

Additionally, these results show the power of this type of study, and draw the attention to some unresolved problems of European phylogeography. It would be very interesting to further explore, for example, the pattern of extended but genetically more uniform distributions north of the Alps (as observed in *E. euryale isarica* and other species), and more southern refugial populations which regularly show more scattered pattern of distribution but higher levels of genetic diversity.

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### PERSPECTIVE

## Speciation with gene flow could be common

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### Abstract

The likelihood of speciation in the face of homogenizing gene flow (i.e. without complete geographical isolation) is one of the most debated topics in evolutionary biology. Demonstrating this phenomenon is hampered by the difficulty of isolating the effects of time since population divergence vs. gene flow on levels of molecular genetic differentiation. For example, weak genetic differentiation between taxa could be due to recent divergence, gene flow, or a combination of these factors. Nonetheless, a number of convincing examples of speciation with gene flow have recently

**emerged, owing in part to the development of new analytical methods designed to estimate gene flow specifically. A recent example of speciation with gene flow in salamanders (Niemiller *et al.* 2008) further advances our understanding of this phenomenon, by showing that gene flow between cave and spring salamanders was ongoing during speciation, rather than having occurred after a long period of allopatric divergence. Future work on the ecological and genetic factors reducing gene flow will likely increase our understanding of the conditions that facilitate divergence in the face of gene flow.**

*Keywords:* divergence-with-gene-flow, isolation with migration, migration, reproductive isolation

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The geographical context of speciation is related to levels of gene flow between populations during divergence (Mayr 1963; Gavrillets 2004; Bolnick & Fitzpatrick 2007). At one extreme, gene flow is totally absent during 'allopatric speciation'. At the other extreme, there are no physical barriers to gene flow at all. This represents 'sympatric speciation', which is an extreme case of speciation with gene flow. Intermediate scenarios with partial, but incomplete, physical restrictions to gene flow are also likely (e.g. parapatric speciation). Speciation in the face of gene flow is generally thought to be difficult, because gene flow constrains population differentiation, thereby preventing the evolution of strong reproductive isolation (Mayr 1963; Coyne & Orr 2004). Although theoretical models have now demonstrated that speciation with gene flow is feasible under particular conditions (Gavrillets 2004; Bolnick & Fitzpatrick 2007), empirically demonstrating that speciation occurred in the face of gene flow is difficult. Nonetheless, a number of convincing examples of speciation with gene flow have now emerged, owing to methodological advances and creative approaches to studying the phenomenon (Hey 2006 for review).

An increasingly common test for divergence with gene flow involves using coalescent-based analyses to isolate the roles of time vs. gene flow on levels of genetic divergence, in an 'isolation with migration' model (the IM approach; Hey 2006). A study of speciation in salamanders, published in this issue of *Molecular Ecology* (Niemiller *et al.* 2008), used the IM approach to test whether divergence between spring and cave salamanders occurred with or without gene flow (Fig. 1). In such salamanders, two main speciation scenarios have been advanced: a 'climate-relict' hypothesis which invokes allopatric speciation after cold-adapted species become stranded in caves during climate change, and an 'adaptive-shift' model in which parapatric speciation occurs in the face of gene flow, with divergent selection between cave and surface habitats driving differentiation. Niemiller *et al.* (2008) applied coalescent-based analyses to DNA sequence variation from two mitochondrial and one

nuclear gene, and strongly rejected a model of divergence with zero gene flow, thereby supporting an 'adaptive-shift' scenario involving gene flow.

Other studies employing slightly different approaches suggest that the salamander study, and others employing the IM approach, are not extreme anomalies. For example, studies reporting highly discordant patterns in gene genealogies from different loci support divergence with gene flow (Wang *et al.* 1997; Dopman *et al.* 2005; Bull *et al.* 2006; Putnam *et al.* 2007), because greater genealogical discordance is expected during divergence with gene flow (Hey 2006). Niemiller *et al.* (2008) also report such genealogical discordance. Other studies have focused on the criteria for sympatric speciation proposed by Coyne & Orr (2004) in their book on speciation (e.g. Barluenga *et al.* 2006; Savolainen *et al.* 2006). Finally, other work has inferred divergence with gene flow using the heterogeneity of genetic divergence among loci within the genome (Emelianov *et al.* 2004), geographical patterns of divergence in allopatry vs. sympatry (Grant *et al.* 2005), site-specific genetic differentiation (Panova *et al.* 2006), or patterns of linkage disequilibrium within populations (Nosil *et al.* 2006). In short, methods for detecting gene flow are improving, and their creative use has increased the available examples of speciation with gene flow.

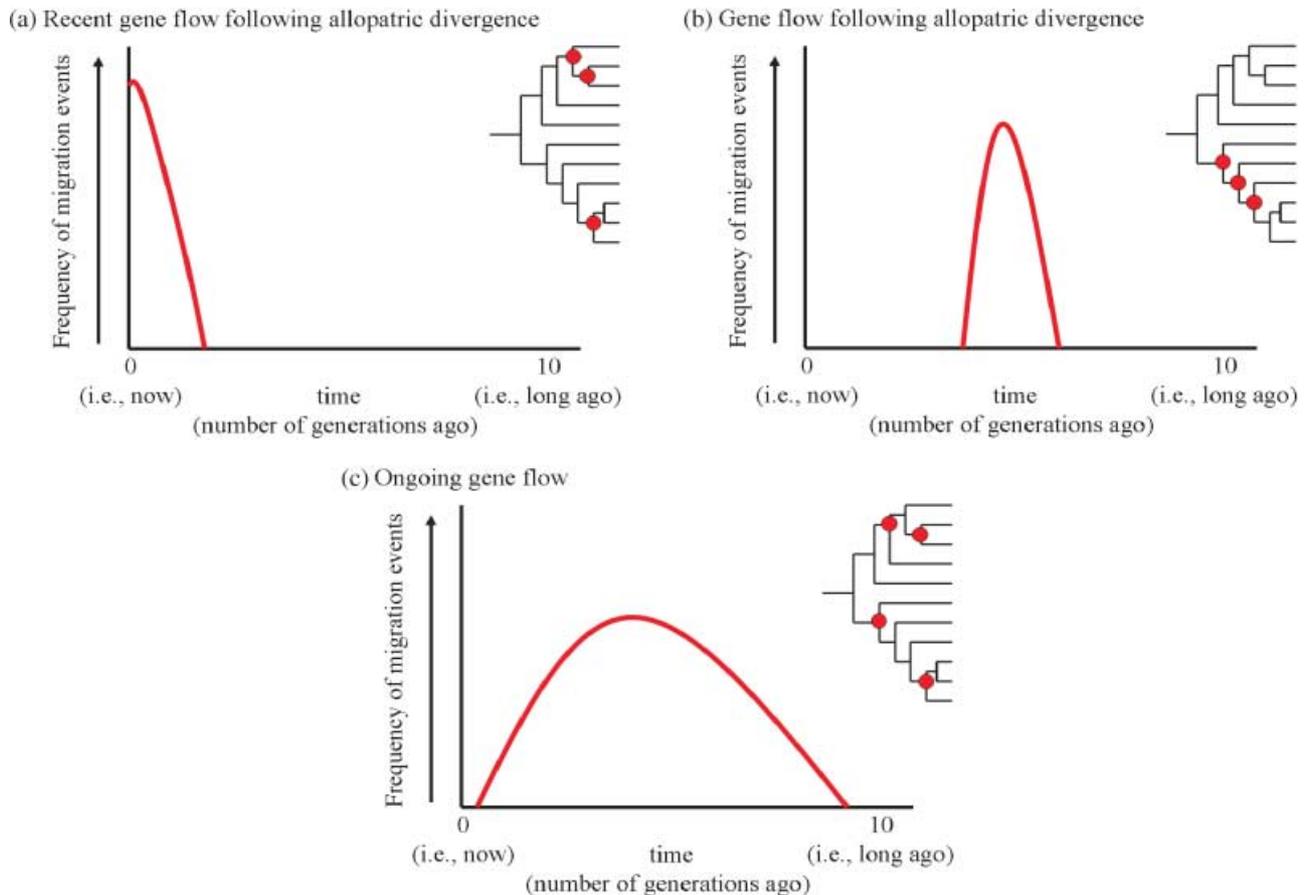
Given convincing cases where gene flow occurred at some point in the speciation process, three major questions emerge: the timing of gene flow relative to the initiation of speciation, the factors which constrain gene flow to facilitate divergence in the face of it, and the generality of the process.

First, a rarely addressed issue is the timing of gene flow. In particular, at what point in the speciation process did gene flow occur? At one extreme, gene flow may have been ongoing during the entire process. At the other extreme, gene flow ensued upon secondary contact, after a long period of allopatric divergence in which partial reproductive isolation accumulated unimpeded by gene flow. In the latter scenario, although there may be some gene flow upon secondary contact, speciation was essentially allopatric. Of course, intermediate scenarios are possible (Rundle & Nosil 2005). The study by Niemiller *et al.* (2008) advances our general understanding of speciation with gene flow by testing when, in this continuum of possible points in time, gene flow occurred. They extend an approach used to address the divergence of chimpanzee subspecies (Won & Hey 2005), and show that the timing of reconstructed migration (i.e. gene flow) events between salamander species was broadly distributed through time. This result is more consistent with continuous or recurrent gene flow during divergence than with secondary contact following a long period of allopatric divergence (Fig. 2).

Second, elucidating the factors that facilitate divergence with gene flow will increase our understanding of how the process occurs, and the conditions that favour it. For example, ecological divergence between populations is likely to be of key importance in facilitating speciation with gene flow. If so, a positive correlation between the degree of adaptive phenotypic population divergence and levels of neutral genetic differentiation, independent from geographical distance, is expected (Nosil *et al.* 2008), because such a pattern indicates that adaptive divergence restricts gene flow. Likewise, tests for the role of genetic factors, such as chromosomal inversions, in



**Fig. 1** Pictures of the salamanders studied by Niemiller *et al.* (2008). The spring salamander (left) (*Gyrinophilus porphyriticus*) is the surface-dwelling progenitor of the cave adapted Tennessee cave salamander (right) (*G. pallescens*) and Berry cave salamander (*G. gulolineatus*). Photo credit: Matthew L. Niemiller.



**Fig. 2** Tests for distinguishing whether gene flow was ongoing during divergence vs. having originated following a long period of allopatric differentiation. Shown are the timing of migration events in IM analyses (following Won & Hey 2005). The X-axes are time (number of generations ago multiplied by the effective neutral mutation rates). The Y-axes are the frequency of migration events in samples at Markov chain Monte Carlo stationarity. The width of a distribution indicates how widely distributed through time migration events were (i.e. how 'ongoing' gene flow was during divergence). Wider distributions correspond to gene flow being more ongoing. Also shown are inferred migration events (red circles at nodes) in gene trees (following Slatkin & Maddison 1989). Patterns expected under three hypothetical scenarios are depicted (in each, the duration of the allopatric period depends on how long ago population divergence was initiated, which is not considered here). (a) Recent gene flow following a period of allopatric divergence. Migration events are highly concentrated over a narrow time interval corresponding to recent time periods. In a gene tree, inferred migration events would be concentrated towards the tips of the phylogeny. (b) Gene flow following allopatric divergence, but where gene flow was not necessarily recent. Migration events are concentrated over a narrow time period, but one which corresponds to a period further back in time. Such patterns might arise if gene flow occurred at a specific point in time in the past, corresponding to when secondary contact occurred. In a gene tree, inferred migration events would be concentrated at a relatively specific part of the tree. (c) A scenario where gene flow was relatively ongoing, with migration events widely distributed through time. This pattern is most similar to the one detected by Niemiller *et al.* (2008). In a gene tree, inferred migration events would be spread throughout the tree.

facilitating divergence with gene flow are warranted (Noor *et al.* 2001; Rieseberg 2001).

Third, as more tests for divergence with gene flow emerge, it will be interesting to assess the generality of the process. The existing evidence, bolstered by the Niemiller *et al.* (2008) study, indicates that divergence with gene flow certainly can occur. But how common and taxonomically widespread is the process? The use of standardized methods (e.g. the IM approach) indicates that meta-analytic techniques can one day be used to address questions concerning generality. Collectively, these avenues of future research will likely increase our understanding of the process of speciation.

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