

NEWS AND COMMENTARY

Speciation

**Selection against migrant pathogens:
the immigrant inviability barrier
in pathogens**

T Giraud

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In a recent Perspective piece in *Evolution* entitled 'Reproductive isolation caused by natural selection against immigrants from divergent habitats', Nosil *et al* (2005) argued that the classification of reproductive isolating barriers commonly used in studies on speciation was incomplete. These classifications usually put forward in chronological order of occurrence, the intrinsic mechanisms impeding the mating of individuals from two populations: from prezygotic barriers (temporal isolation, ecological isolation, behavioural isolation, mechanical isolation and gametic isolation) to postzygotic barriers (zygotic mortality, hybrid inviability, hybrid sterility, F2 breakdown).

Nosil *et al* (2005) described a novel type of barrier, not often recognized, that results from the reduced success of immigrants upon reaching foreign habitats that are ecologically divergent from their native habitat. They highlight that this 'immigrant inviability' barrier is biologically and chronologically distinct from the widely recognized 'habitat isolation' barrier. Habitat isolation is usually considered in terms of reduced migration due to habitat preference, whereas the barrier created by the reduced viability of immigrants acts through habitat-associated fitness differences and reflects the reduced survival of those individuals that do indeed successfully migrate to foreign habitats (Figure 1). Therefore, the two types of barriers may most often result from different genes and refer to different concepts: 'immigrant inviability' is a consequence of selection that is in itself a form of reproductive isolation; conversely, the term 'habitat isolation' usually refers to a form of selection that promotes the evolution of a reproductive barrier or habitat preference. Nosil *et al* (2005) show the relevance of the 'immigrant inviability' barrier in plants and animals by finding numerous examples in a survey of related literature. Obviously, the importance of this barrier is

greater when the other types of isolation, that is, habitat preference, sexual preference, postzygotic barriers and geographic isolation, are lower. Their formal recognition of immigrant inviability should be of great importance to the study of speciation, because concepts play an important role in research, and terminological ambiguity impedes scientific progress.

However, Nosil *et al* (2005) omitted pathogens in their literature survey, a group of organisms of great importance to human affairs, and for which the concept of 'natural selection against immigrants' is particularly relevant. For pathogens, different host species can indeed be considered as divergent habitats, and host shift as migration (McCoy, 2003). Pathogens specialized to a given host that shift onto another host species may not be fit enough to be able to grow and reproduce in this novel host. The reduced viability of host/habitat specialized pathogens in host species other than their native one can thus act as a strong isolating barrier. Given the high number of specialized sibling species complexes in pathogens (De Meeüs *et al*, 1998), such reproductive isolation is likely to be of critical importance in these organisms, and may even explain, to some extent, their high species richness.

Although the effect of natural selection against immigrants in pathogens is quite similar to that in insects parasitizing plants, such as those mentioned by Nosil *et al* (2005), it may be of greater importance in those pathogens with a particular life cycle (Le Gac and Giraud, 2004; Giraud, 2006; Giraud *et al*, 2006). For animals, strong divergent selection can indeed overcome the effect of free movement between environments before they have an opportunity to mate. However, maintaining genetic divergence in the face of free migration through the elimination of migrants implies a very large selective mortality or reduction in fertility (Via *et al*, 2000).

When migration between habitats is unrestricted, that is, in sympatry, some characters such as habitat choice or mate choice are likely to evolve that reduce the exposure to selection caused by migration among habitats. The load imposed by strong selection against immigrants can also be reduced in cases where migration is restricted among habitats because of some degree of allopatry, for instance in parapatry. In fact, the cases cited by Nosil *et al* (2005) where natural selection against immigrants play a role in reproductive isolation all exhibit at least one of these three additional barriers to gene flow, habitat choice, mate choice or some degree of allopatry, in particular for parasitic insect species (see references cited in Table 2 in Nosil *et al*, 2005).

In contrast, some pathogen species have peculiarities in their life cycles that may render the selection against immigrants particularly important compared to other barriers such as allopatry, habitat choice or partner choice (Giraud *et al*, 2006). Many fungal plant pathogens for instance produce huge numbers of spores that have high dispersal ability and are passively dispersed, precluding host choice and rendering unlikely strong restriction of migration among plant species due to geographical separation. Furthermore, some pathogen species have no possibility of dispersal between development on the host and mating (Alexopoulos *et al*, 1996): air-borne spores typically land on a plant, form hyphae that grow within the host and then produce gametes that mate within this individual plant. Such individual pathogens thus necessarily mate with other individuals that were also sufficiently adapted to the same host to be able to develop on it, requiring neither mate choice within the plant nor habitat preference. This contrasts with parasitic insects that are usually free to fly from one host to the other between selection on the host and mating, which reduces the effect of natural selection among immigrants. In pathogen life cycles with no dispersal between selection and mating, reduced viability of immigrants can thus play an important role in reproductive isolation: even when there are no other barriers to gene flow, that is, in complete sympatry, with neither host choice nor mate choice, reproductive isolation can be complete (Giraud *et al*, 2006). Reduced viability of immigrants then contributes to near 100% of the reproductive isolation, representing the main mechanism of divergence (Giraud *et al*, 2006).

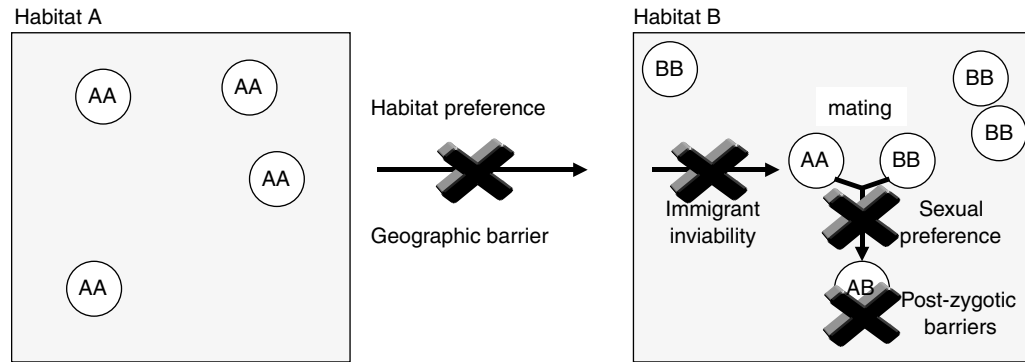


Figure 1 Schematic representation of the different types of reproductive isolation barriers preventing gene flow between two populations present in different habitats, A and B (individuals with genotypes AA and BB, respectively). Only the ‘immigrant inviability’ barrier acts through the same genes as does adaptation to the habitat.

In fact, there are some documented cases in pathogens consistent with an important role of the reduced viability of immigrants as a reproductive isolating barrier that would nicely complement the review by Nosil *et al* (2005), particularly in pathogenic fungi. The fungal Ascomycete *Venturia inaequalis* for instance, is responsible for scab, a major apple disease in most areas of the world; *V. inaequalis* also attacks crab apple, hawthorn, various ornamentals of the genus *Malus*, loquat and other plants (Le Cam *et al*, 2002). In *V. inaequalis*, gametes are produced after a mycelium has grown deep into leaf tissues, so that there is no dispersal between development and mating. *Formae speciales* have recently been described in this pathogen that exhibit no sexual isolation, that is, are completely interfertile *in vitro*, but are so highly specialized on two different host plants, apple and pyracantha, that they cannot crossinfect. Further, molecular marker data show that they exchange no genes in sympatry (Le Cam *et al*, 2002). Dispersing spores have absolutely no possibility of host choice, being wind-borne. Only the ‘natural selection against immigrants from divergent habitats’ can explain such a pattern of reproductive isolation, and it may contribute to 100% of the reproductive isolation in this case. There are many other examples of specialized parasitic ascomycetes that reproduce on their host after mycelial development and have therefore no possibility of dispersal between selection on the host and mating, including the agent of powdery mildew, *Erysiphe graminis* (Alexopoulos *et al*, 1996, pp 462–474). A parasitic life cycle with mating on the host after mycelial development is also found in some other taxa, for instance in Oomycota. Specialized species exist for instance in the genera *Phytophthora* or *Peronospora* that are responsible for

important crop diseases such as the late blight of potato. Mycelia grow inter- or intracellularly and sexual reproduction should therefore occur only between strains infecting the same host individual (Alexopoulos *et al*, 1996, p 711), rendering likely the role of reduced immigrant viability as a reproductive barrier. There are also numerous important nonfungal human pathogens that have a direct life cycle, cannot choose their host, mate within their host and release eggs outside, and for which the reduced immigrant viability may therefore play a critical role. Examples can be found in ascarids, where cryptic specialized species have also been recently detected (Combes, 2001), schistosomes (Théron and Combes, 1995), or bacterial pathogens, which are thought to exchange genes preferentially within their hosts.

In their Perspectives paper, Nosil *et al* (2005) also consider a simple population genetics formalization of their concept of natural selection against immigrants. They rightly point out that, with respect to maintaining reproductive isolation in the face of migration, selection against immigrants is not only selection against heterozygotes, but also against the immigrant homozygotes. They however only consider a single fitness gene in their demonstration and not the rest of the genome, thus focusing on the maintenance of adaptive alleles in the right habitats rather than on true reproductive isolation, which are two distinct phenomena. It has been known for a while that strong selection allows maintenance of adaptive polymorphism when a single adaptive locus is involved (Levene, 1953) but that reproductive isolation does not necessarily follow. Mating events between individuals adapted to different habitats can indeed allow gene flow at loci not linked to the genes involved in host adaptation (Felsenstein, 1981; Rice,

1984), thus preventing neutral genes or genes involved in postzygotic isolation from becoming fixed, even if the fixed polymorphism associated with habitat for adaptive alleles may be maintained by selection. Moreover, if several fitness loci are involved, optimal adaptation on a given host requires the accumulation of all favourable alleles at all loci within a genotype and favourable genetic combinations can also be broken by mating events between individuals adapted to different habitats. For true reproductive isolation to be possible, gene flow must therefore be restricted not only for a single locus under selection but also for neutral genes. In addition, multiple genes under selection must be able to come into linkage disequilibria. These more realistic and complete considerations are lacking from Nosil *et al* (2005), who did not check that the maintenance of adaptive alleles in the island allowed such true reproductive isolation.

The effect of immigrant inviability on reproductive isolation among specialized pathogens has in fact been recently formalized taking into account several genes under selection as well as neutral genes. Giraud *et al* (2006) developed a model to investigate, in haploid pathogens with a life cycle characterized by restricted dispersal between development on the host and mating, the conditions that allow a restriction of gene flow even in the absence of any barrier to gene flow other than reduced immigrant viability. The different host species were in total sympatry, that is, with unrestricted migration among habitats and there was neither host choice nor mate choice. They showed that gene flow can indeed be severely restricted such that even neutral genes do not leak across the host-race barriers and adaptive alleles at independent loci can attain linkage disequilibrium. Increasing the number of fitness loci facilitated

reproductive isolation, which is in stark contrast to other mechanisms of reproductive isolation for which increasing the number of loci usually restricts the possibility of divergence (Gavrilets, 2004). This was because the reduced viability of immigrants allowed linkage disequilibria to arise easily among the fitness genes. As suggested by Nosil *et al* (2005), the fact that selection itself was the cause of reproductive isolation created a pleiotropic relationship between reduced fitness and assortative mating that facilitated the building of linkage disequilibria among fitness genes and then divergence, even at neutral genes.

The model developed by Giraud *et al* (2006) is further useful for illustrating the distinction between the immigrant inviability barrier and the widely recognized 'habitat isolation' barrier, that acts through reduced migration among habitats. The differences between the two types of isolation barriers may be difficult to perceive, but the model clearly shows that immigrant inviability can restrict gene flow without host preference ('habitat isolation') and with-

out the other types of barriers, that is, in complete sympatry and without sexual isolation or postzygotic isolation. The model by Giraud *et al* (2006) clearly shows that selection can act as reproductive isolation ('reduced viability of immigrants') and not only *promotes* the evolution of reproductive barriers (host preference or sexual preference). This supports the claim by Nosil *et al* (2005) that the barrier caused by a reduced viability of immigrants has to be conceptually recognized and to be studied separately if we are to disentangle the mechanisms leading to speciation.

In conclusion, formal recognition of reduced immigrant viability as an isolation barrier is timely and necessary, the differences between habitat isolation and reduced immigrant viability being difficult to perceive. The process of 'natural selection against immigrants from divergent habitats' may be particularly common and important in pathogens, where there exist many documented cases consistent with its occurrence. The model developed by Giraud *et al* (2006) should help to clarify the conditions allowing reduced immi-

grant viability to in fact reduce gene flow.

T. Giraud is at the Ecologie, Systématique et Evolution, UMR 8079 CNRS-UPS-ENGREF, Bâtiment 360, Université Paris-Sud, F-91405 Orsay Cedex, France.

E-mail: Tatiana.Giraud@ese.u-psud.fr

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