

The ripple effects of clines from coevolutionary hotspots to coldspots

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Coevolution has the potential to alter not only the ecological interactions of coevolving partners, but also their interactions with yet other species. The effects of coevolution may ripple throughout networks of interacting species, cascading across trophic levels, swamping competitors, or facilitating survival or reproduction of yet other species linked only indirectly to the coevolving partners. These ripple effects of coevolution may differ among communities, amplifying how the coevolutionary process produces geographic mosaics of traits and outcomes in interactions among species. In a *From the Cover* article in this issue of *Molecular Ecology*, Hague et al. (2022) provide a clear example, using the well-studied interactions between Pacific newts (*Taricha* spp.) and their common garter snake (*Thamnophis sirtalis*) predators in western North America. Pacific newts harbour tetrodotoxin (TTX), which is highly toxic to vertebrate predators. In coevolutionary hotspots, extreme escalation of toxicity in the newts and resistance to toxicity in the snakes have resulted in snake populations that retain high levels of TTX. In two geographic regions, snakes in these hotspot populations have evolved bright, aposematic colours that may act as warning signals to their own vertebrate predators. The warning signals and toxin-resistance alleles in the snake populations decrease clinally away from the coevolutionary hotspots, shaped by a geographically variable mix of selection imposed by the snakes' prey and by their own predators.

The interactions between newts and garter snakes have become one of the best studied examples of how lineages of interacting species coevolve as a geographic mosaic of molecular, chemical, and morphological traits, and ecological outcomes across large geographic scales. Tetrodotoxin (TTX) within Pacific newts is a powerful neurotoxin, fatal to most vertebrate predators. Populations of garter snakes that have evolved the ability to detoxify TTX gain access to newts as prey. In some habitats along the Pacific coast of North America, the newts are abundant. Some country roads even post newt crossing signs to warn drivers of the annual local newt migration to ponds and creeks for breeding.

This new study builds on a highly impressive body of past work on the geographic mosaic of coevolution between Pacific newts and garter snakes in western North America, beginning with a major study published over two decades ago (Brodie et al., 2002). As additional researchers have contributed expertise from other fields, these studies have identified the biochemical mechanisms of toxicity and toxin resistance and found repeated examples of coevolutionary escalation among divergent populations of the newts and the snakes. Strengthening the coevolutionary interpretations even further, recent studies have found that similar covariation in toxicity and resistance to toxicity recurs among different pairs of newt

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and garter snake species distributed across thousands of kilometres (Reimche et al., 2020).

These past studies also have shown that levels of (TTX) in Pacific newts and levels of genetically based toxin resistance in common garter snakes covary among populations in a series of clines distributed from western Canada to California. The ability of snake populations to resist the toxic effects of TTX matches toxin levels in newt populations across these clines and, intriguingly, even overshoots the necessary levels of toxin resistance in some areas.

Using these past results, the new study draws on the natural history observation that common garter snakes vary greatly among species and populations in bright colour patterns, dominated by red (Figure 1). Aposematic (warning) colours are most apparent in regions in which TTX levels in the newts and TTX resistance in the snakes are high, dropping off clinally from these coevolutionary hotspots. The authors show that this is not due to chance. Geographic variation in aposematic coloration in the snakes deviates from the pattern that would be predicted based on divergence in neutral genetic markers (SNPs).

Interpreting clinal covariation in toxicity and aposematic colour patterns as a result of selection rather than neutral divergence is strengthened further by two other results from this study and past studies. Snake populations in Oregon and California are from different phylogeographic lineages, likely separated during the Pleistocene. The clines in newt toxicity and snake resistance in these two regions therefore seem to have arisen from independent events of coevolutionary escalation. Moreover, the genetic basis for achieving high levels of resistance to TTX in snake populations differs between the regions. Tetrodotoxin binds to voltage-gate sodium

channels in motor nerves, preventing transport of sodium ions and resulting in paralysis of skeletal muscles (Geffeney et al., 2005). Snakes in both regions share a repeated first-step mutation that disrupts the toxin from binding to the channels, but populations in Oregon and California populations achieve higher levels of TTX resistance through different alleles (Hague et al., 2017). The same coevolutionary result has therefore been achieved through different genetic mechanisms.

In both regions, snake populations with high frequencies of alleles conferring high TTX resistance are also the snake populations with bright, aposematic coloration. Aposematism and TTX resistance alleles decrease clinally away from these regions of high coevolutionary escalation. Because the snakes retain the toxin from the newts they eat, aposematism in the snakes may therefore be a result of natural selection imposed by avian predators that avoid snakes exhibiting these warning signals. Sexual selection or even disruptive camouflage is always a potential alternative interpretation for the evolution of bright colour patterns, but the clinal covariation of toxicity, resistance, and bright colours makes these alternatives unlikely.

The authors' interpretation of repeated evolution of aposematism in the snakes therefore arises from an elegant intermingling of several complementary kinds of data: phylogeographically independent origin of clines of newt toxicity, genetically independent mechanisms of high TTX resistance in the snakes, and geographic coincidence of toxicity and aposematism. Few studies in coevolutionary biology can approach the interpretative strength of this study with respect to demonstration of direct coevolution between two or more species and the potential evolutionary consequences for interactions with yet other species.



FIGURE 1 Examples of colour variation in populations of the common garter snake (*Thamnophis sirtalis*) that co-occur with toxic newt (*Taricha* spp.). Photo credit: Michael Hague.

The study does not provide direct experimental evidence that vertebrate predators selectively avoid common garter snakes with these suites of bright red signals. There is, though, a long history of past research worldwide, showing avoidance by predators of bright, seemingly aposematic, colour patterns. These past studies include a classic set of experiments completed decades ago by two of the authors, showing avoidance of brightly coloured vertebrate prey by birds (Brodie & Brodie, 1980).

The interactions between newts, common garter snakes, and raptors are but one ecological axis of the potential ripple effects of coevolution and its ecological consequences. Some communities have more than one species of *Taricha* newt and more than one species of garter snake, setting up the possibility of yet other novel coevolutionary trajectories and their ripple effects. In addition, in some areas *Ensatina* salamanders appear very similar to co-occurring newts in morphology and behaviour, suggesting that mimicry may also be another ripple effect (Kuchta et al., 2008). Along yet another trophic axis, TTX may also protect the newts from parasites (Johnson et al., 2018). In ways such as these, the coevolutionary process fuels relentless evolution within networks of interacting species.

These results also are important because they suggest how antagonistic coevolution may sometimes decrease trophic connections between coevolving species and other species within a community, in this case through predator avoidance of brightly coloured snakes. As avoidance by avian, and potentially other, predators varies along coevolutionary clines from hotspots to coldspots, it contributes to the ever-changing ecological consequences of the geographic mosaic of coevolution. These are, then, the kinds of direct and indirect effects, acting within and across communities, which make coevolution such a potentially important process in the organization of the earth's biodiversity.

AUTHOR CONTRIBUTIONS

John N Thompson wrote the article.

CONFLICT OF INTEREST STATEMENT

The authors declare no competing interest.

DATA AVAILABILITY STATEMENT

No data.

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