_j^{i;ii} = \bar{p}_{j;ii} = \frac{\alpha + 2(1-\alpha)p^i}{2-\alpha} \cdot p^i \cdot p_j \ \text{and}\ \bar{p}_{j;ik} = \frac{2(1-\alpha)}{2-\alpha} \cdot 2 \cdot p^i \cdot p^k \cdot p_j\,.$$

Again using formulae (1) it is shown that

$$\bar{P}^{ik} = \frac{2(1-\alpha)}{2-\alpha} \cdot 2 \cdot p^i \cdot p^k,\ \bar{P}^{ii} = \frac{2(1-\alpha)}{2-\alpha} \cdot (p^i)^2 + \frac{\alpha}{2-\alpha} \cdot p^i,$$

which is the well known equilibrium state for positive assortative mating,

$$p_j = \bar{p}_{j|ik} = 2 \cdot \bar{P}_j^{i|ik} = 2 \cdot \bar{P}_j^{k|ik} = \bar{p}_{j|ii} = \bar{P}_j^{i|ii},$$

which proves the complete stochastic independence between the two loci and therefore implies

$$\bar{P}_{jl} = 2 \cdot p_j \cdot p_l, \quad \bar{P}_{jj} = (p_j)^2,$$

and

$$\bar{P}^{ik}_{jl} = 2p^ip^k \cdot p_jp_l \cdot \frac{(1-\alpha)(3-\alpha)}{2-\alpha} \text{ for } i \neq k$$

$$\bar{P}^{ii}_{jl} = \frac{2p_jp_l}{2-\alpha} \cdot [2(1-\alpha)(p^i)^2 + \alpha p^i] \quad \text{for } j \neq l$$

$$\bar{P}^{ii}_{jj} = \frac{p_j^2}{2-\alpha} \cdot [2(1-\alpha)(p^i)^2 + \alpha p^i].$$

Hence the initially stated intuitive expectation is confirmed for $\alpha \neq 1 \neq c$, and there exists just one joint equilibrium state for the two loci, which is characterized by complete stochastic independence between the two loci, Hardy-Weinberg proportions at the B-locus and positive assortative equilibrium at the A-locus.

Now from (4a) one may conclude that two successive generations attain Hardy-Weinberg proportions if and only if $V_j = V'_j = 0$ for all j. This is equivalent to $P^i_j = p^i \cdot p_j$ for all i,j (complete gametic linkage equilibrium) and $V_j = 0$ for all j, as can be confirmed with the help of (3) and (5). Applying (1), (3) and (5) it is shown that the last statement implies $V'_j = 0$ and $P'^i_j = p^i \cdot p_j$.

Consequently gametic linkage equilibrium and $V_j = 0$ for all j is a necessary and sufficient condition for the B-locus separately to attain a persistent Hardy-Weinberg equilibrium state. Thus there is no need to require complete stochastic independence between the two loci.

Concluding Remarks

All derivations in the preceeding sections were based on the fundamental concept that the population can be subdivided into groups, each of which consists of all the individuals having the same genotype at the A-locus. The genotypic structure of the progeny at the B-locus could then be given a representation depending on the variance of the frequency of each B-allele between the groups and the covariance of each pair of B-allele frequencies with respect to the groups [Eq. (4a)].

Now consider a situation where one observes frequencies of single-locus genotypes in the parental and the progeny population, the latter deviating from Hardy-Weinberg proportions. Furthermore, suppose that strict positive assortative mating is known to take place with respect to a character (e.g. flowering times within seed plants) whose different expressions determine the assortment. Then, one would probably begin by trying to explain the frequencies in the progeny population by assuming the locus to participate directly in the genetic control of this character. Equations (3) would serve as a comparison.

If this hypothesis cannot be confirmed, the second step would be to set up a 'hitch-hiking' hypothesis. To enable a comparison with the corresponding Eqs. (4a), it is necessary to subdivide the parental population into groups defined by the different character expressions (flowering times) and compute the allelic frequencies within these groups as well as the overall allelic frequencies. With the resulting variances and covariances inserted into (4a), these equations should reflect the genotypic structure of the progeny population if the hypothesis is true.

This example is sufficiently typical for demonstrating how to apply the theoretical results to the interpretation of experimentally obtained data not only for one locus, but also for two-loci situations where one locus can be considered to be responsible for the mating system (whether artificial or natural).

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Dr. H.-R. Gregorius
Lehrstuhl für Forstgenetik
und Forstpflanzenzüchtung der Universität
Büsgenweg 2
34 Göttingen-Weende
(Federal Republic of Germany)

Appendix

Consider the population to be subdivided into groups that mate at random among one another, as was described in the formulation of the model, and apply the quantities defined to fit this concept. Then the formulae for the genotypic structure of the offspring generation (designated by a prime) can be written down immediately.

For the joint structure of the A and B loci one obtains:

$$P'^{ik}_{jl} = 2\alpha \cdot P^{i|ik}_j \cdot P^{k|ik}_l \cdot P^{ik} + 2(1-\alpha) \cdot P^i_j \cdot P^k_l \text{ for } i \neq k$$

$$P'^{ii}_{jj} = \alpha \cdot \sum_k (P^{i|ik}_j)^2 \cdot P^{ik} + (1-\alpha) \cdot (P^i_j)^2 \qquad (2)$$

$$P'^{ii}_{jl} = 2\alpha \cdot \sum_k P^{i|ik}_j \cdot P^{i|ik}_l \cdot P^{ik} + 2(1-\alpha) \cdot P^i_j \cdot P^i_l \text{ for } j \neq 1$$

Summing Eqs. (2) over i and k results in the structure of the B-locus:

$$P'_{jl} = 2 \cdot \alpha \cdot \sum_{\substack{i,k \\ i \leqslant k}} p_{j|ik} \cdot p_{l|ik} \cdot P^{ik} + 2(1-\alpha) \cdot p_j \cdot p_l \quad \text{for } j \neq l \tag{4}$$

$$P'_{jj} = \alpha \cdot \sum_{\substack{i,k \\ i \leqslant k}} (p_{j|ik})^2 \cdot P^{ik} + (1-\alpha) \cdot (p_j)^2 .$$

It follows that $p'_j = p_j$ and $p'^i = p^i$.

Furthermore, Eqs. (2) and (1) allow computation of the remaining probabilities characterizing the association of alleles at the two loci:

$$\begin{aligned} P'^{i;ik}_j &= \frac{1}{2} \cdot \alpha \cdot c \cdot P^{i;ik}_j + (1-\alpha) \cdot c \cdot P^i_j \cdot p^k + \\ &\quad + \frac{1}{2} \cdot \alpha \cdot (1-c)\, P^{k;ik}_j + \\ &\quad + (1-\alpha)(1-c)\, P^k_j \cdot p^i, \quad \text{for } i \neq k \\ P'^{i;ii}_j &= \frac{1}{2} \cdot \alpha (P^i_j + p_{j;ii}) + (1-\alpha)\, P^i_j \cdot p^i, \end{aligned} \tag{5}$$

$$p'_{j;ik} = \frac{1}{2} \cdot \alpha \cdot p_{j;ik} + (1-\alpha)(P^i_j \cdot p^k + P^k_j \cdot p^i) \quad \text{and}$$

$$p'_{j;ii} = P'^{i;ii}_j ,$$

$$P'^{i}_j = c \cdot P^i_j + \alpha \cdot (1-c) \cdot (p_{j;ii} + \frac{1}{2} \cdot \sum_{\substack{k \\ k \neq i}} p_{j;ik}) + \\ + (1-\alpha) \cdot (1-c) \cdot p^i \cdot p_j .$$