Speciation by Natural and Sexual Selection: Models and Experiments

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ABSTRACT: A large number of mathematical models have been developed that show how natural and sexual selection can cause prezygotic isolation to evolve. This article attempts to unify this literature by identifying five major elements that determine the outcome of speciation caused by selection: a form of disruptive selection, a form of isolating mechanism (assortment or a mating preference), a way to transmit the force of disruptive selection to the isolating mechanism (direct selection or indirect selection), a genetic basis for increased isolation (a one- or two-allele mechanism), and an initial condition (high or low initial divergence). We show that the geographical context of speciation (allopatry vs. sympatry) can be viewed as a form of assortative mating. These five elements appear to operate largely independently of each other and can be used to make generalizations about when speciation is most likely to happen. This provides a framework for interpreting results from laboratory experiments, which are found to agree generally with theoretical predictions about conditions that are favorable to the evolution of prezygotic isolation.

Keywords: sympatric speciation, allopatric speciation, parapatric speciation, reinforcement, mating preferences, assortative mating.

If you thumb through a text on evolutionary biology, you will fall into a comfortable rhythm. A dramatic example of adaptation such as melanism in the peppered moth is followed by an explanation of how advantageous mutations spread in populations. A plot showing the correlation between protein sequence divergence and the time since the most recent common ancestor is followed by a discussion of the neutral theory and other hypotheses for the molecular clock. And on it goes, each evolutionary phenomenon followed by theory that explains it.

The rhythm falters, though, when you come to speciation. This section typically opens with a spectacular example, like the African cichlids, but the follow-up explanation strangely lacks the vocabulary of population genetics. In fact, most discussions of speciation are framed entirely in terms of concepts that Darwin would have been comfortable with: the distinctions between allopatry and sympatry, between pre- and postmating barriers, and so on.

Two reasons are typically given for why we still lack a coherent understanding of speciation in terms of population genetic principles. First, speciation occurs on a time scale that is typically too long to observe directly. Second, it involves interactions between a host of evolutionary factors (spatial structure, nonrandom mating, epistasis, etc.), each of which is difficult enough to understand in isolation.

There is, however, a third reason: theoreticians have balkanized the subject of speciation. Over the last 25 years, about 100 mathematical models for the evolution of prezygotic isolation by selection have been published. Each focuses on a highly specific scenario, for example, sympatric speciation with habitat-specific mating and a female mating preference acting on a male display trait. Further, the great majority of the models are analyzed by simulation, which forces investigators to make a large number of restrictive assumptions that obscure the generalities and relations with other models. While this research program has been critically important for proving what is possible, it does not offer much hope of producing a unified theory to think about and test generalities about speciation.

As much as we would like to fill that lacuna in this article, our goals are more modest. We begin by proposing a list of five elements that can be used to classify all known mechanisms for how natural and sexual selection cause speciation. We illustrate this scheme by using it to organize every published model of speciation by selection that we could find in the literature. By reviewing the theory in this way, we hope to draw attention to the common features

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of existing models. (We also hope to save future workers from duplicating previous efforts; there is a tendency in this field to reinvent, and republish, earlier models.) We then review the experimental literature on speciation to see how those data relate to generalizations from the theory.

This article restricts itself to the evolution of prezygotic isolation. Prezygotic isolation is by far the most critical factor keeping populations separate. Cases where species remain distinct only because of postzygotic isolation are extremely rare, if they exist at all. Postzygotic mechanisms are important for other reasons, of course; they strengthen isolation between some populations, they can provide the motor that can drive evolution of prezygotic isolation, and they give insights into the genetics of population divergence. Theoretical and empirical studies of postzygotic isolation are advancing rapidly, and interested readers should consult the recent reviews on the subject (Wu and Palopoli 1994; Coyne and Orr 1997; Werren 1997; Ramsey and Schemske 1998; Turelli and Orr 2000). A second constraint on the scope of this article is that it deals only with speciation by selection and neglects entirely mechanisms that involve drift (see, e.g., Templeton 1981). The reason is simply one of convenience; there are enough models involving only selection to fill a review.

To assess the roles that different factors play, we need a yardstick of progress toward speciation. Here, we will use linkage disequilibrium as a metric. This is a continuous and quantitative measure of the amount of genetic mixing, as we describe in the next section. Where along the continuum of disequilibria we should draw the line between one and two species is a theological question from which we steer clear.

Five Elements of Speciation by Selection

There are any number of ways that one can organize a discussion of how prezygotic isolation evolves. The geographical context (allopatry vs. sympatry) has traditionally been emphasized, but one could instead organize the discussion around the effects of behavioral mechanisms, say, or the number of loci that affect the traits. What would be most useful is a framework that breaks mechanisms of speciation into a small number of fundamental elements. This way, we can consider the effect of each element and the interactions between them.

In this section, we propose a scheme that deconstructs speciation into five elements. They are relatively independent of one another, so the effects of each on speciation can be understood largely in isolation of the others. To show how existing models relate to these elements, we reviewed every published model of speciation we were able to find in the literature and classified them according to our five elements. The results are shown in table 1. The following subsections discuss each of the elements in turn.

Element 1: A Source of Disruptive Selection

Speciation is the fission of a gene pool. In most hypotheses, the rupture is caused by some kind of disruptive selection that causes the evolution of isolating mechanisms, either directly or indirectly. By "disruptive selection," we mean a deterministic force that generates linkage disequilibrium.

Several kinds of disruptive selection can lead to speciation (table 1, sec. I). Perhaps the simplest is spatial variation in fitness, as emphasized by proponents of allopatric speciation (Mayr 1963). A second way to generate persistent disruptive selection is frequency dependence, as when population densities are independently regulated in different niches (Levene 1953). The term "tension zone" is used to describe this situation when individuals occupying the different niches are separated in space and meet in a hybrid zone (Barton and Hewitt 1985). Competition between similar phenotypes can also produce persistent disruptive selection through frequency dependence. This idea, which has been popular in recent models of speciation (e.g., Dieckmann and Doebeli 1999; Kondrashov and Kondrashov 1999), descends from an argument made by Darwin (1859, chap. 4) that was put into graphical form by Rosenzweig (1978). Here, intermediate phenotypes compete against a large fraction of the population, while extreme phenotypes have fewer competitors and therefore higher fitness.

Models of speciation typically treat spatial variation in fitness and frequency-dependent selection within a locality as different mechanisms for producing disruptive selection. They play the same role, however, and it is not clear that anything is gained by distinguishing between them in this context.

Sexual selection is another source of disruptive selection. (In this article, we use "sexual selection" in a broad sense to mean any kind of nonrandom mating.) If individuals with similar body sizes tend to mate with each other, for example, linkage disequilibrium naturally develops between the loci that contribute to variation in body size. Likewise, when females express mating preferences for different values of a trait expressed in males, linkage disequilibrium develops between the preference and trait loci (O'Donald 1979; Lande 1981; Kirkpatrick 1982).

Sexual selection has fundamentally different consequences for speciation than does natural selection. Sexual selection is more effective in generating disequilibria and hence new species. The reason is that recombination frustrates natural selection by breaking apart favorable combinations of alleles. Nonrandom mating, however, brings together alleles at different loci, which allows recombi-

Table 1: Models of speciation classified by five major elements

	References[a]
I. A form of disruptive selection:	
A. Fitnesses vary in space	1, 3–7, 9, 12, 13, 21, 22, 25, 26, 34, 38, 49, 51–53, 55
B. Frequency-dependent natural selection:	
1. Two niches with independent density regulation	10, 12, 14, 15, 20, 25–30, 32, 37, 44, 45, 60
2. Tension zone	23, 25, 26, 37, 48
3. Competition within a niche	2, 8, 11, 12, 14–16, 25–30, 32, 39, 41, 43, 45, 46, 50, 60, 61
C. Sexual selection	2, 11, 17, 18, 24–26, 31, 33, 35, 38–40, 42, 48, 54, 56–59, 62
II. A prezygotic isolating mechanism:	
A. Mating preferences	16–18, 23, 24, 26, 30, 31, 33, 34–36, 40, 42, 43, 48–52, 54, 56–59, 61, 62
B. Assortment traits (including geographical isolation)	1, 3–9, 11–15, 20–22, 25, 27–29, 31, 32, 37–39, 41, 45, 47, 48, 50, 51, 53, 55, 60
C. A geographical setting:	
1. Allopatry	18, 24, 33, 35, 42, 49
2. Parapatry	1, 3–7, 12, 13, 21–23, 25, 26, 34, 36, 38, 40, 47, 51–53, 55
3. Sympatry	2, 6, 8–12, 14–17, 20, 25–32, 37,39, 41, 43–46, 48, 50, 54, 56–62
III. Transmitting the force of selection to the isolating mechanism:	
A. Direct selection	5, 6, 11, 20, 25, 27, 28, 31, 32, 37–39, 45, 48–50, 53–57
B. Indirect selection	1, 3–10, 12–18, 20–23, 25, 26, 28–30, 33, 34–37, 40, 42, 43, 47, 50–53, 55, 58–62
IV. A genetic basis for increased isolation:	
A. One-allele mechanisms	1, 3, 6, 8, 10, 12–15, 21–23, 29, 37, 47, 50, 51
B. Two-allele mechanisms	4, 5, 7, 9, 11, 13, 16–19, 21, 22, 24–33, 34–40, 42, 43, 45, 48–62
V. An initial condition:	
A. Divergence initially low	2, 8, 10–12, 14–17, 20, 28–32, 37, 39, 41, 43, 45, 50, 58–62
B. Divergence initially large (including geographical isolation)	1, 3–7, 9, 12, 13, 18, 21–27, 29, 31, 33, 34–36, 38, 40, 42, 47–49, 51–57, 61

[a] Numbers correspond to references as follows: (1) Balkau and Feldman 1973, (2) Bernstein et al. 1985, (3) Cain et al. 1999, (4) Caisse and Antonovics 1978, (5) Crosby 1970, (6) de Meeûs et al. 1993, (7) Dickinson and Antonovics 1973, (8) Dieckmann and Doebeli 1999, (9) Diehl and Bush 1989, (10) Doebeli 1996, (11) Drossel and McKane 2000, (12) Endler 1977, (13) Felsenstein 1981, (14) Fialkowski 1988, (15) Fialkowski 1992, (16) Gibbons 1979, (17) Higashi et al. 1999, (18) Iwasa and Pomiankowski 1995, (19) Johnson and Wade 1996, (20) Johnson et al. 1996, (21) Kawecki 1996, (22) Kawecki 1997, (23) Kelly and Noor 1996, (24) Kiester et al. 1984, (25) Kirkpatrick 2000, (26) Kirkpatrick and Servedio 1999, (27) Kondrashov 1983*a*, (28) Kondrashov 1983*b*, (29) Kondrashov 1986, (30) Kondrashov and Kondrashov 1999, (31) Kondrashov and Shpak 1998, (32) Kondrashov et al. 1998, (33) Lande 1981, (34) Lande 1982, (35) Lande and Kirkpatrick 1988, (36) Liou and Price 1994, (37) Maynard Smith 1966, (38) Moore 1981, (39) Noest 1997, (40) Payne and Krakauer 1997, (41) Pimm 1979, (42) Pomiankowski and Iwasa 1998, (43) Ramadevan and Deakin 1990, (44) Rausher 1984, (45) Rice 1984, (46) Rosenzweig 1978, (47) Sanderson 1989, (48) Sawyer and Hartl 1981, (49) Schluter and Price 1993, (50) Seger 1985, (51) Servedio 2000, (52) Servedio and Kirkpatrick 1997, (53) Slatkin 1982, (54) Spencer et al. 1986, (55) Stam 1982, (56) Sved 1981*a*, (57) Sved 1981*b*, (58) Takimoto et al. 2000, (59) Turner and Burrows 1995, (60) Udovic 1980, (61) van Doorn et al. 1998, (62) Wu 1985.

nation to unite them in a single gamete. Recombination therefore helps to generate, rather than break down, the disequilibria favored by nonrandom mating.

We can illustrate this point with a toy model of speciation that has two unlinked loci. It is a "toy" because it is so simplified that it cannot capture most of the five elements of speciation, but it is useful to make some basic observations. Imagine that the two loci contribute equally to a trait that causes assortative mating and that is also the target of disruptive natural selection. Each locus has two alleles, and each allele has a frequency of one-half.

Progress toward speciation is measured by the linkage

disequilibrium, D, between the two loci among zygotes. In a random mating population with no natural selection, D evolves to a value of 0. At the other extreme, a value of D of one-fourth represents two populations that are completely reproductively isolated. (For those who would prefer to think about a single diploid locus rather than two haploid loci, the analog of D there is the homozygote excess, which also ranges from 0 to one-fourth. In fact, what follows translates to a single diploid locus in which the recombination rate between the maternally and the paternally inherited alleles is 1.)

This model allows us to experiment with the effects of natural and sexual selection on speciation. Sexual selection takes the form here of assortative mating, whose intensity is measured by the parameter A. A value of $A = 0$ corresponds to random mating, while $A = 1$ implies only individuals with the same phenotype mate. In the toy model, A is assumed to be fixed and so cannot evolve. The strength of disruptive natural selection is measured by S, where $S = 0$ reflects equal survival of all genotypes and $S = 1$ means that intermediate individuals never survive. The appendix describes our assumptions about mating and natural selection in more detail and gives the equation for how D evolves.

The consequences of assortative mating and disruptive natural selection are shown in figure 1. With free recombination, even complete lethality of the intermediate genotypes gets a population only halfway to speciation: the maximum for D is one-eighth. But with sufficiently strong assortative mating, complete reproductive isolation is possible: the theoretical limit of one-fourth for D can be reached. The upshot is that nonrandom mating (or sexual selection, broadly construed) is more powerful than natural selection in causing a gene pool to fission. A second point is that speciation does not require the spread of new genes. With strong assortative mating, for example, disequilibrium will rapidly build up in a population that initially has none. (This corresponds to a trajectory running up the right side of the top panel in fig. 1.) One could imagine that happening when a change in environmental conditions suddenly increases the accuracy with which individuals choose their mates (van Doorn et al. 1998).

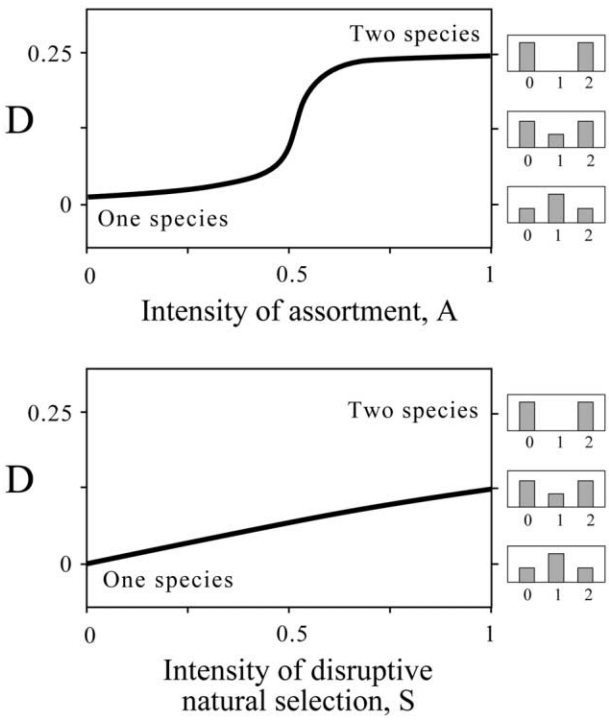

Figure 1: Comparison of the efficacy of assortative mating versus disruptive natural selection in generating linkage disequilibrium D according to the model described in the appendix. Insets at the right show the distribution of phenotypes corresponding to different values of D. *Top*, equilibrium for D under different strengths of assortment A, with $S = 0.1$. *Bottom*, equilibrium for D under different strengths of disruptive selection for $A = 0$.

Element 2: A Prezygotic Isolating Mechanism

Prezygotic isolating mechanisms can be grouped according to whether they depend on assortative mating or on a mating preference (table 1, sec. II). We say that assortative mating occurs when there is a correlation between the phenotypes of mating individuals with respect to a single trait expressed in both sexes. Many animals mate assortatively based on body size, and many plants mate on the basis of pollinators (which they influence through flower morphology, phenology, etc.). Populations of both animals and plants are often reproductively isolated by habitat choice and the time of year (and even the time of day) that they mate. Phenotypic variation in these kinds of traits typically generates assortative mating as an automatic by-product. Assortative mating therefore works in many situations where there is no way for individuals actively to compare their phenotypes.

Isolation in some animals is produced by mating preferences expressed in one sex (typically females) that act on display traits expressed in the other (typically males). A variation on this theme is found in flowering plants that are pollinated by animals. A plant's "mating preference" in this case is in effect expressed in an entirely different species, the pollinator.

Here again there is the opportunity to unify models of speciation. Assortment and mating preferences can be treated as a single form of prezygotic isolation by regarding

assortment as the special case where a mating preference acts on itself.

The Geographical Setting

One of Mayr's great legacies for our understanding of speciation was his emphasis on the importance of biogeography (Mayr 1963; see Coyne 1994). As a result, the geographical context of speciation—the allopatry versus parapatry versus sympatry continuum—is traditionally viewed as the most important factor in speciation (table 1, sec. II.C).

Our list of fundamental elements for speciation can be simplified, however, if we view geography as simply another form of assortative mating. Consider geography as a genetic locus. Each geographical location then represents a different allele. Migration is replaced by a form of frequency-dependent mutation at the geography locus; movement between populations is equivalent to mutation of both alleles at the geography locus. That locus enforces the most extreme form of assortative mating since only individuals that carry the same allele at the geography locus are allowed to mate.

The evolutionary dynamics of a population with this form of assortative mating are exactly equivalent to those of a geographically structured population. Although this equivalence may at first seem obscure, it is useful for three reasons. First, it shows that we can simplify thinking about speciation by treating geography as just one more type of assortative mating; geography does not need to be modeled separately. Second, allopatry and sympatry do not need to be treated as qualitatively distinct situations. Third, the correspondence between geography and assortment helps make clear why allopatric speciation is so powerful and so prevalent: it is an exceedingly accurate form of assortative mating. Very few other types of assortative mating guarantee that only individuals carrying the same allele at a single locus will mate together. Combining this with ubiquitous spatial variation in selection produces a potent engine for generating new species. It may well be critical to the great majority of speciation events, as argued by Mayr (1963).

Element 3: A Way to Transmit the Disruptive Selection to the Isolating Mechanism

Disruptive selection will only cause speciation if its force is somehow transmitted to the genes causing prezygotic isolation. There are two broad categories of mechanisms that can do the job: direct selection and indirect selection (table 1, sec. III).

We say that direct selection operates on a mating preference or assortment trait if the genes that influence that character also directly affect survival or fecundity (Kirkpatrick and Ryan 1991). Direct selection has probably caused the evolution of prezygotic isolation in many flowering plants. Populations of monkeyflowers (*Mimulus*) that have invaded serpentine soils flower earlier in the season than those on other soils. Serpentine soils dry out early in the year, and natural selection may have favored early flowering as an adaptation to ensure that the plants reproduce before they senesce (Macnair and Gardner 1998). Thus, direct natural selection acting on phenology may have caused reproductive isolation from later-flowering populations that live on other soils as a side effect.

The most compelling proposals for how sympatric speciation might happen also depend on direct selection. Many herbivorous insects and parasites mate on their hosts. Ecological pressures to expand the range of acceptable hosts act as a form of direct selection on a trait (habitat preference) that produces isolation pleiotropically (Bush 1975; Rice 1987). Sexual selection as well as natural selection can generate direct selection on assortment traits. (That is not possible with mating preferences since they are a cause but not a target of sexual selection.) Some forms of assortment give a mating advantage to extreme phenotypes. In theory, that alone can be enough to cause one population to fission into two (Kondrashov and Shpak 1998).

Indirect selection is the second broad category of mechanisms that transmit the force of disruptive selection to the prezygotic isolating mechanism. It occurs when the genes that affect the isolating mechanism are genetically correlated (in linkage disequilibrium) with the genes that are the direct target of natural or sexual selection.

The most celebrated example of indirect selection in speciation is reinforcement (Dobzhansky 1940). Indirect selection is responsible for reinforcement since it is driven by selection on maladaptive gene combinations that interfere with development and fertility, not selection acting directly on the genes that affect mating preferences. (The distinction between direct and indirect selection breaks down, however, when there is complete postzygotic isolation; the two modes become identical.) The correlation between the hybrid incompatibility genes and the preference genes is caused by hybridization itself, which introduces sets of alleles from each species (see Kirkpatrick and Servedio 1999).

Indirect selection can be driven by natural selection, acting, for example, on the low viability of hybrids. It can also result from sexual selection. Reinforcement can also happen when hybrid offspring are perfectly viable but have low mating success (Coyne and Orr 1998; Kirkpatrick and Servedio 1999). Sympatric speciation can occur by the same mechanism, at least in principle. Models have shown that if females within a population prefer very different

kinds of males, that can generate disruptive selection on a display trait and generate disequilibrium between the preference loci themselves. If variation in mating preferences is extremely large, a single population can split into two reproductively isolated groups (Wu 1985; Turner and Burrows 1995; Higashi et al. 1999; Kondrashov and Kondrashov 1999; Takimoto et al. 2000). Aside from the question of how likely these conditions might be in nature, a problem for this idea is that without ecological divergence, competition will drive one or the other of the new species to extinction (Kondrashov et al. 1998).

All else equal, direct selection is more efficient than indirect selection. The reason is simple: the force of indirect selection is transmitted to the genes causing prezygotic isolation via linkage disequilibrium, which acts something like a car clutch that is slipping. The impact of selection is mitigated by the imperfect genetic correlation between these two sets of genes. This theoretical observation is the basis for suggestion that direct selection may often be more important than indirect selection in the evolution of mating preferences within species (Kirkpatrick 1987; Kirkpatrick and Ryan 1991; Kirkpatrick and Barton 1997). Hybridizing species, however, might be an important exception. Here, selection can be particularly intense, and the linkage disequilibria can be large. Reinforcement is therefore exactly the situation where indirect selection is expected to be most powerful.

Element 4: A Genetic Basis for Increased Isolation

Felsenstein (1981) identified a fundamental distinction that determines how prezygotic isolation evolves, what he termed the one-allele/two-allele dichotomy (table 1, sec. IV). In two-allele mechanisms, isolation is strengthened when two different alleles spread in the two nascent species. Most scenarios for the evolution of prezygotic isolation fall in this category. One example is the evolution of different mating preferences in two populations. A second is when two plant populations become isolated because an allele for early flowering is fixed on one and an allele for late flowering is fixed in the other. Thus, two-allele mechanisms can work with both mating preferences and assortment.

In one-allele mechanisms, by contrast, isolation increases when the same allele is fixed in both populations. The spread of a mutation that increases philopatry is one example. A second is an allele that decreases the length of the flowering season in a plant. If populations already differ in their mean flowering date, then the new allele will decrease the amount of overlap and so decrease the amount of gene flow between them. A third example is the spread of a gene that causes animals of similar size to mate with each other.

These three examples illustrate the important point that one-allele mechanisms require that there already be differentiation based on some sort of two-allele mechanism. A gene that increases the number of matings between individuals of similar size contributes to speciation only when there is already genetic variation for size. In keeping with the discussion above, geographical isolation can be viewed as a kind of two-allele mechanism. Thus, an allele that increases philopatry contributes to speciation only if the population lives in two or more localities.

The importance of the distinction between one- and two-allele mechanisms is that hybridization affects them very differently. A two-allele mechanism builds up genetic differences between populations, while hybridization tends to erase those differences. That is, two-allele mechanisms lead to a tension between selection, which favors divergence of the populations, and gene flow, which works against it. This antagonism is absent in one-allele mechanisms. Consequently, one-allele mechanisms are more powerful than two-allele mechanisms.

Because gene flow inhibits divergence with two-allele mechanisms, it has sometimes been suggested that reinforcement will be thwarted unless postzygotic isolation is virtually complete (e.g., Butlin 1989; Rice and Hostert 1993). That view is not supported by more recent theory, which shows that reinforcement by two-allele mechanisms can work under quite general conditions (e.g., Liou and Price 1994; Kirkpatrick and Servedio 1999; Kirkpatrick, in press). Furthermore, reinforcement by one-allele mechanisms is completely unimpeded by gene flow (Kelly and Noor 1996; Servedio 2000).

The distinction between direct and indirect selection is orthogonal to the distinction between one- and two-allele mechanisms; all four combinations of factors are possible. In principle, the most effective combination is a one-allele mechanism driven by direct selection. Interestingly, examples are not common. Possible candidates are island populations of animals and plants. Direct selection favors decreased dispersal since most propagules are literally lost at sea. The loss of dispersal mechanisms then allows the isolated populations to diverge into new species. Most cases of prezygotic isolation, however, seem to involve two-allele mechanisms (e.g., Bradshaw et al. 1995). Perhaps a reason that one-allele mechanisms are not more conspicuous in nature is that the appropriate genetic variation is relatively rare, a kind of evolutionary constraint to speciation (Felsenstein 1981).

At the other extreme, a particularly weak combination of factors is indirect selection driving a two-allele mechanism. Nevertheless, this is the classic scenario proposed for reinforcement: different mating preferences evolve in two distinct populations as the result of selection against unfit hybrids. While the models discussed above show that

reinforcement can indeed work under these conditions, they have not answered the question of whether reinforcement can close off gene flow between two populations entirely.

Element 5: An Initial Condition

Virtually all genetic models of speciation have been motivated by the problems of sympatric speciation and reinforcement (table 1, sec. V). Accordingly, they either consider what happens when a population starts near panmixia (if the question is sympatric speciation) or when two populations start with strong isolation (if the question is reinforcement).

The initial condition is important because the outcome of speciation depends not only on ecology and genetics but also on history. That is, the number of species that we end up with is determined in part by the number with which we start (Kondrashov and Shpak 1998). This is illustrated with our toy model in figure 2. When assortative mating based on genotype is weak, the population will evolve toward an equilibrium with small D regardless of where it begins. In this case, secondary contact between two isolates will end in fusion no matter how much they diverged in allopatry, and speciation fails. But with strong assortment, two outcomes are possible. If D is initially below a threshold, then the population will settle down to a low equilibrium value of D. However, if D is sufficiently large to begin with, then a large value for D will result, and speciation succeeds. With extremely strong assortative mating, we can get sympatric speciation from a population that starts with little or no disequilibrium. Most scenarios for sympatric speciation envision a second phase in which the strength of assortment (or other barrier to hybridization) is further strengthened. This second phase is reinforcement, which works the same way regardless of whether the initial divergence happened in sympatry or allopatry.

Two implications follow. First, reinforcement can occur in some situations where sympatric speciation cannot. When assortment is strong (e.g., with $A = 0.8$ in fig. 2), a population that is initially in linkage equilibrium ($D = 0$) will remain one species; sympatric speciation will not occur. But if D is initially large (e.g., because two populations diverged in allopatry and then came into secondary contact), the two subpopulations will remain distinct. There is then the opportunity for reinforcement to happen, that is, for assortative mating to be strengthened through evolution at other loci.

The second point is that reinforcement can fail in two very different ways. If assortment is too weak, populations may fuse before reinforcement has a chance to succeed (Liou and Price 1994). While fusion is occurring, there is a race between the evolution of new barriers to interbreeding and the impending coalescence, and it seems that very unusual circumstances would be needed for reinforcement to win in this situation. More work is needed here; a major gap in speciation theory is the lack of general conclusions for when fusion will and will not occur.

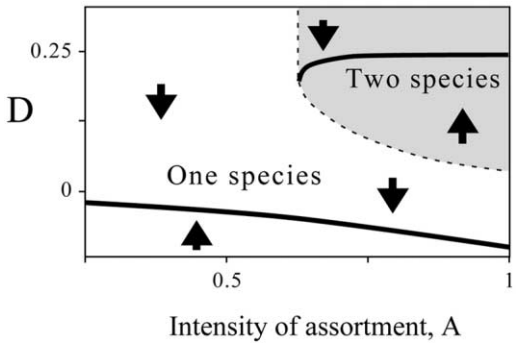

Figure 2: Equilibria for the two-locus model under different strengths of assortment A. The case shown includes weak stabilizing natural selection, $S = -0.1$. For sufficiently strong assortment ($A > 0.62$), a one-species equilibrium ($D \approx 0$) and a two-species equilibrium ($D \approx 0.25$) are both stable. The two-species equilibrium will be reached if the initial disequilibrium is sufficiently large (*shaded region*).

Reinforcement can also fail even if the populations do not fuse. This happens when reinforcement is prevented by other evolutionary forces (e.g., when hybridization frustrates a two-allele mechanism) or when the populations simply lack the appropriate genetic variation to allow further isolation to evolve. Distinguishing between the ways that reinforcement can fail will be important in our discussion of the experimental data below.

Conclusions about Models

Our review of the theoretical literature shows there are many ideas about how prezygotic isolation can evolve by selection. Considering all combinations of the five elements listed in table 1, we calculate that there are 240 possible scenarios. Of those, it seems that only 94 combinations have been modeled to date. Opportunistic theoreticians can rejoice; apparently there are 146 models still to be published.

That suggestion is, of course, facetious. Modeling every recombinational possibility of ingredients is an efficient algorithm for generating publications (and pulping trees) but not a good way to discover general principles. Several important conclusions have come from specific models, for example, that sympatric speciation and reinforcement can indeed work. A major next step will be to understand

what combinations of factors are most important in producing new species in nature. The scheme of five elements sketched above may be useful for that goal since it leads to several generalizations. The next section tests some of those conclusions using the results of laboratory experiments on speciation by selection.

Theory Meets Data

A hurdle to testing hypotheses about speciation is that it usually cannot be observed directly in the wild. An alternative strategy is to study the conditions that can lead to speciation in the laboratory. In an important and influential article, Rice and Hostert (1993) reviewed over 50 experimental studies of speciation. Table 2 reorganizes those studies in light of the discussion in the last section. It is not possible to classify the experiments in exact parallel with the taxonomy of models given in table 1 because we typically do not have critical information, for example, whether isolation is evolving via a one- or two-allele mechanism. Nevertheless, we can draw some useful conclusions. In keeping with this article's focus on selection, we omit the experiments that test the effects of drift.

One group of experiments (table 2, sec. I.A) simulate the evolution of prezygotic isolation in hybridizing populations when there is complete postzygotic isolation (what Rice and Hostert [1993] called the "destroy-all-the-hybrids" experiments). Stronger prezygotic isolation evolved fairly frequently, in 11 of 19 studies. That pattern is consistent with theory: complete postzygotic isolation generates direct selection for prezygotic isolation, which is an efficient mechanism for speciation. The reasons for the failures are not known; presumably the appropriate genetic variation was missing (Ödeen and Florin 2000). An interesting question is how often opportunities for speciation are not realized in nature because of genetic constraints. Other experiments selected divergently on allopatric populations (table 2, sec. I.B). A striking pattern is that prezygotic isolation has appeared in eight of eight studies, the result of indirect selection that is presumably mediated by pleiotropy (Rice and Hostert 1993).

A second group of experiments simulate sympatric speciation. They ask when divergence will occur when there is gene flow and initially little disequilibrium (table 2, sec. II.A). In one such series of studies, Rice and Salt (1988, 1990) looked at sympatric speciation under direct selection. They selected divergently on habitat choice in an organism that mates within its chosen habitat (*Drosophila*). They observed a dramatic response, with the percentage of flies returning to their natal habitat increasing from 53% to 100% over the course of 35 generations. The experiments again agree with the theoretical conclusion that direct selection is a powerful way to generate new species.

Other experimental tests of sympatric speciation use indirect selection (table 2, sec. II.A.2). For example, Hostert (1997) constructed a base population of *Drosophila* that was polymorphic for an eye color mutation and applied varying intensities of selection against offspring whose parents had different eye color genotypes. This protocol generates indirect selection for divergent mating preferences so that between-group matings become less common. Unless genetic variation for mate choice based on eye color was already segregating in the base population, successful speciation would also require a two-allele mechanism.

There are thus several factors that theory predicts made

Table 2: Experimental studies of speciation

	Success	Mixed	Failure
I. No gene flow:			
A. Direct selection	2, 5, 8, 17–19, 21–23, 25, 34	12–14	1, 10, 11, 24, 33
B. Indirect selection	3, 6, 7, 9, 16, 18, 20, 30		
II. With gene flow:			
A. Low initial divergence:			
1. Direct selection	26–28		
2. Indirect selection	18, 30, 32	4	18 experiments reviewed in 16, 17, 31
B. High initial divergence:			
1. Indirect selection			15, 29, 35

Note: Numbers correspond to references as follows: (1) Barker and Cummins 1969, (2) Barker and Karlsson 1974, (3) Burnet and Connolly 1974, (4) Coyne and Grant 1972, (5) Crossley 1974, (6) de Oliveira and Cordeiro 1980, (7) del Solar 1966, (8) Dobzhansky et al. 1976, (9) Dodd 1989, (10) Ehrman 1964, (11) Ehrman 1969, (12) Ehrman 1971, (13) Ehrman 1973, (14) Ehrman 1979, (15) Ehrman et al. 1991, (16) Grant and Mettler 1969, (17) Hostert 1997, (18) Hurd and Eisenberg 1975, (19) Kessler 1966, (20) Kilias et al. 1980, (21) Knight et al. 1956, (22) Koepfer 1987, (23) Koopman 1950, (24) Koref-Santibanez and Waddington 1958, (25) Paterniani 1969, (26) Rice 1985, (27) Rice and Salt 1988, (28) Rice and Salt 1990, (29) Robertson 1966, (30) Soans et al. 1974, (31) Spiess and Wilke 1984, (32) Thoday and Gibson 1962, (33) van Dijken and Scharloo 1979, (34) Wallace 1953, (35) Wallace 1982.

the evolution of isolation difficult in this group of experiments: the populations started out well mixed (with low *D*), selection was indirect, and a one-allele mechanism may not have been possible. Indeed, speciation under these conditions has been rare in the lab; only three studies (Thoday and Gibson 1962; Soans et al. 1974; Hurd and Eisenberg 1975) saw isolation evolve, while in 21 others (including Hostert 1997), it did not.

The last group of experiments are of reinforcement: the evolution of increased isolation by indirect selection, starting with large *D* (table 2, sec. II.B). Three such experiments have been done, and isolation evolved in none of them. The way in which the failures occurred is significant. All three experiments saw the populations fuse (i.e., the large initial *D* collapsed to a value near 0) before isolation could evolve. We are unaware of any experimental test of reinforcement that have looked for the evolution of prezygotic isolation in populations that remained genetically distinct, a situation generally thought to be quite common in nature.

Lab experiments on speciation set up conditions under which isolation might evolve and then ask whether it does. In addition to telling us when speciation might happen, these experiments could provide valuable information about how it happens. In cases where isolation does appear in the lab, it would be very interesting to know whether its basis is a one- or two-allele mechanism, whether it evolved by direct or indirect selection, and so forth.

Discussion

Perhaps the best hope for arriving at a general conceptual understanding of speciation is to proceed in two steps. The first is to decompose the evolution of prezygotic isolation into a minimal number of fundamental elements. The second step is to study the effects of each of those factors in isolation from the others, to the extent possible. We have made a preliminary stab at organizing the major factors above, but other schemes may prove to be more useful. Regardless of how it is achieved, we see no reason that all the diverse biogeographic, ecological, behavioral, and genetic scenarios that have been proposed for speciation cannot ultimately be housed under a single theoretical roof.

Reaching that goal will greatly simplify thinking about speciation. It will also provide a useful framework for interpreting empirical results. In their review of the experiments, a major conclusion that Rice and Hostert (1993) drew was that reinforcement does not work unless postzygotic isolation is complete. Their review, however, did not distinguish between experiments in which *D* was initially low and those where it was high (i.e., tests of sympatric speciation vs. tests of reinforcement). Furthermore, in cases where *D* was initially high, the review did not distinguish between experiments where fusion occurred and those where it did not. Taking those factors into account suggests there has not yet been an experiment favorable to finding reinforcement with incomplete postzygotic isolation. Our conclusion is therefore that the experimental case against reinforcement is far from compelling.

We restricted ourselves here to mechanisms based on selection. Another force that could produce prezygotic isolation is drift. In principle, two populations that are geographically isolated might drift apart in their mating preferences or assortment traits so much that they do not interbreed on secondary contact (Nei 1976; Lande 1981; Nei et al. 1983; Wu 1985; Gavrilets 1999). The role of drift in speciation has been controversial ever since Mayr's (1963) discussions of "genetic revolutions," and it has been challenged on both theoretical and empirical grounds (Barton and Charlesworth 1984; Rice and Hostert 1993). One hope for resolving this issue is the prospect of locating the genes responsible for prezygotic isolation. Both direct and indirect selection should leave their signatures there in patterns of nucleotide divergence and polymorphism. Conversely, sequence data consistent with divergence by drift would call into question the role of selection in speciation.

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APPENDIX

The Model

This appendix describes the highly simplified model that we used to illustrate several points about speciation in the text. The model is of two equivalent haploid loci, each of which has two alleles called "+" and "−" that are at

frequencies of one-half. We will simply assume that some form of selection maintains this polymorphism. The loci contribute additively to a trait, and so an individual's phenotype is determined by whether it carries zero, one, or two of the + alleles.

Since the allele frequencies are fixed (by assumption), linkage disequilibrium is the only thing that evolves. It changes in response to three forces: natural (or viability) selection, assortative mating, and recombination. The intensity of disruptive natural selection is quantified by S, where $1 - S$ is the viability of individuals that carry one + allele relative to those that carry either zero or two. Thus, $S = 0$ means that all genotypes survive equally, and $S = 1$ means that only the extreme $(-, -)$ and $(+, +)$ genotypes survive. Negative values of S correspond to stabilizing natural selection that favors individuals that carry a single + allele.

A simple kind of assortative mating occurs in which individuals most often mate with others carrying the same number of + alleles. The intensity of assortment is measured by A, where $A = 0$ implies random mating and $A = 1$ implies perfect assortment. Specifically, we assume that the frequencies of matings between two genotypes is proportional to

$$(1 - A)^{(n_1 - n_2)^2} f_1 f_2,$$

where n_1 and n_2 are the number of + alleles they carry and f_1 and f_2 are the frequencies of those genotypes in the population. This mating rule is a discrete version of a Gaussian mating preference. It produces frequency-dependent selection that favors common genotypes, and we emphasize that this is not the only form of assortative mating possible. After mating, haploid offspring are produced following free recombination.

The dynamics of the linkage disequilibrium are given by

$$\Delta D = \frac{-64(6A^2 - 4A^3 + A^4 - 4AS + 2S^2)D^3 - 16[2A^4 - 8A^3 + 12A^2 - 8A - 3(S-2)S]D^2 - 4[4 + 6A^2 - 4A^3 + A^4 + 4A(S-2) - 4S]D - S(S-2)}{4[6A^2 - 4A^3 + A^4 + 4A(S-2) + 2(S-2)^2 + 32(-4A + 6A^2 - 4A^3 + A^4 + 4S - 2S^2)D + 64(6A^2 - 4A^3 + A^4 - 4AS + 2S^2)D^2]}.$$

The equilibria are those values of D for which $\Delta D = 0$. These can be found using, for example, *Mathematica* (Wolfram 1999). Graphs of the results for some parameter values are shown in figures 1 and 2.

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