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# Change in frequency of a rare mutant allele: A general formula and applications to partial inbreeding models

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**Abstract.** We deduce and prove a general formula to approximate the change in frequency of a mutant allele under weak selection, when this allele is introduced in small frequency into a population which was previously at a fixation state. We apply the formula to autosomal genes in partial selfing models and to autosomal as well as sex-linked genes in partial sib mating models. It is shown that the fate of a rare mutant allele depends not only on the selection parameters, the inbreeding coefficient and the reproductive values of the sexes in sex-differentiated populations, but also on coefficients of relatedness between mates. This is interpreted as a kin selection effect caused by inbreeding per se.

## 1. Introduction

An approximate adaptive topography for partially inbred populations evolving under weak selection was proposed some time ago by Wright (1942). This topography is a function of the population state which involves, apart from the selection parameters, Wright's fixation index, $F$, also called the inbreeding coefficient, and the reproductive values of the sexes in the case of a sex-differentiated population. Without sex differences, the adaptive topography proposed is $F$ times the mean fitness of inbred individuals plus $(1 - F)/2$ times the mean fitness of outbred individuals. Such an adaptive topography was first designed to predict the change in the frequency of any given gene, this change being given by the derivative of this topography with respect to an increase in the frequency of this gene alone. This will be refered to as *Wright's formula*.

In the case of a partial selfing population undergoing weak selection, it has been shown (Nagylaki, 1992, 1997) that, at least after enough generations have passed and as long as the population is far enough from equilibrium, the population evolves so that to go upward the adaptive topography proposed by Wright. In the case of a partial sib mating population without sex differences, the change in the frequency of a mutant allele, after enough generations have passed and as long as the mutant

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allele is rare, does not completely agree with Wright's formula, as pointed out by Pollak (1995). Actually, in this case, Wright's adaptive topography has to be multiplied by $(1 + r)$, where $r$ is the coefficient of correlation between the frequencies of the mutant allele in two mates, in order to yield a correct approximation for the change in frequency of the mutant allele in the population. Nevertheless, since the missing multiplicative factor is always positive, Wright's formula still correctly predicts the increase or decrease of gene frequencies, as long as the terms neglected in the approximation remain smaller. Thererofe, in this case, we can say that Wright's formula is *qualitatively valid*, although it is not *quantitatively valid*.

In Pollak's (1995) paper, there are claims that are made without formal proofs. Moreover, it is of interest to know whether or not Wright's formula remains generally valid to predict the increase or decrease of gene frequencies in populations with inbreeding, that is, qualitatively valid. Finally, there is a need to interpret the effect of inbreeding on the change of gene frequencies that makes quantitatively invalid Wright's formula.

In this paper, we deduce and prove a general formula to approximate the change in frequency of a mutant allele under weak selection, when introduced in small frequency into a population which was previously at a fixation state. This can be used to study the fate of the mutant allele when rare and get conditions for its invasion or extinction. It is assumed that the population state can be described by a $n$-dimensional vector whose entries represent the frequencies of group types (actually, genotypes or mating types) carrying the mutant allele and that the linear approximation for the transformation of this vector near the origin from one generation to the next is given by a non-negative matrix which is smooth enough with respect to the intensity of selection and whose at least some power is positive. The formula is applied to autosomal genes in a partial selfing model and autosomal as well as sex-linked genes in a partial sib mating model. Exact conditions for invasion of a rare mutant allele are deduced. We address the question of the quantitative and qualitative validity of Wright's formula in such models and we discuss the effect of inbreeding from a kin selection perspective.

## 2. Framework and basic results

We are interested in the fate of a mutant allele under weak selection, when introduced in small frequency into an infinite population at fixation. Let $\mathbf{x} = (x_1, x_2, \ldots, x_n)$ be a frequency vector describing the population state such that $\mathbf{x} = \mathbf{0}$, that is, the state with zero everywhere, corresponds to the fixation of a particular gene. Actually, $x_1, x_2, \ldots, x_n$ will represent frequencies of types, genotypes or mating types, carrying the mutant allele. Let $T$ be the transformation for the population state from one generation to the next, assuming discrete non-overlapping generations, such that $\mathbf{x}' = T(\mathbf{x})$ denotes the frequency vector in the next generation, given that it is $\mathbf{x}$ in the current generation. Assume that $T$ is smooth enough with respect to $\mathbf{x}$ in the neighborhood of the fixation state $\mathbf{x} = \mathbf{0}$. Let $\mathbf{M}(s)$ be the matrix of linear approximation of the recurrence equations defined by $T$ near the fixation state, so that

$$\mathbf{x}' = \mathbf{M}(s)\mathbf{x} + O(\|\mathbf{x}\|^2), \tag{1}$$

where $\|\mathbf{x}\|$ represents some norm of the vector $\mathbf{x}$, $s$ measures the intensity of selection and $O(\|\mathbf{x}\|^2)$ denotes a function in $\mathbf{x}$ such that $\|O(\|\mathbf{x}\|^2)\|/\|\mathbf{x}\|^2$ remains bounded as $\|\mathbf{x}\|^2$ goes to 0. We will assume that the parameter $s$ is positive and small, which models weak selection, the limiting case $s = 0$ corresponding to neutrality. The matrix $\mathbf{M}(s)$ is necessarily non-negative and the leading eigenvalue of this matrix will determine the fate of the mutant allele in the population if $s$ is small enough and as long as the mutant allele remains rare enough.

Suppose that the non-negative matrix $\mathbf{M}(s)$ is such that there exists some integer $k$ for which the matrix $\mathbf{M}(s)^k$ displays only positive entries for every $s \geq 0$, that is, $\mathbf{M}(s)$ is primitive for every $s \geq 0$. By the Perron-Frobenius theory (see, e.g., Gantmacher, 1959, Seneta, 1981), the greatest eigenvalue in modulus, denoted by $\rho(s)$, is simple, positive and strictly dominates the other eigenvalues in modulus. Furthermore, there exist left and right eigenvectors associated to $\rho(s)$, denoted by $\boldsymbol{\xi}$(s) and $\boldsymbol{\eta}(s)$ respectively, which exhibit only positive entries, and such positive eigenvectors are necessarily associated to the leading eigenvalue $\rho(s)$.

In absence of selection ($s = 0$), the Hardy-Weinberg law (see, e.g., Crow and Kimura, 1970) will guarantee that the frequency of the mutant allele will be invariant from one generation to the next. This frequency, denoted by $p$, will be given by $\mathbf{f}^{\mathrm{T}}\mathbf{x} = \sum_i f_i x_i$ (T for transpose), where $f_i$ represents the frequency of the mutant allele in the mutant type $i$ for $i = 1, \ldots, n$ and $\mathbf{f} = (f_1, \ldots, f_n)$. Therefore $\mathbf{f}$ will be a positive left eigenvector for the eigenvalue 1, which entails $\rho(0) = 1$ with $\boldsymbol{\xi}(0) = \mathbf{f}$. For $s$ small, let $\dot{\rho}(s)$ and $\dot{\mathbf{M}}(s)$ denote the derivatives of $\rho(s)$ and $\mathbf{M}(s)$ with respect to $s$. These derivatives exist if $\mathbf{M}(s)$ is smooth enough with respect to $s$, which will be assumed. We are now ready to state a first result under the above assumptions (proof in Appendix).

**Result 1.** *The leading eigenvalue of* $\mathbf{M}(s)$ *for s small is approximated by*

$$\rho(s) = 1 + \dot{\rho}(0)s + O(s^2),$$

*where*

$$\dot{\rho}(0) = \frac{\boldsymbol{\xi}(0)^{\mathrm{T}}\,\dot{\mathbf{M}}(0)\boldsymbol{\eta}(0)}{\boldsymbol{\xi}(0)^{\mathrm{T}}\boldsymbol{\eta}(0)},$$

$\boldsymbol{\xi}(0)$ *and* $\boldsymbol{\eta}(0)$ *being positive left and right eigenvectors of* $\mathbf{M}(0)$ *for the eigenvalue* 1.

Actually, we can even go further and approximate the change in frequency of the mutant allele when rare from one generation to the next (proof in Appendix).

**Result 2.** *Let* $p^{(k)}$ *be the frequency of a rare mutant allele at generation k in a population previously at fixation. Under weak selection (s small enough) and for k sufficiently large, but not too large in the case* $\dot{\rho}(0) > 0$*, the change in frequency of the rare mutant allele is approximated by*

$$\Delta p^{(k)} = p^{(k+1)} - p^{(k)} = \dot{\rho}(0)\,p^{(k)}s + \textit{smaller terms}.$$

Invasion or extinction of the mutant allele when rare will thus depend upon the sign of $\dot{\rho}(0)$. In effect, if $\dot{\rho}(0) < 0$, then $\rho(s) < 1$, for $s$ sufficiently small, and the mutant allele will eventually disappear in the population if its initial frequency is small enough. Conversely, if $\dot{\rho}(0) > 0$, then $\rho(s) > 1$, for $s$ sufficiently small, and extinction is precluded, which means protection of the mutant allele in the population (see, e.g., Lessard and Karlin,1982, and references therein). The case $\dot{\rho}(0) = 0$ is a degenerate case that would require a quadratic approximation for $\rho(s)$.

In the next sections, we apply Results 1 and 2 to genetic models with partial inbreeding, namely partial selfing and partial sib mating, and deduce conditions for the spread of a rare mutant allele.

## 3. Partial selfing model

Consider a single locus with two alleles, say $A_1$ and $A_2$, in an infinite diploid population undergoing discrete non-overlapping generations. Assume that every individual of the population can reproduce, either by selfing with probability $\alpha$ ($0 < \alpha < 1$), or by random outcrossing with the complementary probability $1 - \alpha$. Let $P_{11}$, $P_{12}$ and $P_{22}$ denote the frequencies of the genotypes $A_1A_1$, $A_1A_2$ and $A_2A_2$, respectively, in the population. Then, the frequencies of the alleles $A_1$ and $A_2$ are

$$p_1 = P_{11} + \frac{1}{2}P_{12} \quad \text{and} \quad p_2 = P_{22} + \frac{1}{2}P_{12}.$$

Moreover, let the genotypes $A_1A_1, A_1A_2, A_2A_2$ have the respective selective values $w_{11} = 1 + h_{11}s$, $w_{12} = 1 + h_{12}s$, $w_{22} = 1 + h_{22}s$. Here, zygotic selection is applied through viability differences, that is, the genotypic selective values are proportional to the probabilities of survival from conception to maturity. It is assumed that the selective values are not all equal. Let us recall that $s$ is assumed to be positive and small.

If $P_{11}$, $P_{12}$ and $P_{22}$ designate the genotypic frequencies among the zygotes in the current generation at the time of conception, then the genotypic frequencies among the adults in the current generation, after selection but before mating, are

$$P_{11}^* = \frac{w_{11}P_{11}}{w_{11}P_{11} + w_{12}P_{12} + w_{22}P_{22}}, \; P_{12}^* = \frac{w_{12}P_{12}}{w_{11}P_{11} + w_{12}P_{12} + w_{22}P_{22}},$$
$$P_{22}^* = \frac{w_{22}P_{22}}{w_{11}P_{11} + w_{12}P_{12} + w_{22}P_{22}}.$$

After mating and reproduction, the genotypic frequencies among the zygotes in the next generation are given by the equations

$$P'_{11} = \alpha\left[P_{11}^* + \frac{1}{4}P_{12}^*\right] + (1-\alpha)\left[P_{11}^* + \frac{1}{2}P_{12}^*\right]^2,$$
$$P'_{12} = \alpha\left[\frac{1}{2}P_{12}^*\right] + 2(1-\alpha)\left[P_{11}^* + \frac{1}{2}P_{12}^*\right]\left[P_{22}^* + \frac{1}{2}P_{12}^*\right],$$
$$P'_{22} = \alpha\left[P_{22}^* + \frac{1}{4}P_{12}^*\right] + (1-\alpha)\left[P_{22}^* + \frac{1}{2}P_{12}^*\right]^2.$$

Here, we assume Mendelian segregation of genes, no fertility differences between the mating types and no gametic selection. It is useful to note that under these assumptions, mating and reproduction do not change the allelic frequencies, that is,

$$p_1' = P_{11}' + \frac{1}{2}P_{12}' = P_{11}^* + \frac{1}{2}P_{12}^* = p_1^*,$$

and

$$p_2' = 1 - p_1' = 1 - p_1^* = p_2^*.$$

Figure 1 below summarizes the life cycle in the population and the notation used for the genotypic and allelic frequencies. Of course, at each stage of the life cycle, the genotypic and allelic frequencies sum up to 1.

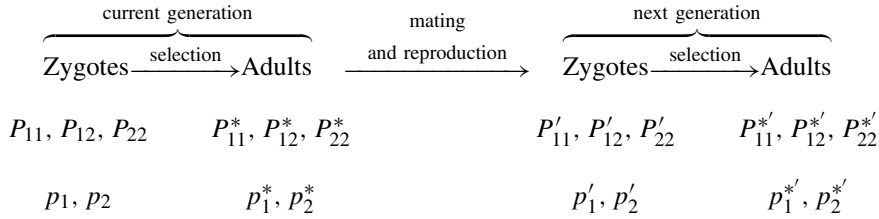


**Fig. 1.** Life cycle and notation for genotypic and allelic frequencies in the partial selfing model.

Let us suppose that allele $A_1$ is rare in the population. Developing the recurrence equations for $P_{11}$, $P_{12}$ near fixation of $A_2$ ($P_{11}$, $P_{12} \cong 0$) yields the matrix of linear approximation

$$\mathbf{M}(s) = \begin{bmatrix} \alpha\,(1 + d_{11}s) & \frac{\alpha}{4}\,(1 + d_{12}s) \\ 2(1-\alpha)\,(1 + d_{11}s) & \left(1 - \frac{\alpha}{2}\right)(1 + d_{12}s) \end{bmatrix} + O(s^2),$$

where $d_{1j} = h_{1j} - h_{22}$, for $j = 1, 2$. One can easily deduce $\mathbf{M}(0)$ and calculate its eigenvalues, which are

$$\lambda_1 = 1,\ \lambda_2 = \frac{\alpha}{2}.$$

As expected, we have $\rho(0) = 1$. Left and right positive eigenvectors associated to this eigenvalue 1 are given respectively by

$$\boldsymbol{\xi}(0)^{\mathrm{T}} = (2, 1) \quad \text{and} \quad \boldsymbol{\eta}(0)^{\mathrm{T}} = (\alpha, 4\,(1-\alpha))\,.$$

Now, using Result 1, we find that

$$\dot{\rho}(0) = F d_{11} + (1 - F)\, d_{12}, \tag{2}$$

where

$$F = \frac{\alpha}{2 - \alpha}.$$

Here, $F$ is the inbreeding coefficient at equilibrium in the partial selfing model when there is no selection, that is, when $s = 0$ (Wright, 1921). Nagylaki (1997)

confirmed that the above value of $F$ can be used as an approximation in the case of weak selection (see also Pollak and Sabran, 1992).

Equation (2) allows us to obtain necessary and sufficient conditions for non extinction of $A_1$ when it is rare and selection is weak. Recall that $d_{1j} = h_{1j} - h_{22}$ for $j = 1, 2$. Therefore, $d_{1j} > 0$ means that $A_1A_j$ is fitter than $A_2A_2$ for $j = 1, 2$.

**Result 3.** *If selection is weak enough in the partial selfing model, allele* $A_1$ *is preserved from extinction if and only if*

*(i)* $d_{12} > 0, d_{11} \leq 0$ *and* $\alpha < \frac{2d_{12}}{2d_{12}-d_{11}} = \alpha_0$, *or*
*(ii)* $d_{12} < 0, d_{11} > 0$ *and* $\alpha > \alpha_0$, *or*
*(iii)* $d_{12} \geq 0$ *and* $d_{11} > 0$.

This result agrees with those obtained by Nagylaki (1997) who achieved a complete dynamical analysis of the partial selfing model under weak selection. For studies of the partial selfing model under arbitrary selection parameters, see, e.g., Kimura and Ohta (1971) and Rocheleau and Lessard (2000).

## 4. Partial sib mating model

The complete study of the partial sib mating model with selection bears some difficulties due to the non-linearity of the transformation equations which must be expressed in terms of the mating types. Again, consider a single autosomal locus with two alleles, $A_1$ and $A_2$, in an infinite diploid population undergoing discrete non-overlapping generations. Let $p_1, p_2$ and $q_1, q_2$ be the allelic frequencies in males and females, respectively. The frequencies of the genotypes $A_1A_1, A_1A_2, A_2A_2$ are denoted by $P_{11}$, $P_{12}$, $P_{22}$ in males and $Q_{11}$, $Q_{12}$, $Q_{22}$ in females. Every individual is given a fixed probability $\beta$ of sib mating and the complementary probability $1 - \beta$ of random mating ($0 < \beta < 1$). As a generalized version of the common non sex-differentiated selection model, we shall assign different viability values depending upon the sexes. These values for $A_1A_1, A_1A_2, A_2A_2$ will be $f_{11} = 1 + u_{11}s$, $f_{12} = 1 + u_{12}s$, $f_{22} = 1 + u_{22}s$ in females and $m_{11} = 1 + v_{11}s, m_{12} = 1 + v_{12}s, m_{22} = 1 + v_{22}s$ in males. It is assumed that the selective values are not all equal in at least one of the sexes. Figure 2 below schematizes the life cycle from one generation to the next.

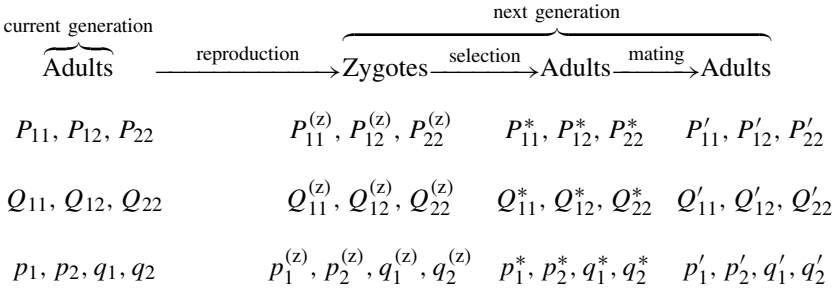


**Fig. 2.** Life cycle and notation for genotypic and allelic frequencies in males and females in the partial sib mating model.

**Table 1.** Male×female mating types in the current generation and male×female couples of sibs produced in the next generation.

| Male × female mating type | Frequency | Zygotes | Male × female couples of sibs |
|---|---|---|---|
| $(A_1A_1 \times A_1A_1)$ | $x_1$ | $A_1A_1$ | $(A_1A_1 \times A_1A_1)$ |
| $(A_1A_1 \times A_1A_2)$ | $x_2$ | $\frac{1}{2}A_1A_1{:}\frac{1}{2}A_1A_2$ | $\frac{1}{4}(A_1A_1 \times A_1A_1){:}\frac{1}{4}(A_1A_1 \times A_1A_2)$ $\frac{1}{4}(A_1A_2 \times A_1A_1){:}\frac{1}{4}(A_1A_2 \times A_1A_2)$ |
| $(A_1A_2 \times A_1A_1)$ | $x_3$ | $\frac{1}{2}A_1A_1{:}\frac{1}{2}A_1A_2$ | $\frac{1}{4}(A_1A_1 \times A_1A_1){:}\frac{1}{4}(A_1A_1 \times A_1A_2)$ $\frac{1}{4}(A_1A_2 \times A_1A_1){:}\frac{1}{4}(A_1A_2 \times A_1A_2)$ |
| $(A_1A_1 \times A_2A_2)$ | $x_4$ | $A_1A_2$ | $(A_1A_2 \times A_1A_2)$ |
| $(A_2A_2 \times A_1A_1)$ | $x_5$ | $A_1A_2$ | $(A_1A_2 \times A_1A_2)$ |
| $(A_1A_2 \times A_1A_2)$ | $x_6$ | $\frac{1}{4}A_1A_1{:}\frac{1}{2}A_1A_2{:}\frac{1}{4}A_2A_2$ | $\frac{1}{16}(A_1A_1 \times A_1A_1){:}\frac{1}{8}(A_1A_1 \times A_1A_2){:}$ $\frac{1}{8}(A_1A_2 \times A_1A_1)$ $\frac{1}{16}(A_1A_1 \times A_2A_2){:}\frac{1}{16}(A_2A_2 \times A_1A_1){:}$ $\frac{1}{4}(A_1A_2 \times A_1A_2)$ $\frac{1}{8}(A_1A_2 \times A_2A_2)){:}\frac{1}{8}(A_2A_2 \times A_1A_2){:}$ $\frac{1}{16}(A_2A_2 \times A_2A_2)$ |
| $(A_1A_2 \times A_2A_2)$ | $x_7$ | $\frac{1}{2}A_1A_2{:}\frac{1}{2}A_2A_2$ | $\frac{1}{4}(A_1A_2 \times A_1A_2){:}\frac{1}{4}(A_1A_2 \times A_2A_2)$ $\frac{1}{4}(A_2A_2 \times A_1A_2){:}\frac{1}{4}(A_2A_2 \times A_2A_2)$ |
| $(A_2A_2 \times A_1A_2)$ | $x_8$ | $\frac{1}{2}A_1A_2{:}\frac{1}{2}A_2A_2$ | $\frac{1}{4}(A_1A_2 \times A_1A_2){:}\frac{1}{4}(A_1A_2 \times A_2A_2)$ $\frac{1}{4}(A_2A_2 \times A_1A_2){:}\frac{1}{4}(A_2A_2 \times A_2A_2)$ |
| $(A_2A_2 \times A_2A_2)$ | $x_9$ | $A_2A_2$ | $(A_2A_2 \times A_2A_2)$ |

Clearly, at each stage of the life cycle, the frequencies of the genotypes and alleles in males and females must sum up to 1. In a mated couple, we have to distinguish the sex of each member. Let $x_1, \ldots, x_9$ designate the frequencies of the mating types in the population, as illustrated in Table 1.

We shall now derive the recurrence equations for the frequencies of the mating types from one generation to the next. The genotypic frequencies in the male and female adults, respectively, of the current generation in terms of the frequencies of the mating types are

$$P_{11} = x_1 + x_2 + x_4,\ P_{12} = x_3 + x_6 + x_7,\ P_{22} = x_5 + x_8 + x_9,$$

and

$$Q_{11} = x_1 + x_3 + x_5,\ Q_{12} = x_2 + x_6 + x_8,\ Q_{22} = x_4 + x_7 + x_9,$$

with $P_{11} + P_{12} + P_{22} = 1$ and $Q_{11} + Q_{12} + Q_{22} = 1$. The frequency of allele $A_1$, in the male and female adults, respectively, is

$$p_1 = P_{11} + \frac{1}{2}P_{12} = x_1 + x_2 + x_4 + \frac{1}{2}(x_3 + x_6 + x_7)$$

and

$$q_1 = Q_{11} + \frac{1}{2}Q_{12} = x_1 + x_3 + x_5 + \frac{1}{2}(x_2 + x_6 + x_8).$$

The adults of the current generation reproduce and the zygotes of the next generation are in the proportions indicated in Table 1. The genotypic frequencies of the zygotes just after conception are

$$\begin{aligned}
P_{11}^{(z)} &= Q_{11}^{(z)} = x_1 + \frac{1}{2}x_2 + \frac{1}{2}x_3 + \frac{1}{4}x_6,\\
P_{12}^{(z)} &= Q_{12}^{(z)} = \frac{1}{2}x_2 + \frac{1}{2}x_3 + x_4 + x_5 + \frac{1}{2}x_6 + \frac{1}{2}x_7 + \frac{1}{2}x_8,\\
P_{22}^{(z)} &= Q_{22}^{(z)} = \frac{1}{4}x_6 + \frac{1}{2}x_7 + \frac{1}{2}x_8 + x_9.
\end{aligned}$$

After selection, the genotypic frequencies among the zygotes in the population are modified so that, before mating, they are given by

$$\begin{aligned}
P_{11}^{*} &= \frac{m_{11}P_{11}^{(z)}}{T_M}, \quad P_{12}^{*} = \frac{m_{12}P_{12}^{(z)}}{T_M}, \quad P_{22}^{*} = \frac{m_{22}P_{22}^{(z)}}{T_M},\\
Q_{11}^{*} &= \frac{f_{11}Q_{11}^{(z)}}{T_F}, \quad Q_{12}^{*} = \frac{f_{12}Q_{12}^{(z)}}{T_F}, \quad Q_{22}^{*} = \frac{f_{22}Q_{22}^{(z)}}{T_F},
\end{aligned}$$

where

$$\begin{aligned}
T_M = {} & m_{11}\left(x_1 + \frac{1}{2}x_2 + \frac{1}{2}x_3 + \frac{1}{4}x_6\right)\\
& + m_{12}\left(\frac{1}{2}x_2 + \frac{1}{2}x_3 + x_4 + x_5 + \frac{1}{2}x_6 + \frac{1}{2}x_7 + \frac{1}{2}x_8\right)\\
& + m_{22}\left(\frac{1}{4}x_6 + \frac{1}{2}x_7 + \frac{1}{2}x_8 + x_9\right),\\
T_F = {} & f_{11}\left(x_1 + \frac{1}{2}x_2 + \frac{1}{2}x_3 + \frac{1}{4}x_6\right)\\
& + f_{12}\left(\frac{1}{2}x_2 + \frac{1}{2}x_3 + x_4 + x_5 + \frac{1}{2}x_6 + \frac{1}{2}x_7 + \frac{1}{2}x_8\right)\\
& + f_{22}\left(\frac{1}{4}x_6 + \frac{1}{2}x_7 + \frac{1}{2}x_8 + x_9\right).
\end{aligned}$$

Finally, the recurrence equations for the frequencies of the mating types from one generation to the next, taking into account that a proportion $\beta$ of matings are between sibs (see Table 1) and a proportion $1 - \beta$ occur at random, are

$$
\begin{aligned}
x_1' &= (1-\beta)\, P_{11}^* Q_{11}^* + \beta f_{11} m_{11} \left(x_1 + \tfrac{1}{4}x_2 + \tfrac{1}{4}x_3 + \tfrac{1}{16}x_6\right)/T_{\mathrm{FS}},\\
x_2' &= (1-\beta)\, P_{11}^* Q_{12}^* + \beta f_{12} m_{11} \left(\tfrac{1}{4}x_2 + \tfrac{1}{4}x_3 + \tfrac{1}{8}x_6\right)/T_{\mathrm{FS}},\\
x_3' &= (1-\beta)\, P_{12}^* Q_{11}^* + \beta f_{11} m_{12} \left(\tfrac{1}{4}x_2 + \tfrac{1}{4}x_3 + \tfrac{1}{8}x_6\right)/T_{\mathrm{FS}},\\
x_4' &= (1-\beta)\, P_{11}^* Q_{22}^* + \beta f_{22} m_{11} \left(\tfrac{1}{16}x_6\right)/T_{\mathrm{FS}},\\
x_5' &= (1-\beta)\, P_{22}^* Q_{11}^* + \beta f_{11} m_{22} \left(\tfrac{1}{16}x_6\right)/T_{\mathrm{FS}},\\
x_6' &= (1-\beta)\, P_{12}^* Q_{12}^*\\
&\quad + \beta f_{12} m_{12} \left(\tfrac{1}{4}x_2 + \tfrac{1}{4}x_3 + x_4 + x_5 + \tfrac{1}{4}x_6 + \tfrac{1}{4}x_7 + \tfrac{1}{4}x_8\right)/T_{\mathrm{FS}},\\
x_7' &= (1-\beta)\, P_{12}^* Q_{22}^* + \beta f_{22} m_{12} \left(\tfrac{1}{8}x_6 + \tfrac{1}{4}x_7 + \tfrac{1}{4}x_8\right)/T_{\mathrm{FS}},\\
x_8' &= (1-\beta)\, P_{22}^* Q_{12}^* + \beta f_{12} m_{22} \left(\tfrac{1}{8}x_6 + \tfrac{1}{4}x_7 + \tfrac{1}{4}x_8\right)/T_{\mathrm{FS}},\\
x_9' &= (1-\beta)\, P_{22}^* Q_{22}^* + \beta f_{22} m_{22} \left(\tfrac{1}{16}x_6 + \tfrac{1}{4}x_7 + \tfrac{1}{4}x_8 + x_9\right)/T_{\mathrm{FS}},
\end{aligned}
\tag{3}
$$

where

$$
\begin{aligned}
T_{\mathrm{FS}} &= f_{11}m_{11}\left(x_1 + \frac{1}{4}x_2 + \frac{1}{4}x_3 + \frac{1}{16}x_6\right) + (f_{12}m_{11} + f_{11}m_{12})\\
&\quad \times \left(\frac{1}{4}x_2 + \frac{1}{4}x_3 + \frac{1}{8}x_6\right) + (f_{22}m_{11} + f_{11}m_{22})\left(\frac{1}{16}x_6\right)\\
&\quad + f_{12}m_{12}\left(\frac{1}{4}x_2 + \frac{1}{4}x_3 + x_4 + x_5 + \frac{1}{4}x_6 + \frac{1}{4}x_7 + \frac{1}{4}x_8\right)\\
&\quad + (f_{22}m_{12} + f_{12}m_{22})\left(\frac{1}{8}x_6 + \frac{1}{4}x_7 + \frac{1}{4}x_8\right)\\
&\quad + f_{22}m_{22}\left(\frac{1}{16}x_6 + \frac{1}{4}x_7 + \frac{1}{4}x_8 + x_9\right).
\end{aligned}
$$

Now, assuming that allele $A_1$ is rare in the population ($x_1, x_2, \ldots, x_8 \cong 0$), the recurrence equations (3) yield the matrix of linear approximation $\mathbf{M}(s)$ (see Appendix A.4), up to terms of order $s$ and with the notation

$$d_{1j}^{\mathrm{f}} = u_{1j} - u_{22} \text{ and } d_{1j}^{\mathrm{m}} = v_{1j} - v_{22},$$

for $j = 1, 2$. The matrix $\mathbf{M}(0)$ is easily obtained and its eigenvalues in decreasing order (calculated by Mathematica) are all positive and given by

$$
\begin{aligned}
&\lambda_1 = 1, \lambda_2 = \frac{2\beta + \sqrt{4\beta^2 + 16\beta}}{8}, \lambda_3 = \frac{\beta}{2}, \lambda_4 = \frac{\beta}{4},\\
&\lambda_5 = \frac{2\beta - \sqrt{4\beta^2 + 16\beta}}{8}, \lambda_6 = \lambda_7 = \lambda_8 = 0.
\end{aligned}
$$

Positive left and right eigenvectors, respectively, associated to the eigenvalue 1 are

$$\boldsymbol{\xi}(0)^{\mathrm{T}} = (4, 3, 3, 2, 2, 2, 1, 1)$$

and

$$
\begin{aligned}
\boldsymbol{\eta}(0)^{\mathrm{T}} &= \left(\frac{\beta\,(2+\beta)}{16\,(2-\beta)\,(1-\beta)}, \frac{\beta}{4\,(2-\beta)}, \frac{\beta}{4\,(2-\beta)}, \frac{1}{4}, \frac{1}{4}, 1, \frac{5\beta^2 - 20\beta + 16}{4\beta\,(2-\beta)},\right.\\
&\quad \left.\frac{5\beta^2 - 20\beta + 16}{4\beta\,(2-\beta)}\right).
\end{aligned}
$$

Result 1 permits us to obtain

$$\dot{\rho}(0) = (1+r)\left[F\left(\frac{d_{11}^{\mathrm{f}} + d_{11}^{\mathrm{m}}}{2}\right) + (1-F)\left(\frac{d_{12}^{\mathrm{f}} + d_{12}^{\mathrm{m}}}{2}\right)\right], \tag{4}$$

where

$$F = \frac{\beta}{4-3\beta} \quad \text{and} \quad r = \frac{\beta}{2-\beta} = \frac{2F}{1+F}.$$

The coefficient $F$ is the inbreeding coefficient at equilibrium in the partial sib mating model without selection as shown by Ghai (1969). The coefficient $r$ is known as the coefficient of relationship (Wright, 1922) and it represents the coefficient of correlation between two mated individuals relative to their frequencies of $A_1$ at the specified locus (see, e.g., Li, 1976). Since $F > 0$ and $r > 0$, the sign of $\dot{\rho}(0)$ is completely determined by those of $d_{11}^{\mathrm{f}}, d_{11}^{\mathrm{m}}, d_{12}^{\mathrm{f}}$ and$d_{12}^{\mathrm{m}}$.

If we assume equal selective values for the sexes ($u_{11} = v_{11}, u_{12} = v_{12}$ and $u_{22} = v_{22}$) and define $d_{1j} = d_{1j}^{\mathrm{f}} = d_{1j}^{\mathrm{m}}$ for $i, j = 1, 2$, equation (4) reduces to

$$\dot{\rho}(0) = (1+r)\left[Fd_{11} + (1-F)\,d_{12}\right]. \tag{5}$$

It should be noted that equation (5) agrees with one derived less rigorously by Pollak (1995) for the same model.

A detailed analysis of equation (4) also allows us to determine necessary and sufficient conditions under which invasion of allele $A_1$ will occur under weak selection when it is rare in the population. We define

$$h_{ij} = \frac{u_{ij} + v_{ij}}{2} \text{ and } d_{1j} = h_{1j} - h_{22},$$

for $i, j = 1, 2$. Therefore, as in the partial selfing model, $d_{1j} > 0$ means that $A_1A_j$ is fitter than $A_2A_2$, for $j = 1, 2$, if the fitness of a genotype is defined as the average fitness of that genotype in females and males, giving the same weight to the fitnesses in the two sexes.

**Result 4.** *If selection is weak enough in the partial sib mating model for autosomal genes, allele* $A_1$ *is preserved from extinction if and only if*

*(i)* $d_{12} > 0, d_{11} \leq 0$ *and* $\beta < \frac{4d_{12}}{4d_{12}-d_{11}} = \beta_0$, *or*
*(ii)* $d_{12} < 0, d_{11} > 0$ *and* $\beta > \beta_0$, *or*
*(iii)* $d_{12} \geq 0$ *and* $d_{11} > 0$.

## 5. Partial sib mating model for sex-linked genes

In this model, we suppose that females possess two genes at the concerned locus while males have only one. Thus, the female population is diploid at this locus whereas the male population is haploid. Given two alleles, $A_1$ and $A_2$, we assign selective values $f_{11} = 1 + u_{11}s$, $f_{12} = 1 + u_{12}s$, $f_{22} = 1 + u_{22}s$ to the female genotypes $A_1A_1, A_1A_2, A_2A_2$ and selective values $m_1 = 1 + v_1s, m_2 = 1 + v_2s$ to the male genotypes $A_1, A_2$. These selective values are not all equal in at least

**Table 2.** Mating types in the current generation and couples of sibs produced in the next generation for a sex-linked locus.

| Mating type | Frequency | Zygotes | | Couples of sibs |
|---|---|---|---|---|
| | | females | males | |
| $(A_1A_1 \times A_1)$ | $x_1$ | $A_1A_1$ | $A_1$ | $(A_1A_1 \times A_1)$ |
| $(A_1A_2 \times A_1)$ | $x_2$ | $\frac{1}{2}A_1A_1{:}\frac{1}{2}A_1A_2$ | $\frac{1}{2}A_1{:}\frac{1}{2}A_2$ | $\frac{1}{4}(A_1A_1 \times A_1){:}\frac{1}{4}(A_1A_1 \times A_2)$ |
| | | | | $\frac{1}{4}(A_1A_2 \times A_1){:}\frac{1}{4}(A_1A_2 \times A_2)$ |
| $(A_2A_2 \times A_1)$ | $x_3$ | $A_1A_2$ | $A_2$ | $(A_1A_2 \times A_2)$ |
| $(A_1A_1 \times A_2)$ | $x_4$ | $A_1A_2$ | $A_1$ | $(A_1A_2 \times A_1)$ |
| $(A_1A_2 \times A_2)$ | $x_5$ | $\frac{1}{2}A_1A_2{:}\frac{1}{2}A_2A_2$ | $\frac{1}{2}A_1{:}\frac{1}{2}A_2$ | $\frac{1}{4}(A_1A_2 \times A_1){:}\frac{1}{4}(A_1A_2 \times A_2)$ |
| | | | | $\frac{1}{4}(A_2A_2 \times A_1){:}\frac{1}{4}(A_2A_2 \times A_2)$ |
| $(A_2A_2 \times A_2)$ | $x_6$ | $A_2A_2$ | $A_2$ | $(A_2A_2 \times A_2)$ |

one of the sexes. All possible mating types and their frequencies are depicted in Table 2. The genotypic frequencies in the male and female adults, respectively, in the current generation are given by

$$P_1 = x_1 + x_2 + x_3, \quad P_2 = x_4 + x_5 + x_6,$$

and

$$Q_{11} = x_1 + x_4, \quad Q_{12} = x_2 + x_5, \quad Q_{22} = x_3 + x_6,$$

with $P_1 + P_2 = 1$ and $Q_{11} + Q_{12} + Q_{22} = 1$. Then, the frequency of allele $A_1$ in the male and female adults, respectively, is

$$p_1 = P_1 = x_1 + x_2 + x_3 \qquad \text{and} \qquad q_1 = Q_{11} + \frac{1}{2}Q_{12} = x_1 + x_4 + \frac{1}{2}(x_2 + x_5).$$

After mating and reproduction of the adults in the current generation, the genotypic frequencies in male and female zygotes, respectively, in the next generation are

$$P_1^{(z)} = x_1 + \frac{1}{2}x_2 + x_4 + \frac{1}{2}x_5, \quad P_2^{(z)} = \frac{1}{2}x_2 + x_3 + \frac{1}{2}x_5 + x_6,$$

and

$$Q_{11}^{(z)} = x_1 + \frac{1}{2}x_2, \quad Q_{12}^{(z)} = \frac{1}{2}x_2 + x_3 + x_4 + \frac{1}{2}x_5, \quad Q_{22}^{(z)} = \frac{1}{2}x_5 + x_6.$$

After selection among the zygotes, these genotypic frequencies become

$$P_1^* = \frac{m_1 P_1^{(z)}}{T_M}, \quad P_2^* = \frac{m_2 P_2^{(z)}}{T_M},$$
$$Q_{11}^* = \frac{f_{11} Q_{11}^{(z)}}{T_F}, \quad Q_{12}^* = \frac{f_{12} Q_{12}^{(z)}}{T_F}, \; Q_{22}^* = \frac{f_{22} Q_{22}^{(z)}}{T_F},$$

where

$$T_{\mathrm{M}} = m_1\left(x_1 + \frac{1}{2}x_2 + x_4 + \frac{1}{2}x_5\right) + m_2\left(\frac{1}{2}x_2 + x_3 + \frac{1}{2}x_5 + x_6\right),$$
$$T_{\mathrm{F}} = f_{11}\left(x_1 + \frac{1}{2}x_2\right) + f_{12}\left(\frac{1}{2}x_2 + x_3 + x_4 + \frac{1}{2}x_5\right) + f_{22}\left(\frac{1}{2}x_5 + x_6\right).$$

Assuming a probability $\beta$ of sib mating and $1-\beta$ of random mating ($0 < \beta < 1$), the recurrence equations for the frequencies of the mating types from one generation to the next are

$$\begin{aligned}
x_1' &= (1-\beta)\, Q_{11}^* P_1^* + \beta f_{11} m_1\left(x_1 + \frac{1}{4}x_2\right)/T_{\mathrm{FS}},\\
x_2' &= (1-\beta)\, Q_{12}^* P_1^* + \beta f_{12} m_1\left(\frac{1}{4}x_2 + x_4 + \frac{1}{4}x_5\right)/T_{\mathrm{FS}},\\
x_3' &= (1-\beta)\, Q_{22}^* P_1^* + \beta f_{22} m_1\left(\frac{1}{4}x_5\right)/T_{\mathrm{FS}},\\
x_4' &= (1-\beta)\, Q_{11}^* P_2^* + \beta f_{11} m_2\left(\frac{1}{4}x_2\right)/T_{\mathrm{FS}},\\
x_5' &= (1-\beta)\, Q_{12}^* P_2^* + \beta f_{12} m_2\left(\frac{1}{4}x_2 + x_3 + \frac{1}{4}x_5\right)/T_{\mathrm{FS}},\\
x_6' &= (1-\beta)\, Q_{22}^* P_2^* + \beta f_{22} m_2\left(\frac{1}{4}x_5 + x_6\right)/T_{\mathrm{FS}},
\end{aligned}$$

where

$$\begin{aligned}
T_{\mathrm{FS}} = {} & f_{11}m_1x_1 + \frac{1}{4}\left(f_{11}+f_{12}\right)\left(m_1+m_2\right)x_2 + f_{12}m_2x_3 + f_{12}m_1x_4\\
& + \frac{1}{4}\left(f_{12}+f_{22}\right)\left(m_1+m_2\right)x_5 + f_{22}m_2x_6.
\end{aligned}$$

Near the fixation state of allele $\mathrm{A}_2$, the matrix of linear approximation $\mathbf{M}(s)$, ignoring terms of order $s^2$ or smaller and using the notation $d_1^{\mathrm{m}} = v_1 - v_2$ and $d_{1j}^{\mathrm{f}} = u_{1j} - u_{22}$, for $j = 1, 2$, reads as

$$\begin{bmatrix}
\beta\left(1 + d_{11}^{\mathrm{f}}s + d_1^{\mathrm{m}}s\right) & \frac{\beta}{4}\left(1 + d_{11}^{\mathrm{f}}s + d_1^{\mathrm{m}}s\right) & 0 & 0 & 0\\
0 & \frac{\beta}{4}\left(1 + d_{12}^{\mathrm{f}}s + d_1^{\mathrm{m}}s\right) & 0 & \beta\left(1 + d_{12}^{\mathrm{f}}s + d_1^{\mathrm{m}}s\right) & \frac{\beta}{4}\left(1 + d_{12}^{\mathrm{f}}s + d_1^{\mathrm{m}}s\right)\\
(1-\beta)\left(1 + d_1^{\mathrm{m}}s\right) & \left(\frac{1-\beta}{2}\right)\left(1 + d_1^{\mathrm{m}}s\right) & 0 & (1-\beta)\left(1 + d_1^{\mathrm{m}}s\right) & \left(\frac{2-\beta}{4}\right)\left(1 + d_1^{\mathrm{m}}s\right)\\
(1-\beta)\left(1 + d_{11}^{\mathrm{f}}s\right) & \left(\frac{2-\beta}{4}\right)\left(1 + d_{11}^{\mathrm{f}}s\right) & 0 & 0 & 0\\
0 & \left(\frac{2-\beta}{4}\right)\left(1 + d_{12}^{\mathrm{f}}s\right) & \left(1 + d_{12}^{\mathrm{f}}s\right) & (1-\beta)\left(1 + d_{12}^{\mathrm{f}}s\right) & \left(\frac{2-\beta}{4}\right)\left(1 + d_{12}^{\mathrm{f}}s\right)
\end{bmatrix}$$

The matrix $\mathbf{M}(0)$ is easily deduced and its eigenvalues (calculated by Mathematica), in decreasing order, are

$$\lambda_1 = 1,\ \lambda_2 = \frac{2\beta + \sqrt{4\beta^2 + 16\beta}}{8},\ \lambda_3 = \frac{\beta}{2},\ \lambda_4 = \frac{2\beta - \sqrt{4\beta^2 + 16\beta}}{8},\ \lambda_5 = -\frac{1}{2}.$$

Positive left and right eigenvectors of $\mathbf{M}(0)$ associated to the eigenvalue 1 are given by

$$\boldsymbol{\xi}(0)^{\mathrm{T}} = (3, 2, 1, 2, 1) \quad \text{and} \quad \boldsymbol{\eta}(0)^{\mathrm{T}} = \left( \frac{\beta}{4\,(1-\beta)},\ 1,\ \frac{4-3\beta}{2\beta},\ \frac{1}{2},\ \frac{4-3\beta}{\beta} \right).$$

Result 1 yields

$$\overset{\bullet}{\rho}(0) = \left( \frac{2}{3} + \frac{1}{3} r_{Y\to X} \right) \left[ F d_{11}^{\mathrm{f}} + (1-F)\, d_{12}^{\mathrm{f}} \right] + \left( \frac{1}{3} + \frac{2}{3} r_{X\to Y} \right) d_1^{\mathrm{m}}, \qquad (6)$$

where

$$F = \frac{\beta}{4-3\beta},\ r_{Y\to X} = \frac{\beta}{2-\beta} \text{ and } r_{X\to Y} = \frac{\beta}{4-3\beta}.$$

Again, $F$ represents the inbreeding coefficient in females at equilibrium in absence of selection. The coefficient $r_{Y\to X}$ represents the coefficient of regression of the frequency of $A_1$ genes carried by the male of a mated couple ($Y$) on the frequency of $A_1$ genes carried by the female of this couple ($X$), when there is no selection and the population is at equilibrium. The coefficient $r_{X\to Y}$ is defined analogously. It must be noted that when females and males are both diploid at the given locus, then

$$r = r_{Y\to X} = r_{X\to Y} = \frac{\beta}{2-\beta}.$$

Proof of this assertion and derivation of the regression coefficients are found in the Appendix. One should observe that the dissymmetry of the recurrence equations is reflected into the expression of $\overset{\bullet}{\rho}(0)$. In effect, the contribution of each sex is weighted by its corresponding coefficient of regression. The fractions $\frac{2}{3}$ and $\frac{1}{3}$ correspond to reproductive values of females and males, respectively, and are proportional to the contributions of the two sexes at the sex-linked locus in question.

A detailed analysis of equation (6) gives the following result, where

$$d_{12} = \frac{2}{3}\,(u_{12} - u_{22}) + \frac{1}{3}\,(v_1 - v_2) \text{ and } d_{11} = \frac{1}{2}\,(u_{11} - u_{22}) + \frac{1}{2}\,(v_1 - v_2)\,.$$

**Result 5.** *If selection is weak enough in the partial sib mating model for sex-linked genes, allele* $A_1$ *is preserved from extinction if and only if*

*(i)* $d_{12} > 0, d_{11} \le 0$ *and* $\beta < \frac{3d_{12}}{3d_{12}-d_{11}} = \beta_1$, *or*
*(ii)* $d_{12} < 0, d_{11} > 0$ *and* $\beta > \beta_1$, *or*
*(iii)* $d_{12} \ge 0$ *and* $d_{11} > 0$.

## 6. Discussion

Result 1 provides a general criterion for determining the fate of a mutant allele introduced into a population at fixation when selection is weak enough and the mutant allele is rare enough. If the derivative with respect to the intensity of selection, denoted by $s$, of the leading eigenvalue $\rho(s)$ of the linearized transformation for the population state near fixation, represented by the matrix $\mathbf{M}(s)$, is positive at $s = 0$, then the mutant allele is preserved from extinction. On the contrary, if

this derivative is negative, then the mutant allele goes extinct. In the degenerate case where this derivative would be 0, a quadratic analysis would be required (see, e.g., Lessard and Karlin, 1982). The expression given in Result 1 for this derivative evaluated at $s = 0$ can be traced back to Taylor (1985) in a context of sex allocation when a mutant strategy, say a sex ratio $m + s$, is confronted to a resident strategy, say a sex ratio $m$. In this context, a derivative equal to zero when $s = 0$ characterizes an evolutionary equilibrium strategy $m$. In general, when the matrix $\mathbf{M}(s)$ is non-negative and $\mathbf{M}(s)^k$ is positive for some integer $k$, this derivative is equal to 0 at $s = 0$ if and only if the derivative of the characteristic polynomial of $\mathbf{M}(s)$ at $s = 0$ is 0 (see, e.g., Taylor and Bulmer, 1980). Actually, the sign of the derivative of the leading eigenvalue is then the same as the sign of the derivative of the characteristic polynomial (Courteau and Lessard, 2000). In practice, this property facilitates the application of Result 1 to decide about the invasion or extinction of a rare mutant gene since the characteristic polynomial is generally easier to compute than the leading eigenvalue.

Result 2 on the change in frequency of a rare mutant allele from one generation to the next may seem obvious as outlined by Taylor (1989), but a careful analysis has to be performed. The main difficulty lies on the fact that the frequency of the mutant allele, $p$, is not generally the component of the population state in the direction of the leading left eigenvector for the matrix $\mathbf{M}(s)$ unless $s = 0$. We must also make sure that the terms of order different from $ps$ in the change of the gene frequency after enough generations have passed are smaller than $ps$ (this excludes functions of order $sp^2$ or $ps^2$ for instance) and do not depend on the number of generations that have elapsed, as long as the mutant allele is rare enough and selection is weak enough. We have shown that this is the case under mild regularity conditions.

Results 1 and 2 have been deduced in a framework of an infinite population described by genotype frequencies or mating type frequencies, but this framework can be extended to a more general situation of a population structured into mating groups. Then, we would have to take into account the relative contributions of the groups and the relative contributions of the sexes in the expression of the gene frequencies.

Application of Results 1 and 2 to autosomal genes in partial selfing or partial sib mating populations, confirms some previous results obtained in the case of weak selection (see, e.g., Pollak and Sabran, 1992, and Nagylaki, 1997, for the case of partial selfing, and Pollak, 1995, for the case of partial sib mating). In random mating populations, a rare mutant allele at an autosomal locus invades a population at fixation if and only if the mutant heterozygote has a selective advantage over the resident homozygote ($d_{12} > 0$). With partial selfing or partial sib mating, this condition may be neither sufficient, in the case where the mutant homozygote is less fit than the resident homozygote ($d_{11} < 0$), nor necessary, in the case where the mutant homozygote is fitter than the resident homozygote ($d_{11} > 0$), in both cases if the selfing or sib mating rate is large enough. In that case, the threshold value is higher for the rate of sib mating than for the rate of selfing, and this is so since sib mating creates less inbreeding than selfing at the same rate. The effect of inbreeding on autosomal genes is to produce more homozygotes in the population and, as its level increases, it can overcome the fitness effect of overdominance or

underdominance of the heterozygotes, but not the effect of directional selection, on the fate of a mutant allele. In the case of dominance of the resident allele ($d_{12} = 0$), a necessary and sufficient condition for invasion of a mutant allele is that the mutant homozygote is fitter than the resident homozygote ($d_{11} > 0$).

In sex-differentiated populations with partial sib mating, all the above results apply with the fitness of a genotype being defined as an average of the fitnesses of that genotype in females and males. In the case of autosomal genes, this average gives the same weight to each of the sexes. In the case of sex-linked genes, the weighting of the fitnesses in females and males differs in the calculation of $d_{12}$ and $d_{11}$. In the former, the fitnesses in females weigh twice the fitnesses in males, while in the latter, they weigh the same. The reason is that, in outbred individuals, each of the two genes in females counts as much as the gene in males, but in inbred individuals, both count as one since they are the same by descent.

The approximation for the change in frequency of a mutant allele when rare in a population undergoing weak selection does not always agree with Wright's (1942) formula. Although this formula proves to be quantitatively valid in the case of partial selfing, it turns out that it is only qualitatively valid in the case of autosomal genes in partial sib mating populations. This confirms a finding of Pollak (1995). Actually, it is likely that Wright's formula is quantitatively valid only for a few particular cases like partial selfing. It is also likely that it is qualitatively valid only in symmetric cases as illustrated by our result on sex-linked genes in partial sib mating populations. In this case, the formula is neither quantitatively nor qualitatively valid. This happens because, in sex-differentiated populations, the correct approximation under the assumption of weak selection involves not only the inbreeding coefficient and the reproductive values of the sexes, but also coefficients of regression of the frequency of the mutant allele in one mate on the frequency in the other, all calculated as if there were no selection.

In the case of autosomal genes, the coefficients of regression reduce to coefficients of correlation, which are symmetric, while the reproductive values of the sexes are equal to $\frac{1}{2}$ since both sexes contribute equally to future generations. Considering this case without sex differences in a partial sib mating population and making the reasonable assumption, among others, that the inbreeding coefficient $F$ can be calculated ignoring selection if selection is weak enough as in a partial selfing population, Pollak (1995) gets a correct approximation for the change in frequency of a rare allele, denoted by A, and explains the presence of the coefficient of correlation between two mates relative to their frequencies of A, denoted by $m$, as follows: "*. . . because full sibs are more likely to have the same alleles than a random pair of individuals, a positive correlation between mates is induced in their frequencies of A. This results in a second increase within a generation in the frequency of A, which is m times as large as that from viability selection.*"

In the case of sex-linked genes, the reproductive values of the females and males are 2/3 and 1/3, respectively, since the contribution of females to future generations is twice that of the males. Moreover, an individual who carries a rare mutant allele and who survives to reproduce will contribute to the reproduction of its mate and this will cause a second change in the frequency of the mutant allele, weighted by the reproductive value of the sex of the mate times the coefficient of regression

of the frequency of the mutant allele in the mate on the corresponding frequency in the individual. Assuming weak selection, this coefficient is approximated by the expected fraction of genes in the mate that are identical by descent to one or more genes in the individual. Such a coefficient, called a coefficient of relatedness, has been encountered in kin selection models (see, e.g., Hamilton, 1970, Lessard, 1992). What is interesting here is that a classical viability selection model without interactions between kin affecting viability can be put into the framework of kin selection theory, which is still controversial, when there is inbreeding. The reason is that there are interactions between kin that affect their reproductive success and these take place at mating.

## Appendix

### *A.1. Proof of Result 1*

For a better understanding of our analysis, we state the Perron-Frobenius theorem for primitive matrices (see, e.g., Seneta, 1981, or Gantmacher, 1959, for a proof ).

**Perron-Frobenius theorem.** *Suppose* $\mathbf{M}$ *is a* $n \times n$ *non-negative primitive matrix. Then there exists an eigenvalue* $\rho$ *such that:*

(a) $\rho$ *is real, strictly positive and is a simple root of the characteristic equation of* $\mathbf{M}$*;*
(b) $\rho > |\lambda|$ *for every eigenvalue* $\lambda \neq \rho$*;*
(c) *associated to* $\rho$ *are strictly positive left and right eigenvectors,* $\boldsymbol{\xi}$ *and* $\boldsymbol{\eta}$*, which are unique to constant multiples; in fact,* $\rho$ *is the only eigenvalue of* $\mathbf{M}$ *which admits strictly positive eigenvectors;*
(d) *as* $k \to \infty$, $\frac{\mathbf{M}^k}{\rho^k} \to \frac{\boldsymbol{\eta}\boldsymbol{\xi}^{\mathrm{T}}}{\langle \boldsymbol{\xi}, \boldsymbol{\eta} \rangle}$, *where* $\langle \boldsymbol{\xi}, \boldsymbol{\eta} \rangle = \sum_i \xi_i \eta_i$.

Since the non-negative matrix $\mathbf{M}(s)$ is supposed to be primitive, by assertion (c) of the Perron-Frobenius theorem, there exist strictly positive eigenvectors associated to $\rho(s)$, the greatest eigenvalue of $\mathbf{M}(s)$ in modulus. Let $\boldsymbol{\xi}(s)^{\mathrm{T}} = (\xi_1(s), \ldots, \xi_n(s))$ and $\boldsymbol{\eta}(s)^{\mathrm{T}} = (\eta_1(s), \ldots, \eta_n(s))$ be strictly positive left and right eigenvectors, respectively, associated to $\rho(s)$. For the sake of simplicity, assume that the scalar product of these eigenvectors equals 1, that is, $\langle \boldsymbol{\xi}(s), \boldsymbol{\eta}(s) \rangle = \sum_i \xi_i(s)\eta_i(s) = 1$. More explicitly, we have

$$\boldsymbol{\xi}(s)^{\mathrm{T}}\mathbf{M}(s) = \rho(s)\boldsymbol{\xi}(s)^{\mathrm{T}}$$

and

$$\mathbf{M}(s)\boldsymbol{\eta}(s) = \rho(s)\boldsymbol{\eta}(s), \tag{A.1}$$

where the superscript T denotes matrix transposition. Taking the derivative with respect to $s$ on both sides of the second equation in (A.1) (this is feasible since the entries of $\mathbf{M}(s)$ are supposed smooth enough), we obtain

$$\dot{\mathbf{M}}(s)\boldsymbol{\eta}(s) + \mathbf{M}(s)\dot{\boldsymbol{\eta}}(s) = \dot{\rho}(s)\boldsymbol{\eta}(s) + \rho(s)\dot{\boldsymbol{\eta}}(s).$$

Hence, multiplying on the left by $\boldsymbol{\xi}(s)^{\mathrm{T}}$, we find

$$\boldsymbol{\xi}(s)^{\mathrm{T}}\dot{\mathbf{M}}(s)\boldsymbol{\eta}(s) + \boldsymbol{\xi}(s)^{\mathrm{T}}\mathbf{M}(s)\dot{\boldsymbol{\eta}}(s) = \dot{\rho}(s)\boldsymbol{\xi}(s)^{\mathrm{T}}\boldsymbol{\eta}(s) + \rho(s)\boldsymbol{\xi}(s)^{\mathrm{T}}\dot{\boldsymbol{\eta}}(s). \quad \text{(A.2)}$$

But, from the first equality in (A.1) and since $\boldsymbol{\xi}(s)^{\mathrm{T}}\boldsymbol{\eta}(s) = 1$, equation (A.2) reduces to

$$\dot{\rho}(s) = \boldsymbol{\xi}(s)^{\mathrm{T}}\dot{\mathbf{M}}(s)\boldsymbol{\eta}(s).$$

Developing $\rho(s)$ in Taylor series around 0 yields

$$\rho(s) = \rho(0) + \dot{\rho}(0)s + O(s^2), \quad \text{(A.3)}$$

with $\dot{\rho}(0) = \boldsymbol{\xi}(0)^{\mathrm{T}}\dot{\mathbf{M}}(0)\boldsymbol{\eta}(0)$.

It remains to show that $\rho(0) = 1$. To this end, we express the frequency of the rare mutant gene in the population as $p = \mathbf{f}^{\mathrm{T}}\mathbf{x}$, where $\mathbf{f}$ denotes the vector of the rare mutant gene frequency in the different mutant types and $\mathbf{x}$ is the vector of the frequencies of the different types containing the rare mutant gene. With no selection in the population, that is, when $s = 0$, there is invariance of the allelic frequencies, that is, the allelic frequencies remain unchanged from one generation to the next (this is the first part of the Hardy-Weinberg law). Formally, we have $p' = \mathbf{f}^{\mathrm{T}}\mathbf{x}' = \mathbf{f}^{\mathrm{T}}\mathbf{x} = p$, and therefore, $\mathbf{f}^{\mathrm{T}}\mathbf{M}(0)\mathbf{x} = \mathbf{f}^{\mathrm{T}}\mathbf{x}$, which yields

$$\mathbf{f}^{\mathrm{T}}\mathbf{M}(0) = \mathbf{f}^{\mathrm{T}}, \text{ for all } \mathbf{x} \geq \mathbf{0}.$$

This implies that $\lambda = 1$ is one of the eigenvalue of $\mathbf{M}(0)$. But, since $\mathbf{f}$ has strictly positive entries by definition and that a strictly positive eigenvector is necessarily one associated to the greatest eigenvalue $\rho(0)$, this implies that $\rho(0) = 1$. Moreover, by part (c) of the Perron-Frobenius theorem, we have that $\boldsymbol{\xi}(0)$, the left eigenvector of $\mathbf{M}(0)$, is a multiple of the vector $\mathbf{f}$. It will be assumed throughout, without loss of generality, that $\boldsymbol{\xi}(0) = \mathbf{f}$ and $\sum_i \xi_i(s) = \sum_i f_i$, for every $s \geq 0$. This completes the proof of Result 1.

*A.2. Proof of Result 2*

As in the proof of Result 1, $\mathbf{M}(s)$ is non-negative and primitive. In the complex vector space $\mathbf{C}^n$, one can always represent the matrix $\mathbf{M}(s)$ in a Jordan canonical form, that is,

$$\mathbf{M}(s) = \mathbf{P}(s)\mathbf{J}(s)\mathbf{P}(s)^{-1}.$$

Let $\lambda_1(s), \lambda_2(s), \ldots, \lambda_n(s)$ be the eigenvalues (not necessarily distinct) of $\mathbf{M}(s)$. Let

$$\mathbf{P}(s) = \left[\boldsymbol{\varphi}_1(s), \boldsymbol{\varphi}_2(s), \ldots, \boldsymbol{\varphi}_n(s)\right],$$
$$\mathbf{P}(s)^{-1} = \left[\boldsymbol{\psi}_1(s), \boldsymbol{\psi}_2(s), \ldots, \boldsymbol{\psi}_n(s)\right]^{\mathrm{T}}.$$

By the Perron-Frobenius theorem, the right (and the left) eigenvector associated to the greatest eigenvalue in modulus $\rho(s)$ of $\mathbf{M}(s)$ forms a one-dimensional

subspace of $\mathbf{C}^n$. Without loss of generality, let $\lambda_1(s) = \rho(s)$, $\boldsymbol{\varphi}_1(s) = \boldsymbol{\eta}(s)$ and $\psi_1(s) = \boldsymbol{\xi}(s)$. Then, we can write

$$\mathbf{M}(s) = \left[\boldsymbol{\eta}(s), \boldsymbol{\varphi}_2(s), \ldots, \boldsymbol{\varphi}_n(s)\right] \begin{bmatrix} \rho(s) & \mathbf{0} \\ \mathbf{0} & \mathbf{B}(s) \end{bmatrix} \left[\boldsymbol{\xi}(s), \psi_2(s), \ldots, \psi_n(s)\right]^{\mathrm{T}},$$

where $\mathbf{B}(s)$ is a $(n-1) \times (n-1)$ matrix formed of Jordan blocks associated to the eigenvalues of $\mathbf{M}(s)$ different from $\rho(s)$. Because the column vectors of $\mathbf{P}(s)$ form a basis of the whole space, we can express each vector $\mathbf{x} \neq \mathbf{0}$ of the space as a linear combination of these vectors. Actually, we have

$$\mathbf{x} = c_1 \boldsymbol{\eta}(s) + \sum_{i \geq 2} c_i \boldsymbol{\varphi}_i(s), \tag{A.4}$$

where $c_1 = \boldsymbol{\xi}(s)^{\mathrm{T}}\mathbf{x}$, $c_i = \psi_i(s)^{\mathrm{T}}\mathbf{x}$, for $i = 2, \ldots, n$, and at least one of the $c_i$ is different from 0.

In the following, we shall use, for each $s > 0$ fixed, the norm $\|\cdot\|$ defined by $\|\mathbf{x}\| = \sum_i \xi_i(s)\,|x_i|$ for every vector $\mathbf{x}$. The norm of the matrix $\mathbf{M}(s)$ is defined as

$$\|\mathbf{M}(s)\| = \sup_{\mathbf{x}\neq\mathbf{0}} \frac{\|\mathbf{M}(s)\mathbf{x}\|}{\|\mathbf{x}\|} \tag{A.5}$$

Note that

$$\|\mathbf{M}^k(s)\mathbf{x}\| \leq \|\mathbf{M}^k(s)\|\|\mathbf{x}\|, \tag{A.6}$$

for every vector $\mathbf{x}$ and every integer $k \geq 1$. We also have the following lemma.

**Lemma 1.** *For any integer $k \geq 1$, $\left\|\mathbf{M}^k(s)\right\| = \rho^k(s)$.*

*Proof of lemma 1.* Let $k = 1$. Using equation (A.5), we obtain

$$\begin{aligned}
\|\mathbf{M}(s)\| &= \sup_{\mathbf{x}\neq\mathbf{0}} \frac{\sum_i \xi_i(s) \left|\sum_j m_{ij}(s) x_j\right|}{\|\mathbf{x}\|} \\
&\leq \sup_{\mathbf{x}\neq\mathbf{0}} \frac{\sum_i \xi_i(s) \sum_j m_{ij}(s) \left|x_j\right|}{\|\mathbf{x}\|} \\
&= \sup_{\mathbf{x}\neq\mathbf{0}} \frac{\sum_j \sum_i \xi_i(s) m_{ij}(s) \left|x_j\right|}{\|\mathbf{x}\|} \\
&= \sup_{\mathbf{x}\neq\mathbf{0}} \frac{\sum_j \rho(s)\xi_j(s) \left|x_j\right|}{\|\mathbf{x}\|} \\
&= \rho(s) \sup_{\mathbf{x}\neq\mathbf{0}} \frac{\|\mathbf{x}\|}{\|\mathbf{x}\|} \\
&= \rho(s).
\end{aligned}$$

Moreover, letting $\mathbf{x} = \boldsymbol{\eta}(s)$ in equation (A.6) gives

$$\rho(s) = \|\rho(s)\boldsymbol{\eta}(s)\| = \|\mathbf{M}(s)\boldsymbol{\eta}(s)\| \leq \|\mathbf{M}(s)\|\|\boldsymbol{\eta}(s)\| = \|\mathbf{M}(s)\|,$$

since $\|\boldsymbol{\eta}(s)\| = 1$. The rest of the proof is easily achieved by induction on $k$.

A crucial result ensues from Lemma 1 and is provided below.

**Lemma 2.** *For* $\mathbf{x} \geq \mathbf{0}$, $\mathbf{x} \neq \mathbf{0}$ *sufficiently close to* $\mathbf{0}$, *we have* $\|\mathbf{x}'\| < \|\mathbf{x}\|$ *if* $\rho(s) < 1$ *and* $\|\mathbf{x}'\| > \|\mathbf{x}\|$ *if* $\rho(s) > 1$.

*Proof of lemma 2.* Taking the scalar product with $\boldsymbol{\xi}(s)$ on both sides of equation (1) yields

$$\|\mathbf{x}'\| = \rho(s)\|\mathbf{x}\| + O(\|\mathbf{x}\|^2).$$

If $\rho(s) < 1$, then it suffices to choose $\|\mathbf{x}\|$ sufficiently small so that $O(\|\mathbf{x}\|^2) < (1 - \rho(s))\|\mathbf{x}\|$ to have $\|\mathbf{x}'\| < \|\mathbf{x}\|$. If $\rho(s) > 1$, then $\|\mathbf{x}'\| > \|\mathbf{x}\|$ as soon as $\|\mathbf{x}\|$ is small enough to have $O(\|\mathbf{x}\|^2) > (1 - \rho(s))\|\mathbf{x}\|$. This completes the proof of Lemma 2.

Now, let $\mathbf{x}^{(k)} > \mathbf{0}$ denote the vector of frequencies in the $k^{\text{th}}$ generation. Then, iterating equation (1) gives

$$\begin{aligned}\mathbf{x}^{(k)} &= \mathbf{M}^k(s)\mathbf{x}^{(0)} + \mathbf{M}^{k-1}(s)O\left(\left\|\mathbf{x}^{(0)}\right\|^2\right) + \mathbf{M}^{k-2}(s)O\left(\left\|\mathbf{x}^{(1)}\right\|^2\right) + \cdots \\ &\quad + O\left(\left\|\mathbf{x}^{(k-1)}\right\|^2\right). \end{aligned} \tag{A.7}$$

But the above expression can be simplified, as stated in the following result.

**Lemma 3.** *If* $\rho(s) < 1$, *then* $\mathbf{x}^{(k)} = \mathbf{M}^k(s)\mathbf{x}^{(0)} + O(\left\|\mathbf{x}^{(0)}\right\|^2)$, *for* $\mathbf{x}^{(0)}$ *sufficiently close to* $\mathbf{0}$, *where the function* $O(\left\|\mathbf{x}^{(0)}\right\|^2)$ *does not depend upon the value of k. On the other hand, if* $\rho(s) > 1$, *then* $\mathbf{x}^{(k)} = \mathbf{M}^k(s)\mathbf{x}^{(0)} + O(\left\|\mathbf{x}^{(k-1)}\right\|^2)$, *for* $\mathbf{x}^{(k-1)}$ *sufficiently close to* $\mathbf{0}$.

*Proof of lemma 3.* First, let us examine the case $\rho(s) < 1$. We shall show that the sum

$$S = \mathbf{M}^{k-1}(s)O(\left\|\mathbf{x}^{(0)}\right\|^2) + \mathbf{M}^{k-2}(s)O(\left\|\mathbf{x}^{(1)}\right\|^2) + \cdots + O(\left\|\mathbf{x}^{(k-1)}\right\|^2) \tag{A.8}$$

in equation (A.7) is a function of order $\left\|\mathbf{x}^{(0)}\right\|^2$ and does not depend upon the value of $k$. Using Lemma 1 and Lemma 2, we have that

$$\begin{aligned}&\frac{\|S\|}{\left\|\mathbf{x}^{(0)}\right\|^2} \\ &\leq \frac{\left\|\mathbf{M}^{k-1}(s)\right\|\left\|O(\left\|\mathbf{x}^{(0)}\right\|^2)\right\| + \left\|\mathbf{M}^{k-2}(s)\right\|\left\|O(\left\|\mathbf{x}^{(1)}\right\|^2)\right\| + \cdots + \left\|O(\left\|\mathbf{x}^{(k-1)}\right\|^2)\right\|}{\left\|\mathbf{x}^{(0)}\right\|^2} \\ &= \rho^{k-1}(s)\frac{\left\|O(\left\|\mathbf{x}^{(0)}\right\|^2)\right\|}{\left\|\mathbf{x}^{(0)}\right\|^2} + \rho^{k-2}(s)\frac{\left\|O(\left\|\mathbf{x}^{(1)}\right\|^2)\right\|}{\left\|\mathbf{x}^{(1)}\right\|^2}\frac{\left\|\mathbf{x}^{(1)}\right\|^2}{\left\|\mathbf{x}^{(0)}\right\|^2} + \cdots \\ &\quad + \frac{\left\|O(\left\|\mathbf{x}^{(k-1)}\right\|^2)\right\|}{\left\|\mathbf{x}^{(k-1)}\right\|^2}\frac{\left\|\mathbf{x}^{(k-1)}\right\|^2}{\left\|\mathbf{x}^{(0)}\right\|^2} \leq \rho^{k-1}(s)c + \rho^{k-2}(s)c + \cdots + c \leq \frac{c}{1-\rho(s)}, \end{aligned}$$

for some constant $c$, as soon as $\left\|\mathbf{x}^{(0)}\right\|^2$ is small enough. On the other hand, if $\rho(s) > 1$, the function in (A.8) can be shown to be of order $\left\|\mathbf{x}^{(k-1)}\right\|^2$ as long as $\left\|\mathbf{x}^{(k-1)}\right\|^2$ is small enough. This clearly shows that (A.8) depends upon $k$ only in the case $\rho(s) > 1$. This completes the proof of Lemma 3.

Two other important results are provided below.

**Lemma 4.** *If $\rho(s) < 1$, then $\mathbf{x}^{(k)} = \left\|\mathbf{x}^{(k)}\right\| (\boldsymbol{\eta}(s) + O(s))$, for k large enough. On the other hand, if $\rho(s) > 1$, the above equality remains valid for k large enough but not too large.*

*Proof of lemma 4.* Let us write $\mathbf{x}^{(0)} = \left\|\mathbf{x}^{(0)}\right\| \boldsymbol{\eta}(s) + \left[\mathbf{x}^{(0)} - \left\|\mathbf{x}^{(0)}\right\| \boldsymbol{\eta}(s)\right]$. Multiplying on the left by $\mathbf{M}^k(s)$ and using Lemma 3 in the case $\rho(s) < 1$, we find that

$$\mathbf{x}^{(k)} = \rho^k(s)\left\|\mathbf{x}^{(0)}\right\| \left[\boldsymbol{\eta}(s) + \frac{\mathbf{M}^k(s)}{\rho^k(s)} \left(\frac{\mathbf{x}^{(0)}}{\left\|\mathbf{x}^{(0)}\right\|} - \boldsymbol{\eta}(s)\right)\right] + O(\left\|\mathbf{x}^{(0)}\right\|^2).$$

But it can be shown, using (A.4) and assertion (d) of the Perron-Frobenius theorem, that

$$\boldsymbol{v} = \frac{\mathbf{M}^k(s)}{\rho^k(s)} \left(\frac{\mathbf{x}^{(0)}}{\left\|\mathbf{x}^{(0)}\right\|} - \boldsymbol{\eta}(s)\right) \to \mathbf{0}, \text{ as } k \to \infty,$$

uniformly for $\mathbf{x}^{(0)} \geq \mathbf{0}, \mathbf{x}^{(0)} \neq \mathbf{0}$. Thus, there exists an integer $N$ such that, for $k \geq N$, all the entries of $\boldsymbol{v}$ are smaller than $s$ in absolute value. If we let $\left\|\mathbf{x}^{(0)}\right\| < \left(\rho^N(s)\right) s$, then $\mathbf{x}^{(N)} = \rho^N(s) \left\|\mathbf{x}^{(0)}\right\| (\boldsymbol{\eta}(s) + O(s))$. Therefore, $\left\|\mathbf{x}^{(N)}\right\| = \rho^N(s) \left\|\mathbf{x}^{(0)}\right\| (1 + O(s))$, which implies that $\mathbf{x}^{(N)} = \left\|\mathbf{x}^{(N)}\right\| (\boldsymbol{\eta}(s) + O(s))$. Finally, for $k \geq N$, we conclude that $\mathbf{x}^{(k)} = \left\|\mathbf{x}^{(k)}\right\| (\boldsymbol{\eta}(s) + O(s))$, since $\left\|\mathbf{x}^{(k-N)}\right\| \leq \left\|\mathbf{x}^{(0)}\right\| < \left(\rho^N(s)\right) s$. The case $\rho(s) > 1$ is treated analogously, the difference being that $k$ must be large enough so that all the entries of $\boldsymbol{v}$ are bounded by $s$, but not too large so that $\left\|\mathbf{x}^{(k)}\right\| < \left(\rho^N(s)\right) s$. This completes the proof of Lemma 4.

**Lemma 5.** *For s small enough, we have $\|\mathbf{x}\| = p\,(1 + O(s))$.*

*Proof of lemma 5.* For $s$ small enough, $\mathbf{x} \geq \mathbf{0}$, $\mathbf{x} \neq \mathbf{0}$ and $p = \sum_i f_i x_i$, we can write

$$\|\mathbf{x}\| = \sum_i \xi_i(s) x_i = \sum_i (f_i + O(s)) x_i = p + O(s) \left[\frac{\sum_i x_i}{\sum_i f_i x_i}\right] p = p\,(1 + O(s))\,,$$

since $\sum_i x_i \,/ \sum_i f_i x_i$ is the same for all multiples of $\mathbf{x}$ and continuous on the compact set $\mathbf{x} \geq \mathbf{0}$, $\mathbf{x} \neq \mathbf{0}$, $\|\mathbf{x}\| = 1$, and is therefore bounded. This completes the proof of Lemma 5.

We are now ready to complete the proof of Result 2. Using Lemma 5, equation (1) for $s$ small enough can be expressed as

$$\mathbf{x}' = \mathbf{M}(s)\mathbf{x} + O(p^2). \tag{A.9}$$

Therefore, recalling that $\Delta p$ is defined as the change in frequency of the rare mutant gene from one generation to the next, we get

$$\Delta p = p' - p = \mathbf{f}^{\mathrm{T}}(\mathbf{x}' - \mathbf{x}) = \mathbf{f}^{\mathrm{T}}\left(\mathbf{M}(s) - \mathbf{I}\right)\mathbf{x} + O(p^2). \tag{A.10}$$

When $s = 0$, we know that $\Delta p = 0$ and, consequently, we must have $O(p^2) = 0$, which implies that $O(p^2)$ in (A.10) is in fact a function $O(p^2)s$, if it is assumed smooth enough. Thus, using Lemma 5, equation (A.10) can be rewritten as

$$\begin{aligned}
\Delta p &= \mathbf{f}^{\mathrm{T}}\left(\mathbf{M}(s) - \mathbf{M}(0)\right)\mathbf{x} + s\,O(p^2) \\
&= \mathbf{f}^{\mathrm{T}}\left(\dot{\mathbf{M}}(0)s + O(s^2)\right)\mathbf{x} + s\,O(p^2) \\
&= \mathbf{f}^{\mathrm{T}}\dot{\mathbf{M}}(0)\mathbf{x}s + \left(\mathbf{f}^{\mathrm{T}}O(s^2)\frac{\mathbf{x}}{\|\mathbf{x}\|}\right)\|\mathbf{x}\| + s\,O(p^2) \\
&= \mathbf{f}^{\mathrm{T}}\dot{\mathbf{M}}(0)\mathbf{x}s + p\,O(s^2) + s\,O(p^2).
\end{aligned}$$

Finally, for values of $k$ as defined in Lemma 4, we conclude from Lemma 5 that

$$\begin{aligned}
p^{(k+1)} - p^{(k)} &= \mathbf{f}^{\mathrm{T}}\dot{\mathbf{M}}(0)\mathbf{x}^{(k)}s + p^{(k)}O(s^2) + s\,O(p^{(k)^2}) \\
&= \mathbf{f}^{\mathrm{T}}\dot{\mathbf{M}}(0)\left[\|\mathbf{x}^{(k)}\|\left(\boldsymbol{\eta}(s) + O(s)\right)\right]s + p^{(k)}O(s^2) + s\,O(p^{(k)^2}) \\
&= \mathbf{f}^{\mathrm{T}}\dot{\mathbf{M}}(0)\left[p^{(k)}\left(1 + O(s)\right)\left(\boldsymbol{\eta}(0) + O(s)\right)\right]s + p^{(k)}O(s^2) \\
&\quad + s\,O(p^{(k)^2}) \\
&= \mathbf{f}^{\mathrm{T}}\dot{\mathbf{M}}(0)\boldsymbol{\eta}(0)p^{(k)}s + p^{(k)}O(s^2) + s\,O(p^{(k)^2}) \\
&= \dot{\rho}(0)p^{(k)}s + p^{(k)}O(s^2) + s\,O(p^{(k)^2}).
\end{aligned}$$

This completes the proof of Result 2.

*A.3. Coefficients of regression for the partial sib mating models*

Let $X$ be the random variable that gives the frequency of $A_1$ genes carried by the female of a mated couple chosen at random in a diploid population. The random variable $Y$ is defined analogously for the male of the same mated couple. In the following, we shall use the fact that the inbreeding coefficient $F$ is the coefficient of correlation between two uniting gametes, the value assigned to a gamete being the number, 0 or 1, of gene $A_1$ that it carries (Wright, 1922). If there is no selection and the population is at equilibrium, this coefficient is equal to the probability that the two uniting gametes are identical by descent (Malécot, 1948; see, e.g., Crow and Kimura, 1970). In the partial sib mating model, it is known (Ghai, 1969) that $F = \beta \,/ (4 - 3\beta)$.

*Autosomal genes* When females and males are both diploid at the locus considered, let $X = (X_1 + X_2)/2$ and $Y = (Y_1 + Y_2)/2$, where subscript 1 refers to a female gamete and subscript 2 to a male gamete. Hence, the random variables $X_1$, $X_2$, $Y_1$

and $Y_2$ take on values 1 or 0 depending upon the gene $A_1$ is carried or not by the corresponding gamete. By definition, we have that

$$r = \frac{\mathrm{Cov}(X, Y)}{\sqrt{\mathrm{Var}(X)}\sqrt{\mathrm{Var}(Y)}} = \frac{\mathrm{Cov}(X_1 + X_2, Y_1 + Y_2)}{\mathrm{Var}(X_1 + X_2)},$$

because $\mathrm{Var}(X) = \mathrm{Var}(Y)$, since the frequency of $A_1$ at equilibrium is the same in both female and male populations. Therefore, we infer that

$$r = \frac{4\mathrm{Cov}(X_1, Y_1)}{2\mathrm{Var}(X_1) + 2\mathrm{Cov}(X_1, X_2)} = \frac{2F}{1+F} = r_{Y\to X} = r_{X\to Y} = \frac{\beta}{2-\beta},$$

since $F = \frac{\mathrm{Cov}(X_1,X_2)}{\mathrm{Var}(X_1)} = \frac{\mathrm{Cov}(X_1,Y_1)}{\mathrm{Var}(X_1)}$. In the above equation, $r_{Y\to X}$ is the coefficient of regression of the frequency of $A_1$ genes carried by the male of a mated couple $(Y)$ on the frequency of $A_1$ genes carried by the female of this couple $(X)$. Likewise, $r_{X\to Y}$ represents the coefficient of regression of the frequency of $A_1$ genes carried by the female of a mated couple $(X)$ on the frequency of $A_1$ genes carried by the male of this couple $(Y)$.

*Sex-linked genes* This time, we define $X = (X_1 + X_2)/2$ and $Y = Y_1$, so that

$$r_{Y\to X} = \frac{\mathrm{Cov}(X, Y)}{\mathrm{Var}(X)} = \frac{2\mathrm{Cov}(X_1, Y_1)}{\mathrm{Var}(X_1) + \mathrm{Cov}(X_1, X_2)} = \frac{2F}{1+F} = \frac{\beta}{2-\beta},$$
$$r_{X\to Y} = \frac{\mathrm{Cov}(X, Y)}{\mathrm{Var}(Y)} = \frac{\mathrm{Cov}(X_1, Y_1)}{\mathrm{Var}(Y_1)} = F = \frac{\beta}{4-3\beta}.$$

*A.4. Matrix of linear approximation for autosomal genes in partial sib mating populations*

$$\begin{bmatrix}
\beta\left(1+d_{11}^{\mathrm{f}}s+d_{11}^{\mathrm{m}}s\right) & \frac{\beta}{4}\left(1+d_{11}^{\mathrm{f}}s+d_{11}^{\mathrm{m}}s\right) & \frac{\beta}{4}\left(1+d_{11}^{\mathrm{f}}s+d_{11}^{\mathrm{m}}s\right) & 0 & 0 & \frac{\beta}{16}\left(1+d_{11}^{\mathrm{f}}s+d_{11}^{\mathrm{m}}s\right) & 0 & 0 \\
0 & \frac{\beta}{4}\left(1+d_{12}^{\mathrm{f}}s+d_{11}^{\mathrm{m}}s\right) & \frac{\beta}{4}\left(1+d_{12}^{\mathrm{f}}s+d_{11}^{\mathrm{m}}s\right) & 0 & 0 & \frac{\beta}{8}\left(1+d_{12}^{\mathrm{f}}s+d_{11}^{\mathrm{m}}s\right) & 0 & 0 \\
0 & \frac{\beta}{4}\left(1+d_{11}^{\mathrm{f}}s+d_{12}^{\mathrm{m}}s\right) & \frac{\beta}{4}\left(1+d_{11}^{\mathrm{f}}s+d_{12}^{\mathrm{m}}s\right) & 0 & 0 & \frac{\beta}{8}\left(1+d_{11}^{\mathrm{f}}s+d_{12}^{\mathrm{m}}s\right) & 0 & 0 \\
(1-\beta)\left(1+d_{11}^{\mathrm{m}}s\right) & \left(\frac{1-\beta}{2}\right)\left(1+d_{11}^{\mathrm{m}}s\right) & \left(\frac{1-\beta}{2}\right)\left(1+d_{11}^{\mathrm{m}}s\right) & 0 & 0 & \left(\frac{4-3\beta}{16}\right)\left(1+d_{11}^{\mathrm{m}}s\right) & 0 & 0 \\
(1-\beta)\left(1+d_{11}^{\mathrm{f}}s\right) & \left(\frac{1-\beta}{2}\right)\left(1+d_{11}^{\mathrm{f}}s\right) & \left(\frac{1-\beta}{2}\right)\left(1+d_{11}^{\mathrm{f}}s\right) & 0 & 0 & \left(\frac{4-3\beta}{16}\right)\left(1+d_{11}^{\mathrm{f}}s\right) & 0 & 0 \\
0 & \frac{\beta}{4}\left(1+d_{12}^{\mathrm{f}}s+d_{12}^{\mathrm{m}}s\right) & \frac{\beta}{4}\left(1+d_{12}^{\mathrm{f}}s+d_{12}^{\mathrm{m}}s\right) & \beta\left(1+d_{12}^{\mathrm{f}}s+d_{12}^{\mathrm{m}}s\right) & \beta\left(1+d_{12}^{\mathrm{f}}s+d_{12}^{\mathrm{m}}s\right) & \frac{\beta}{4}\left(1+d_{12}^{\mathrm{f}}s+d_{12}^{\mathrm{m}}s\right) & \frac{\beta}{4}\left(1+d_{12}^{\mathrm{f}}s+d_{12}^{\mathrm{m}}s\right) & \frac{\beta}{4}\left(1+d_{12}^{\mathrm{f}}s+d_{12}^{\mathrm{m}}s\right) \\
0 & \left(\frac{1-\beta}{2}\right)\left(1+d_{12}^{\mathrm{m}}s\right) & \left(\frac{1-\beta}{2}\right)\left(1+d_{12}^{\mathrm{m}}s\right) & (1-\beta)\left(1+d_{12}^{\mathrm{m}}s\right) & (1-\beta)\left(1+d_{12}^{\mathrm{m}}s\right) & \left(\frac{4-3\beta}{8}\right)\left(1+d_{12}^{\mathrm{m}}s\right) & \left(\frac{2-\beta}{4}\right)\left(1+d_{12}^{\mathrm{m}}s\right) & \left(\frac{2-\beta}{4}\right)\left(1+d_{12}^{\mathrm{m}}s\right) \\
0 & \left(\frac{1-\beta}{2}\right)\left(1+d_{12}^{\mathrm{f}}s\right) & \left(\frac{1-\beta}{2}\right)\left(1+d_{12}^{\mathrm{f}}s\right) & (1-\beta)\left(1+d_{12}^{\mathrm{f}}s\right) & (1-\beta)\left(1+d_{12}^{\mathrm{f}}s\right) & \left(\frac{4-3\beta}{8}\right)\left(1+d_{12}^{\mathrm{f}}s\right) & \left(\frac{2-\beta}{4}\right)\left(1+d_{12}^{\mathrm{f}}s\right) & \left(\frac{2-\beta}{4}\right)\left(1+d_{12}^{\mathrm{f}}s\right)
\end{bmatrix}$$

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