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Genealogy-dependent variation in viability among self-incompatibility genotypes

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Abstract

Many hermaphroditic plants avoid self-fertilization by rejecting pollen that express genetically determined specificities in common with the pistil. The *S*-locus, comprising the determinants of pistil and pollen specificity, typically shows extremely high polymorphism, with dozens to hundreds of specificities maintained within species. This article explores a conjecture, motivated by empirical findings, that the expression of recessive deleterious factors at sites closely linked to the *S*-locus may cause greater declines in the viability of zygotes constituted from more closely related *S*-alleles. Diffusion approximation models incorporating variation in viability among *S*-locus genotypes and antagonistic interactions between a new specificity and its immediate parent specificity are constructed and analyzed. Results indicate that variation in viability tends to reduce the number of specificities maintained in a population at stochastic steady state, and that genealogy-based antagonism reduces the rate of bifurcation of *S*-allele lineages. These effects may account for some of the unusual features observed in empirical studies of *S*-allele genealogies.

1. Introduction

Homomorphic self-incompatibility (SI) in many flowering plants excludes pollen that express genetically determined specificities in common with the pistil (see de Nettancourt, 1977). Under gametophytic SI (GSI), pollen specificity is determined in the gametophyte stage, by the haploid genome of the pollen itself, and under sporophytic SI (SSI), in the sporophyte stage, by the genome of the plant that produced the pollen. Because pollen that express rarer specificities induce the rejection reaction in fewer pistils, SI engenders intense frequency-dependent balancing selection, promoting the invasion and maintenance of rare specificities. Self incompatible plants typically show very high levels of polymorphism at the locus (*S*-locus) which determines specificity, with up to hundreds of *S*-alleles maintained within species (Lawrence, 2000).

To account for the extraordinary allelic diversity observed by Emerson (1938) in natural populations, Wright (1939) developed a diffusion approximation model of GSI. While this model predicts high *S*-allele polymorphism, the dozens of alleles observed by Emerson appeared incompatible with the low estimated population size. Later work by Fisher (1958) and Wright (1960, 1964) led to refinements of the model and its approximations, but the rate

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of mutation to new *S*-alleles required to account for the number of segregating *S*-alleles remained rather beyond the maximum considered likely on the basis of empirical studies of spontaneous and artificial mutations at the *S*-locus (Wright, 1960).

1.1. Genetic structure

Functional studies of induced mutations (reviewed by Golz et al., 2000; Nasrallah et al., 2000) established that the *S*-locus comprises at least two distinct genes, the determinants of pistil and pollen specificity. Absolute linkage between these genes is considered essential to SI function, as crossing-over would permit self-fertilization by generating a haplotype that encodes different pistil and pollen specificities.

Genetic analysis of the *S*-locus has revealed that recombination is greatly reduced or suppressed, not only between the determinants of pistil and pollen specificity, but across large genomic tracts surrounding the *S*-locus. In the system of SSI expressed in species of Brassica, segregating haplotypes encoding different *S*-locus specificities show extensive structural differences, suggesting that conventional crossing-over within the *S*-locus would generate only nonfunctional gametes (Boyes et al., 1997; Suzuki et al., 1999; Nasrallah, 2000). Comprising perhaps hundreds of kilobases (KB), the *S*-locus region in Brassica is gene-rich, containing approximately one expressed gene per 5:4 KB in *B. rapa* (Suzuki et al., 1999). In solanaceous species expressing GSI, the *S*-locus lies in a centromeric region, and the region of greatly reduced recombination extends over at least 1 MB (McCubbin and Kao, 1999; McCubbin et al., 2000).

1.2. Evolutionary analysis

Characterization of the genes that control pistil expression in model systems of SSI (Nasrallah et al., 1985) and GSI (Anderson et al., 1986) revolutionized the evolutionary, as well as genetic and physiological, investigation of SI. By expanding the empirical basis from number and frequency of alleles to include genealogical relationships among alleles, the advent of molecular population genetics has provided much new information relating to the classical conundrum of *S*-locus diversity. However, resolution of genealogical relationships among segregating *S*-allele lineages has only deepened the mystery. Very high rates of origin of new *S*-alleles would imply rapid turnover of *S*-allele lineages, in apparent contradiction with the ancient divergence of lineages segregating within species (Ioerger et al., 1990; Dwyer et al., 1991; Uyenoyama, 1995). Further, analyses of genealogical structure among segregating *S*-alleles sampled from natural populations have revealed significantly long terminal branches relative to expectation based on SI alone (Uyenoyama, 1997). Other systems of balancing selection, including the evolutionarily-independent form of SI expressed in Brassica (Schierup et al., 1998) and the vertebrate major histocompatibility complex (Richman and Kohn, 1999), also exhibit this pattern.

Further, significant departures from equal frequencies among *S*-alleles controlling GSI in *Papaver rhoeas* (field poppy) may reflect linkage of the *S*-locus to factors affecting seed dormancy and albinism (Lawrence and Franklin-Tong, 1994). All structural information available to date in model systems of both SSI and GSI indicates tight linkage between the *S*-locus and perhaps hundreds of expressed genes.

A factor that may account for both the unusual genealogical structure of S -allele genealogies and the apparent pleiotropy of S -alleles is the progressive accumulation of S -allele-specific load due to recessive deleterious mutations at tightly linked sites (Uyenoyama, 1997, 2000). The very low rates of recombination in the vicinity of the S -locus may promote the development of S -allele-specific load. Formation of a zygote comprising recently diverged specificities would result in homozygosis and expression of recessive deleterious mutations in regions flanking the S -locus. Zygote viability or fertility would decline with increasing genealogical relationship between the constituent S -alleles.

1.3. Overview of the analysis

Here, I extend the Wright (1939) model of GSI to accommodate genealogy-dependent viability selection, denoting an association between zygote viability and the time since divergence of the constituent alleles. Such dependence may derive from S -allele-specific load, disequilibrium between S -alleles and deleterious mutations at loci closely linked to the S -locus. In order to accommodate S -allele-specific load, the models relax some of the symmetry assumptions of the Wright model.

Introduction of variation in zygote viability alone is expected to reduce the probability of invasion of new specificities (see, for example, Karlin and Levikson, 1974). In order to provide a means of distinguishing the general effects of variation in viability from the specific effects of genealogy-dependent viability selection, I first consider Model 1, which incorporates a positive variance, but without mean differences, in viability among S -locus genotypes.

Model 2 addresses the primary issue of interest, genealogy-dependent viability selection. In lieu of an explicit representation of the accumulation of deleterious mutations at multiple sites within the S -locus region, I assume that the relative time since divergence between a pair of alleles determines the viability of the zygote they would form. The distribution of divergence time among common S -alleles depends on the process of origin and extinction of specificities.

A rare, newly arisen S -specificity (O) may wander in the boundary layer close to extinction for an extended period before either exiting the population or jumping into the interior (cf. Gillespie, 1994). The probability of invasion of O depends on the distribution of its divergence times from other alleles. In particular, it may have diverged perhaps orders of magnitude more recently from its immediate parent specificity (P) than from other common S -alleles. Model 2 assumes that the identity of the first common S -allele to become extinct during the period in which O resides in the boundary layer is independent of genealogical relationship to O . In the event that it is P that becomes extinct during this period, the distribution of coalescence times between O and the remaining common S -alleles would be comparable to that between any pair of common S -alleles. Alternatively, the presence of P in the population throughout the period in which O is rare is expected to reduce the probability that O will rise to common frequencies.

Variation in zygote viability in combination with antagonism between closely related S -alleles tends to reduce both S -allele number and the rate of bifurcation of S -allele lineages.

Consequently, while allele-specific load may account for some of the features of observed $\mathcal{S}$ -allele genealogies, it would exacerbate the discrepancy between the number of alleles observed in natural populations and current theoretical expectations.

2. Method

In order to describe the analytical approach, I begin with an exposition of the Wright (1939) model of GSI, together with its key approximations and results (see also Uyenoyama and Takebayashi, 2003).

2.1. Wright model

The intense frequency-dependent balancing selection engendered by GSI derives entirely from prezygotic interactions between seed parent and pollen tube, and not at all from variation in postzygotic components of fitness, including fertility or viability. Accordingly, Wright's (1939) model prescribes uniform seed set and viability among genotypes:

$$P'_{ij} = \left[q_i \sum_{k \neq i, j} \frac{P_{jk}}{1 - q_j - q_k} + q_j \sum_{k \neq i, j} \frac{P_{ik}}{1 - q_i - q_k} \right] / 2, \quad (1)$$

in which P_{ij} represents the frequency of $S_i S_j$ zygotes, the prime indicates the offspring generation, q_k is the frequency of $\mathcal{S}$ -allele S_k in the pollen pool, and the denominators ensure equal seed set among genotypes. Because GSI prevents the formation of homozygotes, indices i, j , and k are necessarily distinct.

In general, this recursion system is of very high dimension, reflecting the maintenance of many specificities under GSI. Using an inspired series of approximations, which were later shown to be robust, Wright (1939) succeeded in capturing the joint evolution of genetic drift, mutation, and GSI selection among arbitrary numbers of specificities in a one-dimensional diffusion model. The effective number of alleles (n) corresponds to the inverse of steady-state homozygosity:

$$F = \sum q_i^2 = 1/n, \quad (2)$$

for q_i the frequency of the i th allele (Kimura and Crow, 1964). Wright's approach entails first treating n as a parameter and later determining its relationship to population size and the rate of mutation to new $\mathcal{S}$ -alleles.

Because mating compatibility depends only on identity or nonidentity between pistil and pollen specificities, $\mathcal{S}$ -alleles are exchangeable: the probability distributions of allele frequencies are unchanged under permutation of allele names. Consider a particular $\mathcal{S}$ -allele, S_i , with frequency q , and assume equal frequencies among the $n - 1$ alternative $\mathcal{S}$ -alleles segregating in the population:

$$q_j = (1 - q)/(n - 1), \quad (3)$$

for j different from i . Similarly, assume equal frequencies among all genotypes that bear S_j and equal frequencies among all other genotypes:

$$P_{ij} = P, \quad (4)$$

$$P_{jk} = \frac{1 - P(n-1)}{\binom{n-1}{2}}, \quad (5)$$

$$q = P(n-1)/2, \quad (6)$$

for i, j , and k denoting distinct specificities.

These approximations and substitution of homozygosity for the inverse of allele number ($F = 1/n$) permit reduction of the model to a single recursion:

$$\Delta q = \frac{q(F-q)}{1-3F+2qF}. \quad (7)$$

Wright (1964) further replaced q in the denominator by F ,

$$\Delta q = \frac{q(F-q)}{(1-F)(1-2F)}, \quad (8)$$

to determine the now canonical diffusion equation coefficients:

$$\mu(x) = -ax(x-F) - ux, \quad (9)$$

$$\sigma^2(x) = x(1-2x)/2N, \quad (10)$$

in which N is the effective population size; u the rate of mutation to new S -alleles; and

$$a = \frac{1}{(1-F)(1-2F)} \quad (11)$$

(see Wright, 1969, pp. 405–406). The form of the diffusion coefficient (10) reflects drift due to sampling of zygotes rather than genes (Fisher, 1958, Chapter IV; Wright, 1960). Further, because SI prevents the formation of homozygotes, reproduction requires at least three S -alleles, ensuring nonnegative $\sigma^2(x)$ for any reproducing population.

Wright's diffusion approximation model of GSI contains only two parameters, effective population size (N) and the rate of mutation to new S -specificities (u), with no parameter representing the intensity of the dominant selective force of prezygotic mating exclusion. In (9), GSI selection generates change at a rate proportional to $x(x-F)$. Unless this quantity is comparable in magnitude to $1/2N$, the force of GSI overwhelms drift, causing very rapid changes in frequency. In essence, the diffusion approximation holds only for x near zero or near the deterministic equilibrium $F = 1/n$, with the process jumping instantaneously between these regions (see Sasaki, 1989, 1992; Gillespie, 1983, 1994).

2.2. Determination of homozygosity

Wright's model addresses the change in frequency of a focal S -allele, against a background of $n - 1$ alternative S -alleles, for n corresponding to the inverse of homozygosity (F). Clearly, the value of n is not in fact a parameter, but is assumed to follow a stationary distribution at stochastic steady state. Because extinction is the only boundary that a given S -allele can reach in finite time, a stationary distribution for its frequency does not exist. However, the property of exchangeability of S -alleles permits the number of S -alleles with frequency in a small interval $(\Phi(x)dx)$ to be obtained from the drift and diffusion coefficients describing changes in the frequency of a particular S -allele. Yokoyama and Nei (1979) assumed that $\Phi(x)dx$ is proportional to the Wright–Fisher formula:

$$\Phi(x)dx = C \lim_{n \rightarrow \infty} \frac{2 \int_0^x \mu(\xi)/\sigma^2(\xi) d\xi}{n} \sigma^2(x)dx, \quad (12)$$

with proportionality constant

$$C = 4Nu. \quad (13)$$

From the condition that allele frequencies (x) sum to unity,

$$\int_0^1 x \Phi(x) dx = 1, \quad (14)$$

Yokoyama and Hetherington (1982) derived an implicit solution for $F(=1/n)$:

$$u \sqrt{8N\pi(1-F)} (1-2F)^{N/(1-F)} e^{2FN/[(1-F)(1-2F)]} = 1. \quad (15)$$

These derivations are somewhat heuristic because the notions of stochastic equilibrium and stationary distribution are not well-defined for SI systems: in particular, the ultimate state is extinction, upon the eventual decline of the number of S -alleles in the population to two, at which point GSI would preclude all fertilization (Ewens, 1964).

An alternative derivation of the number of S -alleles involves equating the rate of incorporation and extinction of common specificities (compare analyses of overdominant viability selection by Sasaki, 1989, 1992; Slatkin and Muirhead, 1999). Each of the $2N$ genes in the population gives rise to a new S -allele at rate u , with the rate of origin of new common S -alleles corresponding to

$$\lambda = 2Nuv(1/2N), \quad (16)$$

in which $v(x)$ represents the probability that an allele that appears with initial frequency x increases to frequency $1/n$ before extinction. A fundamental result from diffusion theory (see Karlin and Taylor, 1981, Chapter 15) gives this probability as

$$v(x) = \frac{S(x) - S(0)}{S(1/n) - S(0)}, \quad (17)$$

in which

$$S(y) = \int^y s(\eta) d\eta, \quad (18)$$

$$s(\eta) = e^{-2 \int^\eta \mu(\xi) / \sigma^2(\xi) d\xi}. \quad (19)$$

$S(y)$; called the scale function, expresses the scaling of distance under which the distance of the process from a point is proportional to hitting probability (Karlin and Taylor, 1981, p. 196). Substitution of drift (9) and diffusion (10) coefficients of the Wright model into (17) produces

$$\lambda = 2Nu(a - 2b) = \frac{4NuF}{(1 - F)(1 - 2F)} \quad (20)$$

for a given in (11) and

$$b = \frac{1}{2(1 - F)} + u. \quad (21)$$

As noted by Gillespie (1994) for overdominant viability selection, the probability that a rare allele will escape the boundary layer and jump into the interior is independent of its initial frequency within the boundary layer.

Karlin and Taylor (1981, Chapter 15) show that the expected time for an allele initiated at frequency x to reach either endpoint of the interval (α, β) is

$$2 \left[\frac{S(x) - S(\alpha)}{S(\beta) - S(\alpha)} \right] \int_x^\beta [S(\beta) - S(\xi)] m(\xi) d\xi + 2 \left[\frac{S(\beta) - S(x)}{S(\beta) - S(\alpha)} \right] \int_\alpha^x [S(\xi) - S(\alpha)] m(\xi) d\xi, \quad (22)$$

in which

$$m(\xi) = 1 - [\sigma^2(\xi) s(\xi)]. \quad (23)$$

Reproduction under GSI requires at least three S -alleles, implying

$$\lim_{\beta \rightarrow 1/2} S(\beta) = \infty. \quad (24)$$

This expression indicates that the upper boundary is in effect infinitely distant from the interior. Taking the limit $(\alpha \rightarrow 0, \beta \rightarrow 1/2)$ produces $t(x)$ the expected time for a common S -allele initiated at frequency x to decline to extinction. For the Wright model,

$$t(x) = \frac{2a}{(a - 2b)^2} e^{N(a - 2b)} \left(\frac{2b}{a} \right)^{2Nb} \sqrt{\frac{\pi}{Nb}}. \quad (25)$$

The rate of extinction of any particular S -allele corresponds to the reciprocal of $t(x)$, giving a total rate of extinction among the n common S -alleles maintained in the population of

$$\mu = n/t(x). \quad (26)$$

Equating the rates of origin and extinction ($\lambda = \mu$) determines the number of common alleles ($n = 1/F$). This manipulation, using the drift and diffusion coefficients for the Wright model, confirms the solution of Yokoyama and Hetherington (1982), obtained by a different approach. The proportionality constant C (13) of the stationary distribution of allele numbers may then be determined from the condition that allele frequencies sum to unity (14). This determination completes the Wright model by relating the number of common alleles (n) to the parameters of the model (N and u).

The expressions derived here differ from those given by Vekemans and Slatkin (1994) and Muirhead (2001). In adapting Takahata's (1990) analysis of symmetric overdominance to GSI, Vekemans and Slatkin (1994) followed Takahata in substituting $x/2N$ for the diffusion coefficient $\sigma^2(x) = x(1 - 2x)/2N$ (10). This substitution introduces a factor of $\sqrt{2}$, later considered equivocal by Slatkin and Muirhead (1999). By modifying classical results on the probability of fixation of alleles under viability selection, Muirhead (2001) proposed an expression for the probability of invasion of new S -alleles that differs from (20). She then used it to infer the rate of extinction from the Yokoyama–Hetherington solution (15) for the number of common alleles (n), obtaining an expression different from (25). The results presented here derive from a self-contained analysis of the Wright model.

2.3. Scaling factor

Takahata (1990) suggested that the process of coalescence among symmetrically overdominant alleles in a population of size $2N$ resembles that among neutral alleles in a population of size $2Nf$, for f a scaling factor summarizing the expansion of coalescence times under balancing selection. Coalescence among j neutral lineages in a population of size $2Nf$ occurs at rate

$$\frac{\binom{j}{2}}{2Nf}, \quad (27)$$

and among lineages under balancing selection at rate

$$\frac{\lambda(1 - 1/n)\binom{j}{2}}{\binom{n}{2}} = \frac{\lambda j(j-1)}{n^2}. \quad (28)$$

The expression for balancing selection reflects the rise of a new specificity to common frequencies (λ) without the extinction of its parent specificity ($1 - 1/n$) and coalescence between a pair of the focal j lineages (see Hey, 1992; Takahata et al., 1992). Equating these expressions determines the scaling factor:

$$f = \frac{n^2}{4N\lambda} = \frac{nt(x)}{4N}, \quad (29)$$

in which the latter equality follows from (26) under the assumption of stochastic equilibrium ($\lambda = \mu$).

For the Wright (1939) model,

$$f = \frac{1}{16N^2uaF^3}, \quad (30)$$

in which F is determined by the Yokoyama and Hetherington (1982) solution (15). This expression differs from the quantity given in Vekemans and Slatkin (1994) by the equivocal $\sqrt{2}$ indicated earlier.

3. Model 1: variation in viability

Model 1 addresses variation in viability among zygotes, independent of genealogical relationship between alleles. The change in frequency of a given allele S_i depends on the distribution of viabilities of carriers of S_i relative to noncarriers.

3.1. Drift and diffusion coefficients

Selection due to both prezygotic incompatibility and postzygotic variation in viability determine the frequency of a genotype bearing S -specificities S_i and S_j :

$$TP'_{ij} = \frac{\tau_j}{2} \left[q \sum_{k \neq i,j} \frac{P_{jk}}{1 - q_j - q_k} + q_j \sum_{k \neq i,j} \frac{P_{ik}}{1 - q - q_k} \right] \quad (31)$$

in which P_{ij} denotes the frequency of zygotes with genotype $S_i S_j$; q and q_j the frequencies in the pollen pool of specificities S_i and S_j , respectively, τ_j the viability in the present generation of genotype $S_i S_j$; the prime the frequency among offspring at the time of reproduction; and T the normalizer that ensures that genotypic frequencies sum to unity. Following Wright (1939), I consider changes in the frequency of S_i and assume symmetry among the frequencies of the $n - 1$ remaining common specificities in the population:

$$q_j = \frac{1 - q}{n - 1}, \quad (32)$$

$$P_{ij} = P, \quad (33)$$

$$P_{jk} = \frac{1 - P(n - 1)}{\binom{n - 1}{2}}, \quad (34)$$

for i, j , and k distinct indices. This approximation assumes that the departures from symmetry generated by variation in viability have little effect on the average viability of carriers of S_j . Viability selection does not affect pollen production, implying

$$q = P(n-1)/2. \quad (35)$$

Incorporation of these assumptions and summation over all alternative specificities S_j permit reduction of the recursion to

$$TP' = T2q'/(n-1) = \tau(n-1) \left[\frac{q(1-2q)}{n-3+2q} + P/2 \right], \quad (36)$$

in which τ represents the average viability among genotypes that bear specificity S_i .

Determination of the normalizer T entails construction of a similar recursion for the frequency of genotype $S_j S_k$, in which both specificities differ from S_i . Summing over all such genotypes as before produces

$$\begin{aligned} T(1-2q') \\ = \tau^* \left[\frac{(1-q)(1-2q)(n-3)}{n-3+2q} + P(n-1)/2 \right], \end{aligned} \quad (37)$$

in which τ^* denotes the expected viability among genotypes that do not bear S_i . Summing these recursions produces

$$T = \tau - (\tau - \tau^*) \left[(1-2q) + \frac{2q(nq-1)}{n-3+2q} \right]. \quad (38)$$

An expression for the change in frequency of S_i over one generation follows from (36) and (38):

$$\begin{aligned} T\Delta q = \tau \frac{q(F-q)}{1-3F+2qF} \\ + q(\tau - \tau^*) \left[(1-2q) + \frac{2q(q-F)}{1-3F+2qF} \right]. \end{aligned} \quad (39)$$

Passing to the diffusion limit requires that genetic changes induced by mating incompatibility, viability selection, and drift occur at comparable rates. As in the Wright model, changes due to incompatibility and drift occur on similar time scales if $q(F-q)$ and $1/2N$ are of comparable orders. Terms in (39) which involve differentials in viability ($\tau - \tau^*$) represent the intensity of viability selection. I assume that

$$E \left[\frac{\tau - \tau^*}{\tau} \right] = 0, \quad (40)$$

$$E\left[\left(\frac{\tau - \tau^*}{\tau}\right)^2\right] = \frac{D}{2N}, \quad (41)$$

in which the first equation indicates equal expected viabilities among genotypes formed by randomly pairing S -specificities. Selection intensities of greater order than $1/2N$ would overwhelm the process, while those of lesser order would have negligible effect. Expanding T under the assumption of small selection differentials due to both incompatibility and viability selection produces

$$\Delta q = q \left[\frac{(F - q)}{1 - 3F + 2qF} + \frac{(\tau - \tau^*)}{\tau} (1 - 2q) \right] \times \left[1 + \frac{\tau - \tau^*}{\tau} (1 - 2q) \right]. \quad (42)$$

This expression determines the mean and variance coefficients of the diffusion model:

$$E[\Delta x] = -x(x - F)a + x(1 - 2x)^2 D/2N, \quad (43)$$

$$E[(\Delta x)^2] = [x(1 - 2x)]^2 D/2N, \quad (44)$$

in which x represents the frequency of the focal S -specificity and a corresponds to (11). The form of a (11) reflects Wright's substitution of F for q in the denominator of the first term of (42), an approximation that permits considerable simplification at the cost of little error for large n (see Wright, 1964). Combining these expressions with terms representing the loss of the focal S -specificity through mutation to new S -specificities (rate u) and drift produces the drift and diffusion coefficients for this first model:

$$\mu_1(x) = -x(x - F)a - xu + x(1 - 2x)^2 D/2N, \quad (45)$$

$$\sigma^2(x) = x(1 - 2x)d(x)/2N, \quad (46)$$

in which

$$d(x) = 1 + Dx(1 - 2x). \quad (47)$$

As Karlin and Levikson (1974) found for general diffusion models involving stochastic fluctuations in selection intensity, the variance in the intensity of viability selection ($D/2N$) contributes to the mean displacement ($\mu_1(x)$) as well as to the variance coefficient ($\sigma^2(x)$).

3.2. Rate of origin of new specificities

Substitution of (45) and (46) into the expression for the scale function (19) gives

$$s(\eta) = B(\eta)e^{-NA(\eta)}, \quad (48)$$

for

$$\begin{aligned}
 A(\eta) &= 2b \log(1 - 2\eta) \\
 &+ \frac{a}{D(r_1 - r_2)} [-r_1 \log(r_1 - \eta) + \log(\eta - r_2)] \\
 &+ \frac{2b}{(r_1 - r_2)} [-r_1 \log(r_1 - \eta) + r_2 \log(\eta - r_2)],
 \end{aligned} \tag{49}$$

$$B(\eta) = \frac{1}{d(\eta)} \left(\frac{r_1 - \eta}{\eta - r_2} \right)^{1/[2(r_1 - r_2)]}, \tag{50}$$

in which r_1 and r_2 represent the roots of $d(\eta)$:

$$1 + D\xi(1 - 2\xi) = 2D(r_1 - \xi)(\xi - r_2) = 0 \tag{51}$$

(cf. Karlin and Levikson, 1974). Integration of $s(\eta)$ using Laplace's asymptotic expansion method for large N (see Olver, 1974, Chapter 3) provides the probability of invasion of a new specificity,

$$v_1(x) = 2/A'(0) = a - 2b, \tag{52}$$

for b (21) as defined by Yokoyama and Hetherington (1982).

These expressions indicate that rate of origin of new specificities under the influence of incompatibility and viability selection is

$$\lambda_1 = 2Nu(a - 2b) = 4Nu\alpha F + o(u). \tag{53}$$

Variation in viability (D) affects the rate of origin of new specificities only through its influence on the number of common specificities maintained in the population (n). Examination of the drift coefficient $\mu_1(x)$ (45) indicates that for small x , the term representing GSI dominates the term representing viability selection.

3.3. Rate of extinction of common specificities

Substitution of the drift (45) and diffusion (46) coefficients into the expression for the time to extinction (22) produces

$$t(x) = \sqrt{\frac{\pi d(\hat{x})}{Nb}} \frac{(1 - 2\hat{x})^{2Nb}}{2a\hat{x}^2} L_1(\hat{x})^{Na} L_2(\hat{x}) L_3(\hat{x})^{2Nb}, \tag{54}$$

in which

$$L_1(\hat{x}) = \left[\frac{r_1(\hat{x} - r_2)}{-r_2(r_1 - \hat{x})} \right]^{1/[D(r_1 - r_2)]}, \tag{55}$$

$$L_2(\hat{x}) = \left[\frac{r_1(\hat{x} - r_2)}{-r_2(r_1 - \hat{x})} \right]^{1/[2(r_1 - r_2)]}, \quad (56)$$

$$L_3(\hat{x}) = \left[\left(\frac{r_1}{r_1 - \hat{x}} \right)^{r_1} \left(\frac{-r_2}{\hat{x} - r_2} \right)^{-r_2} \right]^{1/(r_1 - r_2)} \quad (57)$$

for

$$\hat{x} = \frac{a - 2b}{2a} = F - \frac{u}{a}. \quad (58)$$

As is the case for the rate of origin (53), the time to extinction of a common $\mathcal{S}$ -specificity (segregating at frequencies near $1/n$) is, to the order of the approximation of the diffusion model, independent of the initial frequency x .

Application of l'Hôpital's rule indicates that as variation in the intensity of viability selection diminishes to zero,

$$\lim_{D \rightarrow 0} L_1 = e^{2\hat{x}}, \quad (59)$$

with L_2 and L_3 converging to unity. In the limit of negligible D , the time to extinction reduces to (25), corresponding to the Wright model.

3.4. Determination of homozygosity

The number of common $\mathcal{S}$ -alleles ($n = 1/F$) is determined as a balance between the origin and extinction of common specificities. Setting λ_1 (53) equal to $n/t_1(x)$ produces

$$u\sqrt{8N\pi d(F)(1-F)(1-2F)}^{N/(1-F)} L_1(F)^{N/[(1-F)(1-2F)]} \\ \times L_2(F)L_3(F)^{N/(1-F)} = 1 \quad (60)$$

(to order u). In the limit of negligible variation in viability ($D = 0$), this equation reduces to the Yokoyama-Hetherington (1982) solution (15).

4. Model 2: genealogy-dependent selection

Under genealogy-dependent viability selection, zygotes constituted from more recently diverged $\mathcal{S}$ -specificities have lower viability. A rare specificity newly formed by mutation from an existing common specificity diverged from its parent much more recently than from any other common specificity. Model 2 addresses this exceptional relationship between a newly arisen rare specificity and its parent. A subsequent section examines the relationship between zygote viability and the distribution of coalescence times between two randomly chosen common specificities.

4.1. Drift and diffusion coefficients

Let S_i in recursion (31) for $S_i S_j$ represent the newly arisen specificity and S_j a common specificity different from the parent, S_p . The symmetry assumptions now distinguish S_p from the other common specificities:

$$q_j = \frac{1-q}{n-1}, \quad j \neq i, \quad (61)$$

$$P_{ij} = P, \quad j \neq i, p, \quad (62)$$

$$P_{ip} = Q, \quad (63)$$

$$P_{jl} = \frac{1 - [P(n-2) + Q]}{\binom{n-1}{2}}, \quad i \neq j, l. \quad (64)$$

The frequency of S_i corresponds to

$$q = [P(n-2) + Q]/2. \quad (65)$$

Summation over all alternative specificities $S_j (j \neq i, p)$ produces

$$TP' = \frac{\tau}{2} \left[\frac{2q(1-2q)}{n-3+2q} + \frac{P(n-3) + Q}{n-2} \right], \quad (66)$$

in which τ now represents the average viability of zygotes bearing S_i together with a common specificity other than S_p . The recursion for the frequency of the zygote formed from the parent and offspring specificities is

$$TQ' = \frac{\hat{\tau}}{2} \left[\frac{2q(1-2q)}{n-3+2q} + P \right], \quad (67)$$

in which $\hat{\tau}$ represents the viability of $S_i S_p$ zygotes. These expressions determine the recursion for the frequency of S_i :

$$Tq' = \frac{\tau}{4} \left[\frac{2q(1-2q)(n-2)}{n-3+2q} + P(n-3) + Q \right] + \frac{\hat{\tau}}{4} \left[\frac{2q(1-2q)}{n-3+2q} + P \right]. \quad (68)$$

Only a fraction $1/n$ of the zygotes that bear the rare specificity also bear its parent; further, these genotypes have much lower viability than all other genotypes. To obtain a recursion in a single variable, I ignore terms involving Q or $\hat{\tau}$:

$$Tq' = \frac{\tau}{2} \left[\frac{q(1-2q)(n-2)}{n-3+2q} + \frac{q(n-3)}{n-2} \right], \quad (69)$$

in which the normalizer T corresponds to (38), reflecting the rarity of S_i .

The expression for the change in frequency of S_i over one generation becomes

$$T\Delta q = \tau q \left[\frac{F - q}{1 - 3F + 2qF} - \frac{2n - 5 - 2q(n - 3)}{(n - 2)(1 - 3F + 2qF)} \right] + q(\tau - \tau^*) \left[(1 - 2q) + \frac{2q(q - F)}{1 - 3F + 2qF} \right]. \quad (70)$$

This expression describes the change in frequency of specificity S_i only before it becomes common and in the presence of its parent specificity; after that point, the recursion for common specificities (39) governs its evolution. A weighted average, which reduces to the rare specificity recursion (q_r) for small values of q and to the common specificity recursion (q_c) for q near F , approximates the transition between these two selective regimes:

$$\Delta q_w = \frac{(F - q)\Delta q_r + q\Delta q_c}{F}. \quad (71)$$

Substitution of (70) for q_r and (39) for q_c produces

$$T\Delta q_w = \tau q \left[\frac{(F - q)[F + 2q(1 - 3F)]}{2(1 - 3F + 2qF)(1 - 2F)} \right] + q(\tau - \tau^*) \left[(1 - 2q) + \frac{2q(q - F)}{1 - 3F + 2qF} \right]. \quad (72)$$

In both q_r and q_c , n represents the number of common specificities, a set which includes the focal specificity only when it is common (q_c) and not when it is rare (q_r). Assuming as before that terms involving $q(F - q)$ and the viability selection differential ($\tau - \tau^*$) are of the order of the inverse of the population size, the mean displacement coefficient for Model 2 becomes

$$\mu_2(x) = -x(x - F)a \left[\frac{F + 2q(1 - 3F)}{2(1 - 2F)} \right] - xu + x(1 - 2x)^2 \frac{D}{2N}. \quad (73)$$

Expression (46) gives the variance coefficient for this model.

4.2. Rate of origin of new specificities

Drift and diffusion coefficients (73) and (46) imply an invasion probability for a new specificity in the presence of its parent specificity of

$$v_2(x) = \frac{aF^2}{1 - 2F} - 2u. \quad (74)$$

Comparison of (52) and (74) confirms that antagonistic interactions between a new specificity and its parent discourage invasion.

Whether the invasion probability of a particular novel specificity (O) corresponds to (52) or (74) depends on the presence or absence of its immediate parent specificity (P) during the interval before it either jumps into the interior or becomes extinct. Consider the first common specificity to become extinct after the formation of O , while it remains in the

boundary layer between extinction and invasion. Under the assumption that the existence of O in very low frequency has negligible effect on the fate of P , the probability that it is P that becomes extinct is $1/n$; in this event, O invades with probability $v_1(x)$. Alternatively, with probability $(1 - 1/n)$ P persists in the population, implying an invasion probability of $v_2(x)$. Over the long-term, new specificities become common in the population at rate

$$\begin{aligned}\lambda &= 2Nu[v_1(x)/n + v_2(x)(1 - 1/n)] \\ &= 2NuF^2(3 - 5F)[(1 - F)(1 - 2F)^2] + o(u).\end{aligned}\quad (75)$$

Bifurcation of lineages entails the coexistence of a new specificity together with its parent. In the absence of antagonism between P and O , bifurcation occurs at rate $\lambda(1 - 1/n)$, declining in its presence to

$$\begin{aligned}\lambda(1 - r/n) &= 2Nuv_2(x)(1 - 1/n) \\ &= 2NuF^2/(1 - 2F)^2 + o(u).\end{aligned}\quad (76)$$

This expression implies that genealogy-dependent viability selection increases the probability of exclusion of P :

$$\begin{aligned}r &= \frac{v_1(x)}{v_1(x)/n + v_2(x)(1 - 1/n)} \\ &= \frac{2(1 - 2F)}{F(3 - 5F)} + O(u) > 1.\end{aligned}\quad (77)$$

Given the successful invasion of O , P is more likely to have been absent ($r > 1$ for $v_1(x) > v_2(x)$). Even though the existence of O has no effect on the unconditional probability of extinction of P , antagonism between O and P increases the probability of parental extinction conditional on O having invaded.

4.3. Determination of homozygosity

To determine the equilibrium number of common specificities maintained in the population, I set the rate of incorporation of newly derived specificities in the face of possible parental interference (75) equal to the rate of extinction of common specificities, obtained from (54). This formulation reflects that once the new specificity becomes common, the time since divergence from its parent follows the same distribution of divergence times as between any pair of common specificities. To order u , F is implicitly defined by

$$\begin{aligned}uF(3 - 5F)\sqrt{2N\pi d(F)(1 - F)} \\ \times (1 - 2F)^{[N/(1 - F) - 1]}L = 1,\end{aligned}\quad (78)$$

for

$$L = L_1(F)^{N/[(1 - F)(1 - 2F)]}L_2(F)L_3(F)^{N/(1 - F)}.$$

In the limit of negligible variation in viability among zygotes expressing two common specificities ($D=0$), this expression reduces to

$$uF(3-5F)\sqrt{2N\pi(1-F)(1-2F)}^{[N/(1-F)-1]} \times e^{2NF/[(1-F)(1-2F)]} = 1. \quad (79)$$

4.4. Scaling factor

Under genealogy-dependent viability selection, bifurcation of lineages occurs at rate $\lambda(1-r/n)$. With this modification, equating (27) and (28) produces

$$4Nf = \frac{n^2(n-1)}{\lambda(n-r)}, \quad (80)$$

$$f = \frac{1-2F}{8N^2uaF^4},$$

in which (78) determines F .

Expression (30), in which F is determined by the Yokoyama and Hetherington (1982) solution (15), gives the scaling factor for the Wright (1939) model ($r=1$; $D=0$). In Model 1, which incorporates variation in viability ($D>0$) but not parental exclusion ($r=1$), the scaling factor corresponds to (30), but with F determined by (60).

5. Variation in selection intensity

Expression of recessive deleterious mutations in regions cosegregating with the S -locus may induce a relationship between the time since divergence of a pair of specificities and the viability of the zygote formed from that pair. In a given zygote, mutations that arose prior to the divergence of the constituent haplotypes occur in homozygous form and those that arose subsequently in heterozygous form (Fig. 1). Viability declines as genealogical distance declines, reflecting greater proportions of mutations expressed in homozygous form.

I assign the viability of a zygote formed by the fusion of a random pair of common specificities as

$$\tau = 1 - s_1A - s_2B, \quad (81)$$

in which s_1 and s_2 denote selection coefficients representing reductions in viability due to the expression of deleterious mutations in heterozygous and homozygous form, respectively; A the number of deleterious mutations that arose in either lineage since their common ancestor; and B the number that arose before their divergence but after the most recent common ancestor (MRCA) of all specificities currently segregating in the population. Because all individuals in the population carry the mutations borne by the MRCA in homozygous form, those mutations do not affect relative fitness among zygotes. Parameter D , representing variation in viability selection (41), depends upon the distribution of coalescence times of random pairs of specificities.

For τ and τ^* viabilities of zygotes formed from random pairs of specificities, the expected square of the relative difference is close to but somewhat greater than the ratio of squares:

$$E\left[\left(\frac{\tau - \tau^*}{\tau}\right)^2\right] \approx \frac{E[(\tau - \tau^*)^2]}{E[\tau^2]}. \quad (82)$$

Because the numbers of mutations occurring in disjunct time periods are independent,

$$\begin{aligned} E[(\tau - \tau^*)^2] &= E\left[\{s_1(A - A^*) + s_2(B - B^*)\}^2\right] \\ &= 2\{s_1^2 \text{Var}[A] + s_2^2 \text{Var}[B]\}. \end{aligned} \quad (83)$$

The existence of the limiting diffusion requires that the square of the selection coefficients (s_1^2 and s_2^2) be of the order of the effect due to drift ($1/2N$). Because the expectation of τ^2 differs from unity by the square of the selection intensities,

$$\frac{D}{2N} = 2\{s_1^2 \text{Var}[A] + s_2^2 \text{Var}[B]\}. \quad (84)$$

Assumption of a Poisson distribution for mutation number given divergence time implies

$$\text{Var}[A] = 2\nu E[T_c] + (2\nu)^2 \text{Var}[T_c], \quad (85)$$

$$\text{Var}[B] = \nu E[T_2 - T_c] + \nu^2 \text{Var}[T_2 - T_c], \quad (86)$$

(see Hudson, 1990), in which ν denotes the per-haplotype rate of deleterious mutation, T_c the time since divergence of a random pair of specificities, and T_2 the time since the most recent common ancestor of all specificities segregating in the population (Fig. 2).

The focal pair of specificities coalesce in a given generation only if a lineage bifurcated and the specificities represent the two descendant lineages. For a pergeneration probability of coalescence of

$$P = \frac{\lambda(1 - r/n)}{\binom{n}{2}}, \quad (87)$$

the probability generating function (pgf) for the pairwise coalescence time (T_c) is

$$g(z) = \sum_{k=1}^{\infty} z^k Q^{(k-1)} P = \frac{zP}{P - (z-1)Q}, \quad (88)$$

in which P and Q sum to unity. This function yields

$$E[T_c] = \frac{n^2(n-1)}{2\lambda(n-r)} = 2Nf, \quad (89)$$

$$\text{Var}[T_c] = (2Nf)^2 - 1. \quad (90)$$

The expression for $E[T_c]$ confirms a well-known result, with f the scaling factor given by (80); the expression for $\text{Var}[T_c]$ reflects that the pgf incorporates a geometric distribution rather than the exponential distribution customarily used in coalescence theory (see Hudson, 1990).

Once the focal pair of specificities coalesce, the remaining time to the MRCA depends on the number of lineages remaining at that point. Fig. 3 depicts a genealogy among the n distinct $\mathcal{S}$ -specificities segregating in the population. State i corresponds to the section of the genealogy in which i ancestral lineages remain. The probability that the focal pair coalesce at the boundary between states i and $i-1$ is

$$\begin{aligned} \Pr[X = i] &= \frac{2}{i(i-1)} \prod_{j=i-1}^n \left[1 - \frac{2}{j(j-1)} \right] \\ &= \frac{2(n+1)}{i(i+1)(n-1)} = \frac{2(1+F)}{i(i+1)(1-F)}. \end{aligned} \quad (91)$$

Given coalescence at the boundary between states i and $i-1$; the remaining time to the MRCA ($T_2 - T_c$) corresponds to the sum of the lengths of the states from $i-1$ to 2.

Expression (28), with the rate of bifurcation $\lambda(1-1/n)$ replaced by $\lambda(1-r/n)$, provides the rate of termination of state j :

$$P_j = \frac{\lambda(n-r)j(j-1)}{n^2(n-1)} = \frac{j(j-1)}{4Nf} \quad (92)$$

(using (30)). The pgf for the length of state j corresponds to

$$h_j(z) = \sum_{k=1}^{\infty} z^k Q_j^{(k-1)} P_j = \frac{zP_j}{P_j - (z-1)Q_j}, \quad (93)$$

in which P_j and Q_j sum to unity. Independence among states permits formation of the pgf of the time between coalescence and the MRCA ($T_2 - T_c$) as the product over the states. Taking the expectation over the state of coalescence produces

$$h(z) = \sum_{i=2}^n \Pr[X = i] \prod_{j=2}^{i-1} h_j(z). \quad (94)$$

This pgf provides

$$E[T_2 - T_c] = 2Nf(1 - 2/n) = 2Nf(1 - 2F), \quad (95)$$

$$\begin{aligned} \text{Var}[T_2 - T_c] = (4Nf)^2 \frac{2(1+F)}{(1-F)} \sum_{i=3}^n \frac{1}{i(i+1)} \sum_{j=2}^{i-1} \frac{1}{j^2} \\ - E[T_2 - T_c] \{1 + E[T_2 - T_c]\}. \end{aligned} \quad (96)$$

The expression for $E[T_2 - T_c]$ confirms expectation from standard coalescence theory of the difference between the expected times to the MRCA of n lineages ($4N(1 - 1/n)$) and of a random pair of lineages ($2N$).

6. Discussion

Patterns observed in genealogies of S -alleles derived from natural populations motivated this exploration of variation in viability among S -locus genotypes and allele-specific load. Low rates of crossing-over between haplotypes encoding distinct S -specificities may permit the accumulation of recessive deleterious mutations at sites linked to the S -locus. Under full expression of GSI, mutations restricted to a single specificity class never occur in homozygous form. Screening of the effects of homozygous expression of such mutations is postponed until the formation of zygotes comprising haplotypes encoding distinct specificities that descend from the same ancestral specificity. The models introduced here address the effects of variation in viability among zygotes and greater antagonism between more closely related haplotypes on the number of S -alleles maintained in a population and their genealogical relationships. Numerical simulation studies designed to test the analytical results derived from these models are currently underway.

6.1. Variation in zygote viability

Variation in viability among S -locus genotypes, independent of genealogical relationships among alleles, tends to reduce the invasion probability of new specificities. In order to distinguish the effects of variation itself from those due to allele-specific load, I first studied Model 1, in which zygote viability is independent of genealogical relationship between constituent alleles.

Results confirm that variation in viability reduces the number of S -alleles maintained in population (60). This reduction in allele number increases the probability of invasion of new specificities (53). Consequently, variation in viability decreases the period over which a given specificity is common within the population.

6.2. Genealogy-dependent selection

Genealogy-dependent viability selection denotes a positive association between viability of a given zygote and the time since divergence of its constituent haplotypes. S -allele-specific load may contribute to such associations. In a given zygote, mutations that arose after the divergence of the constituent haplotypes occur in heterozygous form, while those that arose

prior to divergence occur in homozygous form. Model 2 addresses the effects of S -allele-specific load by expressing the distribution of viabilities in terms of the distribution of coalescence times between specificities.

Immediately after the appearance of novel specificity (O); before it rises to common frequencies or becomes extinct, the time since divergence from its immediate parent specificity (P) is negligible relative to divergence times among common S -alleles. The presence of P decreases the probability of invasion of O , implying that antagonistic interactions between closely related specificities reduces the rate of bifurcation of S -allele lineages (77). In contrast, the presence of O in very low frequencies is assumed to have no effect on the probability or rate of extinction of P . If P becomes extinct soon after giving rise to O , O is more likely to invade. Over the long-term, the evolutionary dynamics of new specificities reflect a mixture of the two cases, corresponding to the early extinction or persistence of the immediate parental specificity.

6.3. Empirical observations

Model 2 suggests that reductions in viability due to S -allele-specific load are of the order of the product of the square of selection coefficients associated with heterozygous (s_1) and homozygous (s_2) expression of deleterious mutations, the per-haplotype rate of deleterious mutation (ν), and coalescence times among common specificities (see (84) and (86)). Available empirical information is consistent with substantial reductions of this kind. For example, the cosegregation of the S -locus with genomic tracts of considerable size (Boyes et al., 1997; McCubbin and Kao, 1999) suggests high perhaplotype rates of mutation. Further, analyses of S -allele genealogies indicate coalescence times between specificities of the order of tens of millions of years (Ioerger et al., 1990; Dwyer et al., 1991; Uyenoyama, 1995).

Genealogy-dependent viability selection may increase variation in allele frequency (D in (46) and (73)) and reduce both the number of common S -alleles maintained in population (78) and the rate of bifurcation of S -allele lineages (77). The S -allele genealogy of *Solanum carolinense*, which shows the greatest deviations from expectation based on GSI selection, exhibits an apparent reduction in the rate of bifurcation of lineages (Uyenoyama, 1997). Further, this species maintains the smallest number of S -alleles known (Lawrence, 2000).

6.4. Other factors affecting evolutionary dynamics

Both the number of segregating S -specificities and their genealogical relationships to one other depend critically on the mechanism through which new specificities arise. While the Wright model and the extensions considered here portray the origin of a new specificity as a single mutational event, recent experimental studies suggest passage through intermediate states, possibly with altered SI expression (Matton et al., 1999).

That the determinants of pistil and pollen specificity are genetically and physiologically distinct (Golz et al., 2000; Nasrallah et al., 2000) itself suggests that the formation of a new S -specificity requires at least two mutations. Genetic conflicts between the evolutionary interests of the genes that control pistil and pollen function are expected to arise, even though absolute linkage consigns them to a common fate (Uyenoyama and Newbigin, 2000; Uyenoyama et al., 2001). Pollen that express a novel specificity would induce the rejection

reaction in few pistils, promoting the partial breakdown of SI and the appearance of nonreciprocal pollen exclusion among genotypes. Mutations in the pistil gene that restore reciprocal incompatibility by permitting recognition of the new pollen specificity would be favored. The introduction of a new specificity through this evolutionary pathway almost always entails the replacement of the ancestral specificity by the single mutant, expressing the new pollen specificity alone, and of this intermediate by the double-mutant, expressing a new, full-function specificity (Uyenoyama et al., 2001). *S*-allele turnover through this mechanism would rarely permit bifurcation of lineages within populations, with population structure perhaps determining the rate and pattern of branching in *S*-allele genealogies.

Observation of shared characteristics in patterns of *S*-allele diversity, including exceedingly high numbers of specificities and long terminal branches in gene genealogies, suggests the operation of shared processes. Accumulation of recessive deleterious mutations in regions tightly linked to genes that determine specificity represents a general process likely operating across evolutionarily independent SI systems.

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References

- Anderson MA, Cornish EC, Mau S-L, Williams EG, Hoggart R, et al., 1986 Cloning of cDNA for a stylar glycoprotein associated with expression of self-incompatibility in (*Nicotiana alata*). *Nature* 321, 44–48.
- Boyes DC, Nasrallah ME, Vrebalov J, Nasrallah JB, 1997 The self-incompatibility (S) haplotypes of Brassica contain highly divergent and rearranged sequences of ancient origin. *Plant Cell* 9, 237–247. [PubMed: 9061954]
- Dwyer KG, Balent MA, Nasrallah JB, Nasrallah ME, 1991 DNA sequences of self-incompatibility genes from *Brassica campestris* and *B. oleracea*: polymorphism predating speciation. *Plant Mol. Biol* 16, 481–486. [PubMed: 1893115]
- Emerson S, 1938 The genetics of self-incompatibility in *Oenothera organensis*. *Genetics* 23, 190–202. [PubMed: 17246880]
- Ewens WJ, 1964 On the problem of self-sterility alleles. *Genetics* 50, 1433–1438. [PubMed: 14239799]
- Fisher RA, 1958 *The Genetical Theory of Natural Selection*, 2nd Revised Edition. Dover, New York.
- Gillespie J, 1983 Some properties of finite populations experiencing strong selection and weak mutation. *Amer. Nat* 121, 691–708.
- Gillespie J, 1994 Substitution processes in molecular evolution. II. Exchangeable models from population genetics. *Evolution* 48, 1101–1113. [PubMed: 28564487]
- Golz JF, Clarke AE, Newbigin E, 2000 Mutational approaches to the study of self-incompatibility: revisiting the pollen-part mutants. *Ann. Bot* 85 (Suppl. A), 95–103.
- Hey J, 1992 Using phylogenetic trees to study speciation and extinction. *Evolution* 46, 627–640. [PubMed: 28568659]
- Hudson RR, 1990 Gene genealogies and the coalescent process. In: Futuyma D, Antonovics J (Eds.), *Oxford Surveys in Evolutionary Biology*, Vol. 7 Oxford University Press, New York, pp. 1–44.
- Ioerger TR, Clark AG, Kao T.-h., 1990 Polymorphism at the self-incompatibility locus in Solanaceae predates speciation. *Proc. Natl Acad. Sci. USA* 87, 9732–9735. [PubMed: 2263623]
- Karlin S, Levikson B, 1974 Temporal fluctuations in selection intensities: case of small population size. *Theor. Popul. Biol* 6, 383–412.

- Karlin S, Taylor HM, 1981 A Second Course in Stochastic Processes Academic Press, New York.
- Kimura M, Crow JF, 1964 The number of alleles that can be maintained in a finite population. *Genetics* 49, 725–738. [PubMed: 14156929]
- Lawrence MJ, 2000 Population genetics of the homomorphic self- incompatibility polymorphisms in flowering plants. *Ann. Bot* 85 (Suppl. A), 221–226.
- Lawrence MJ, Franklin-Tong VE, 1994 The population genetics of the self-incompatibility polymorphism in *Papaver rhoeas*. IX. Evidence of an extra effect of selection acting on the *S*-locus. *Heredity* 72, 353–364.
- Matton DP, Luu DT, Xike Q, Laublin G, O'Brien M, et al., 1999 Production of an S RNase with dual specificity suggests a novel hypothesis for the generation of new S alleles. *Plant Cell* 11, 2087–2097. [PubMed: 10559436]
- McCubbin AG, Kao T.-h., 1999 The emerging complexity of self-incompatibility (*S*-) loci. *Sex. Plant Reprod* 12, 1–5.
- McCubbin AG, Wang X, Kao T.-h., 2000 Identification of self- incompatibility (*S*-) locus linked pollen cDNA markers in *Petunia inflata*. *Genome* 43, 619–627. [PubMed: 10984173]
- Muirhead CA, 2001 Consequences of population structure on genes under balancing selection. *Evolution* 55, 1532–1541. [PubMed: 11580013]
- Nasrallah JB, 2000 Cell-cell signaling in the self-incompatibility response. *Curr. Opin. Plant Biol* 3, 368–373. [PubMed: 11019803]
- Nasrallah JB, Kao T.-h., Chen C-H, Goldberg ML, Nasrallah ME, 1985 A cDNA clone encoding an *S*-locus-specific glycoprotein from *Brassica oleracea*. *Nature* 326, 617–619.
- Nasrallah ME, Kandasamy MK, Chang M-C, Stadler Z, Lim S, et al., 2000 Identifying genes for pollen-stigma recognition in crucifers. *Ann. Bot* 85 (Suppl. A), 125–132.
- de Nettancourt D, 1977 Incompatibility in Angiosperms Springer, Berlin.
- Olver FWJ, 1974 Asymptotics and Special Functions Academic Press, New York.
- Richman AD, Kohn JR, 1999 Self-incompatibility alleles from *Physalis*: implications for historical inference from balanced genetic polymorphisms. *Proc. Natl Acad. Sci. USA* 96, 168–172. [PubMed: 9874790]
- Sasaki A, 1989 Evolution of pathogen strategies Ph.D. Thesis, Kyushu University, Kyushu, Japan.
- Sasaki A, 1992 The evolution of host and pathogen genes under epidemiological interaction. In: Takahata N (Ed.), *Population Paleo-Genetics Japan Scientific Societies Press, Tokyo*, pp. 247–263.
- Schierup MH, Vekemans X, Christiansen FB, 1998 Allelic genealogies in sporophytic self-incompatibility systems in plants. *Genetics* 150, 1187–1198. [PubMed: 9799270]
- Slatkin M, Muirhead CA, 1999 Overdominant alleles in a population of variable size. *Genetics* 152, 775–781. [PubMed: 10353917]
- Suzuki G, Taki N, Hirose T, Fukui K, Nishio T, et al., 1999 Genomic organization of the S locus: identification and characterization of genes in SLG=SRK region of S9 haplotype of *Brassica campestris* (syn. *rapa*). *Genetics* 153, 391–400. [PubMed: 10471721]
- Takahata N, 1990 A simple genealogical structure of strongly balanced allelic lines and trans-species evolution of polymorphism. *Proc. Natl Acad. Sci. USA* 87, 2419–2423. [PubMed: 2320564]
- Takahata N, Satta Y, Klein J, 1992 Polymorphism and balancing selection at major histocompatibility complex loci. *Genetics* 130, 925–938. [PubMed: 1582567]
- Uyenoyama MK, 1995 A generalized least-squares estimate for the origin of sporophytic self-incompatibility. *Genetics* 139, 975–992. [PubMed: 7713446]
- Uyenoyama MK, 1997 Genealogical structure among alleles regulating self-incompatibility in natural populations of flowering plants. *Genetics* 147, 1389–1400. [PubMed: 9383079]
- Uyenoyama MK, 2000 The evolution of breeding systems. In: Singh RS, Krimbas C (Eds.), *Evolutionary Genetics from Molecules to Morphology Cambridge University Press, New York*, pp. 300–316.
- Uyenoyama MK, Newbigin E, 2000 Evolutionary dynamics of dual-specificity self-incompatibility alleles. *Plant Cell* 12, 310–312. [PubMed: 10715317]

- Uyenoyama MK, Takebayashi N, 2003 Genus-specific diversification of mating types. In: Singh RS, Uyenoyama MK (Eds.), *The Evolution of Population Biology* Cambridge University Press, New York (Chapter 13).
- Uyenoyama MK, Zhang Y, Newbigin E, 2001 On the origin of self-incompatibility haplotypes: transition through self-compatible intermediates. *Genetics* 157, 1805–1817. [PubMed: 11290732]
- Vekemans X, Slatkin M, 1994 Gene and allelic genealogies at a gametophytic self-incompatibility locus. *Genetics* 137, 1157–1165. [PubMed: 7982569]
- Wright S, 1939 The distribution of self-sterility alleles in populations. *Genetics* 24, 538–552. [PubMed: 17246937]
- Wright S, 1960 On the number of self-incompatibility alleles maintained in equilibrium by a given mutation rate in a population of a given size: a reexamination. *Biometrics* 16, 61–85.
- Wright S, 1964 The distribution of self-incompatibility alleles in populations. *Evolution* 18, 609–619.
- Wright S, 1969 *Evolution and the Genetics of Populations, Volume 2: The Theory of Gene Frequencies* University of Chicago Press, Chicago.
- Yokoyama S, Hetherington LE, 1982 The expected number of self- incompatibility alleles in finite plant populations. *Heredity* 48, 299–303.
- Yokoyama S, Nei M, 1979 Population dynamics of sex-determining alleles in honey bees and self-incompatibility alleles in plants. *Genetics* 91, 609–626. [PubMed: 17248901]

Fig. 1.

Deleterious mutations in a region flanking the S -locus mapped on the allelic genealogy of S -specificities S_1 , S_2 , and S_3 : Zygotes constituted from less closely related haplotypes bear fewer mutations in homozygous form: 1 mutation in homozygous form and 3 mutations in heterozygous form for $S_1=S_2$; and 1 homozygous and 4 heterozygous for $S_1=S_3$. Specificities S_2 and S_3 , which diverged from their common ancestor more recently, share 2 mutations.

Fig. 2.

Times to coalescence between S_1 and S_2 (T_c) and among all n S-specificities currently segregating in the population (T_2). Mutations that appeared in specificities S_1 or S_2 since their divergence occur in heterozygous form in S_1S_2 zygotes, while those that appeared before divergence occur in homozygous form.

Fig. 3. Genealogy traced backward in time from the n distinct $\mathcal{S}$ -specificities currently segregating in the population. State j corresponds to the interval in which the current n lineages have j ancestral lineages.