

Predator–Prey Arms Races

Asymmetrical selection on predators and prey may be reduced when prey are dangerous

Edmund D. Brodie III and Edmund D. Brodie Jr.

There is an intuitive appeal to viewing natural struggles among species as arms races between enemies. Consider the sit-and-wait predator in his shiny patrol car who sits behind freeway overpasses waiting to subdue speeding motorists. As drivers became more wary, law enforcement employed radar guns to identify their quarry. This development was easily combated with radar detectors, until police discovered X, K, and Ka bands. Radar detectors were gradually modified to handle each new frequency, but then some jurisdictions passed laws banning the use of radar detectors and police began using “VG-2 detector hunters” to identify motorists with illegal detectors. Stealth and cloaking options are now available that jam the police detector hunter units. Enter police Lidar detectors, which use laser technology to clock and register speed so quickly that drivers have little time to react and reduce their speed. The latest driver defenses not only detect Lidar, but jam the frequency to provide a few

Edmund D. Brodie III (e-mail: edb3@bio.indiana.edu) is an assistant professor in the Department of Biology, Indiana University, Bloomington, IN 47401. Edmund D. Brodie Jr. (e-mail: brodie@biology.usu.edu) is head of the Biology Department at Utah State University, Logan, UT 84322-5305. Their current collaborative research on predator–prey coevolution began in the 1960s, when E. D. B. Jr. was conducting graduate research and E. D. B. III was helping him collect salamanders. © 1999 American Institute of Biological Sciences.

Predator–prey interactions differ from other types of victim–exploiter systems in that selection on predators frequently may be weaker than on prey

more seconds to slow down and avoid capture.

Natural enemies seem to behave in much the same way; improved abilities in one species demand compensatory improvements by its enemies if they are to continue to be successful. However, the use of the arms race analogy to describe an evolutionary phenomenon invokes specific criteria. In an evolutionary race, the players are lineages, not individuals. Steps are taken in evolutionary time (i.e., across generations). Finally, any beneficial step forward in the race by one player must cost the other and vice versa, so that evolutionary changes by one player increase selection on its opponent, causing a concomitant change.

At the center of any arms race are the arms themselves. The interaction that drives any coevolutionary system occurs at a phenotypic interface that comprises the characters that determine the outcome of any confrontation between individuals. These are the traits that both cause

and experience the selection of an evolutionary arms race; consequently, they are the features that become elaborated after generations of interaction.

Reciprocity is the defining feature of coevolutionary interactions in general, and of arms races in particular. Not only must adaptation by one player favor change in its opponent, but the opponent’s adaptation must likewise generate selection on and evolutionary response in the first player. The result is a race in which both players run neck and neck, with well-matched abilities; each step forward by one player necessitates a reciprocal step by the opponent, lest the opponent fall behind. As the metaphor suggests, arms races are interactions in which the players are antagonists that get caught in an escalation of ever-increasing abilities. Although many coevolutionary interactions can be described as arms races, not all of them fit this model. Mutualistic relationships among species, frequency-dependent cycling of traits in enemies, and a range of other dynamic processes all fit the criteria for coevolution but not the pattern of counter-escalation envisioned in an arms race.

The simplicity of the arms race, and the sometimes all too personal familiarity with what it is like to be caught in one, has led biologists to apply this perspective to a wide array of evolutionary interactions between natural enemies. However, the degree of reciprocity and details of selection vary among antagonistic interactions. Predator–prey interac-

tions, especially, may be characterized by asymmetrical selection that precludes arms races (selection on prey is thought to be stronger than on predators). In this article, we use a covariance approach to understanding selection to dissect those components of an interaction that contribute to the strength of selection by one species on another. After evaluating the evidence that selective inequalities exist and are unique to predator-prey systems, we suggest that interactions involving dangerous prey differ from other predator-prey systems and are likely to result in coevolutionary arms races. In support of this view, we describe results from investigations of the roughskin newt (*Taricha granulosa*), which possesses the neurotoxin tetrodotoxin (TTX), and its resistant predator, the red-sided garter snake (*Thamnophis sirtalis*). Within-population variation in this system suggests the potential for evolution of resistance to TTX, and the matched exploitative and defensive abilities among populations fits the predicted pattern for arms races between predator and prey.

Different races, different rules

Antagonistic interactions among natural enemies are often referred to as “victim–exploiter” relationships. This category encompasses the many interspecific interactions wherein one species gains resources from another, including host–parasite, plant–herbivore, and predator–prey interactions. Although there is certainly some commonality to all of these interactions, the vast array of natural histories they represent means that some important differences may be lost by lumping them together. The broad category of victim–exploiter relationships includes interactions that differ in strength, mode, uniformity of selection, and specificity (Thompson 1982, 1994). As a result, the rules of the races differ, and not all victim–exploiter systems are equally likely to satisfy the requisites for coevolutionary interaction.

Many detailed studies of coevolution have been conducted on plants and their herbivores and on hosts and their parasites (see Thompson 1994). The kinds of investigation in these systems range from explora-

tions of parallel radiations of antagonistic taxa (Farrell 1998, Janz and Nylin 1998, Page et al. 1998) to manipulative studies of reciprocal selection and evolutionary change (Fenner and Ratcliffe 1965, Clayton et al. in press). In many of these systems, the phenotypic interface is well understood, not only from a phenotypic perspective but also from a genetic one. For example, studies of wild parsnip have shown not only that the various furanocoumarins produced by wild parsnip have different effects on different species of insect herbivores, but also that genetic correlations among these compounds may constrain the evolution of the overall suite of defensive traits (Berenbaum et al. 1986, Berenbaum and Zangerl 1988). Detailed studies of genotype frequencies have demonstrated that hosts and parasites can be caught on a circular racetrack in which the most common genotypes in two species cycle in a frequency-dependent process. For example, rare genetic clones of the snail *Potamopyrgus* escape infection by the castrating trematode *Microphallus* resulting in increases in their relative frequency and consequently their infectibility as the parasite tracks changes in the host population (Dybdahl and Lively 1998). Even the limits to escalation in arms races that are brought about through costs of adaptation have been investigated, most recently by expressing alternative traits in a common genetic background and investigating their fitness consequences (Simms 1992, Bergelson and Purrington 1996).

Coevolution between predators and prey is relatively less well known. Although the analogy has been widely applied in such systems, many commonly cited examples of predator–prey arms races are actually elaborate defensive adaptations of prey (Cott 1940, Edmunds 1974, Endler 1986), such as the ultrasonic signals emitted by moths to deter bat predators (e.g., Surlykke and Miller 1985, Tougaard et al. 1998) or the elaborate spines and armor plates of stickleback fish that vary geographically with types of predators (Reimchen 1980). These characters have clearly evolved in response to selection from predators, but in most cases there is little evidence of counter-adaptation by their predators. Noteworthy ex-

ceptions to this pattern exist, such as the crabs of Lake Tanganyika, in Africa, and their gastropod prey, both of which exhibit conspicuous specializations that are unusual for freshwater species (West et al. 1991). These crabs possess robust chelae armored with the heavy molariform dentition characteristic of marine crabs that crush and peel mollusk shells, and the sympatric gastropods have thick, coarse-ribbed shells that resist crushing. Similar patterns are present in the fossil record in the form of matched morphological features between prey and predator lineages. Over geological time, shell thickness of bivalves and the drilling abilities of their gastropod predators have increased in a correlated fashion (Vermeij 1994). Although this sort of correlative evidence is suggestive of arms races, it does not unequivocally establish reciprocal selection and evolution between predators and prey.

An alternative explanation for the correlations between prey defense and predator ability has been proposed by Vermeij (1987, 1994), who argues that the principal mode of evolutionary interaction between predators and prey is not coevolution but “escalation.” The distinction between escalation and coevolution is in the agents of selection that drive phenotypic evolution. In escalation, most evolutionary change follows a “top-down” pattern of selection, wherein species evolve in response to their own enemies (e.g., predators or competitors) rather than through a reciprocal interaction between victim and exploiter. For predators and prey, therefore, the prediction is that most evolutionary change in predators is driven by their own predators or competitors not by their prey. For example, increases in both predator and prey speed that are commonly attributed to an arms race might instead result from both species responding to pressure from their respective predators. Similarly, the heavily armored chelae of Lake Tanganyikan crabs may have evolved in response to intraspecific competition (West et al. 1991), and the increased drilling ability of the gastropod predators of the bivalves may have been a correlated response to body size evolution driven by their own predators. Whether or not escalation is a common expla-

nation of evolutionary trends, the hypothesis highlights the uncertainty with which the arms race analogy is applied to predator-prey systems.

If predators and prey are less likely than other natural enemies to be caught in coevolutionary arms races, what are the reasons? That is, what features of the interaction between individual predators and prey do not occur in interactions between other natural enemies, such that coevolutionary races do not ensue? Empirical and theoretical evidence suggests that predators may not be forced to evolve in response to prey adaptations, even though prey almost certainly evolve in response to predation (Abrams 1986, Vermeij 1994, Abrams and Matsuda 1996). Several hypotheses have been offered to explain why predator and prey may not be equal partners in an arms race; these concepts boil down to an issue of the relative strength and likelihood of reciprocal selection. Generally, selection by prey on predators is expected to be much weaker than selection by predators on prey.

A covariance approach to coevolution

An understanding of the quantitative aspects of selection is required to evaluate whether predators and prey do experience different strengths of selection and, if so, whether these differences determine the occurrence of arms races between species. Quantitative geneticists have traditionally separated the phenotypic process of selection from the genetic response that represents evolutionary change. Under this approach, selection is the relationship between phenotypes and fitness (some values of traits are associated with higher fitness than others), and selection can be formalized as the covariance (or correlation) between traits and fitness (Price 1970, Lande and Arnold 1983, Brodie et al. 1995). The advantage of this approach is that the strength of selection can be quantified and modeled using simple statistical concepts. Factors that increase the covariance between phenotype and fitness generate stronger selection, and factors that decrease the covariance reduce the strength of selection.

The covariance approach is usu-

ally used to understand the relationship between fitness and phenotype within the same individual. However, the same statistical relationship can be used to measure the fitness consequences of different environments, including other individuals of the same or different species (e.g., Wolf et al. 1999). The covariance between an individual's fitness and the environment it experiences quantifies the strength of selection resulting from that environment. When the salient environment is another species, as in potential coevolutionary interactions, the covariance of interest is between the fitness of individuals of one species (e.g., predators) and the values of traits at the phenotypic interface in the other species (e.g., prey).

This simple view of selection by one species on another assumes that the relationship between predator fitness and prey phenotype is the same for all values of predator phenotypes. In reality, the situation is more complex because predators with different trait values might be expected to have different fitness relationships with the same prey. The covariance approach can be modified to incorporate this complexity by considering the simultaneous three-way interaction of predator fitness, predator phenotype, and prey phenotype, but the resulting mathematical treatment is not trivial. Consequently, we restrict ourselves here to the simple two-dimensional case, which nevertheless provides a useful heuristic that makes it possible to pinpoint the factors that influence the strength of selection in a two-species interaction.

A covariance is visualized as a bivariate plot (Figure 1). The relationship between two variables increases as the absolute value of the slope increases and as the spread of points around the regression decreases (i.e., as one variable is better predicted by the other). In biological terms, these statistical features can be understood, respectively, as the consequence of the interaction and the predictability of the consequence.

The consequence of the interaction is the expected fitness of an individual that interacts with another individual with a given phenotypic value. If there is little difference be-

tween interacting with the most extreme individuals, then the consequence of the interaction is small and the slope low (Figures 1c and 1d). For prey fleeing from predators, this consequence is essentially the probability of escape from predators of given trait values. If all predators are too slow to catch the prey, then the probability of escape is equivalent for any type of predator, but if predators are well matched to prey ability, the probability of capture will differ between the fastest and slowest predators.

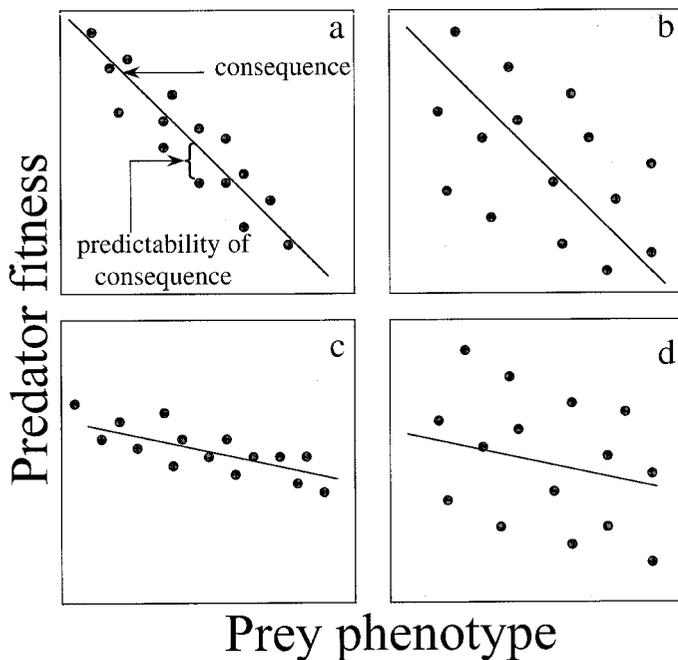
The predictability of the consequence is the likelihood that the expected fitness will be experienced, or the degree to which the fitness of one individual is predicted by the trait of another. Fitness may be relatively unpredictable because the race is run under a variety of environmental conditions, because other traits of predator or prey compensate for deficiencies in the focal trait (e.g., prey may be more distasteful), or because the outcome of a single interaction is only a small component of overall fitness. In other words, if the consequence of an interaction is always enforced, then the predictability is high, but if the consequence can be avoided, then predictability (and therefore selection) is low.

If selection is truly weaker on predators than prey, then there must be differences in either the consequences of interactions or the predictability of these consequences. There are some logical reasons to expect both of these phenomena, but, as we discuss below, some of these explanations are not unique to predator-prey systems, and they are therefore unlikely to explain the relative rarity of coevolution in predator-prey systems. What does appear to be important is that, in most cases, predators may be able to avoid selection imposed by prey. The conspicuous exceptions—and the types of interactions most likely to result in a coevolutionary arms race—are systems in which predators interact with dangerous prey.

I may be hungry, but you're dead

The most commonly cited explanation for why predators may not re-

Figure 1. The covariance relationship between predator fitness and prey phenotype. The strength of selection increases as the covariance increases. Selection resulting from an interaction between species can be viewed by plotting fitness in one species as a function of the traits in the species it interacts with. The two factors that influence the covariance—slope and spread—can be interpreted biologically as, respectively, the consequence of an interaction and the predictability of that consequence.



The slope of the relationship reflects the incremental increase (or decrease) in the expected fitness of a predator that interacts with a prey of given trait value. Steep slopes indicate a severe consequence, whereas shallow slopes indicate a milder consequence. For any given slope, the spread around the average relationship reflects the predictability of predator fitness for a given trait value. The spread is measured as the residual from the regression line; larger residuals indicate less predictability to the outcome, whereas smaller residuals indicate strong predictability. (a) A steep slope with little spread indicates severe and predictable consequences. (b) A steep slope with large spread indicates severe but unpredictable consequences. (c) A shallow slope with little spread indicates mild but predictable consequences. (d) A shallow slope with large spread indicates mild and unpredictable consequences. The life-dinner principle results from differences in the consequences of the interaction between predator and prey (i.e., the difference between [a] and [c]), whereas the ability to avoid selection is captured by differences in the predictability of the consequence (compare [a] with [b] or [c] with [d]). Although we illustrate the covariance approach using the fitness of predators as affected by prey, every interspecific interaction will have a pair of complementary relationships (e.g., for predator-prey systems, prey fitness can also be viewed as a function of predator traits).

spond evolutionarily to prey adaptations is the so-called life-dinner principle (Dawkins and Krebs 1979, Abrams 1986). The life-dinner principle is a characterization of the race between predators and prey that is meant to emphasize the supposed selective asymmetry between the players. If a coyote (*Carnivorous vulgaris*) chases a roadrunner (*Accellaratti incredibilus*), one or the other individual must lose the race (Warner Brothers 1952). If the coyote loses, the roadrunner escapes and the coyote merely loses its dinner, surviving to hunt again (injury resulting from trains, anvils, or ACME products notwithstanding). On the other hand, if the roadrunner loses the race it is caught by the coyote

and killed, resulting in zero future fitness. The consequence of this interaction is clearly more severe for individual prey than for predators, suggesting that selection is stronger on prey than on predators. This asymmetry in selection is assumed to result in faster evolution of prey than predators, leaving predators in the evolutionary dust, unable to keep pace with their prey.

However, this characterization oversimplifies the process of phenotypic evolution, which is actually a combination of selection and inheritance. The evolutionary change in a trait (R) is predicted by the strength of selection (s) and the heritability (h^2 , the percentage of variation in a trait that is controlled by

additive effects of genes; Falconer and Mackay 1996):

$$R = h^2s$$

Even if the running speeds of roadrunners and coyotes were to experience exactly the same strength of selection, speed would evolve more rapidly in the species with greater heritability for the traits at the phenotypic interface. If selection is unequal, as with the life-dinner principle, then the rate of evolution may still be equal if the heritabilities of speed in the two species differ. Because the factors that influence genetic variation are complex and poorly understood (Charlesworth 1987, Price and Schluter 1991), there is little a priori reason to expect heritabilities to be either identical or different. However, an extension of Fisher's fundamental theorem (that the rate of increase in fitness is limited by the amount of additive genetic variance) leads to the prediction that strong selection exhausts genetic variation. Consequently, some researchers expect heritability to be lower for traits under stronger selection (e.g., Mousseau and Roff 1987, Garland et al. 1990). If so, and if selection is truly stronger on prey than predators, then prey defenses should have less genetic variation than predator exploitative abilities. Thus, asymmetry in selection might lead to opposing differences in heritability that would cancel one another out, resulting in comparable rates of phenotypic evolution for both predators and prey.

A casual glance at the foraging adaptations of predators suggests that the life-dinner characterization is also a misjudgment of the strength of selection on predators. If predators truly have little to lose in a race with prey, it is difficult to imagine the forces that shape elaborate foraging adaptations, from the projectile tongues of chameleons to the immobilizing venoms of animals ranging from cone snails to cobras. The extrapolation from races between individuals to evolutionary races between populations must recognize that if a predator loses enough races, it will also lose its life (Abrams 1986).

The situation is made more complex because selection in a two-spe-

cies interaction is dynamic, comprising not only the risks of the race (i.e., life or dinner) but also the relative abilities of the players. The consequence of the interaction depends not on the absolute ability of each species, but on its ability relative to that of its enemy. If the players are well matched, then variation among individual predators could have a large effect on the predicted consequence of a race (Figure 1a). On the other hand, if there is great disparity in relative abilities, no individual predator will represent much of a risk to prey, and the differences between the risks represented by different predators will be minimal (Figure 1c). The slope relating predator ability and prey fitness will be flatter (and selection weaker) than it is in situations in which abilities are better matched. The relative strength of selection on coyotes and roadrunners will therefore change as the average ability of each species (in this case, running speed) changes. Using this perspective, Gavrillets (1997) has modeled the coevolutionary chase and found that the life-dinner principle does hold under some conditions. Assuming that genetic variances are equal and do not change, the victim will outpace the exploiter whenever the victim has more to lose. Conversely, if risk to the exploiter is greater, then a stable equilibrium of matched abilities is predicted. In neither case are predators and prey expected to cycle in an ever-escalating arms race.

But even this dynamic is an oversimplification of natural selection, in that it assumes traits can evolve to infinitely greater values. Whereas directional selection ("the faster the better") is usually imagined for arms races, real biological systems have constraints. Resources used for one feature are unavailable for use in another, and traits specialized to perform one function usually compromise another (e.g., the chameleon tongue is incredibly adept at catching insects at a distance but utterly useless for lapping water out of pools, requiring chameleons to drink dew droplets off vegetation). This limitation to infinite adaptation suggests that selection is more accurately modeled with a stabilizing function, in which the advantage

of a character decreases as it deviates further from its "best" value. Incorporating stabilizing selection into a model that assumes the life-dinner asymmetry can result in some odd dynamics, including stable cycles reminiscent of the Red Queen (i.e., negative frequency-dependent cycling of the most fit type) and the runaway escalation of both species that is characteristic of an arms race (Saloniemi 1993, Dieckmann et al. 1995, Abrams and Matsuda 1996, Gavrillets 1997). Although these dynamics depend on the precise shape of the fitness function, they generally predict either an escalating arms race or a cycling system.

Even if selective inequities do preclude an arms race, they are hardly unique to predator-prey systems. The same sort of asymmetry holds for the bulk of host-parasite and plant-herbivore interactions, although in the opposite direction. In interactions between predators and prey, the exploiter is expected to experience weaker selection than the victim (which could lose its life). By contrast, in other types of victim-exploiter systems, the exploiter may actually have more to lose than the victim. Grazers and herbivores rarely reduce the fitness of a plant to zero but instead eat parts of the plant, leaving the rest with some potential to reproduce. But if a herbivore ingests toxins from the plant or is unable to digest plant tissue due to compounds such as tannins, its fitness may be seriously compromised. Similarly, most parasites do not kill or sterilize their hosts, but they do risk their own lives when they engage in parasitism. For example, bird lice chew feather barbules. This behavior is a minor inconvenience to the bird on a per louse basis, although dense louse loads can sometimes result in sufficient feather damage that a bird can have difficulty thermoregulating and may even die. Each individual louse, on the other hand, risks its life at the bill of the bird, which can crush and kill the louse during preening (Clayton 1991, Clayton et al. in press). Despite this asymmetry in selection, there is little doubt that coevolution occurs in this and other host-parasite systems (and plant-herbivore systems). Selective inequalities therefore seem unlikely

to explain the paucity of coevolutionary interactions between predator and prey.

Dodging the bullet

One of the most conspicuous differences among types of victim-exploiter systems is the intimacy of interaction—that is, the degree to which each species experiences the consequences of engaging the other. Herbivores that sample plant material encounter whatever defenses the plant may have, and the plant that is grazed on undoubtedly experiences the effect of that injury. Any fitness consequences of either defense or grazing are unavoidable for both individuals in such an interaction. Parasites often live in the body of the host, so neither player can avoid the fitness effects of the other. Even ectoparasites such as ticks and mosquitoes, which visit a host for a relatively short time, force an intimate interaction through their physical contact. Prey that are unsuccessful at escape immediately reap the direct consequence of interaction with a predator—death.

By contrast to most players in these victim-exploiter systems, which enforce selection on their partners, predators seem to be able to avoid many of the repercussions of the interaction. Predators that fail to detect a cryptic prey or even fail to capture a prey in a physical chase do not interact physically with the prey. As a result, predators can avoid many of the selective consequences that might follow in a more intimate interaction. Whatever specific defenses the prey might have, from nasty spines to toxic secretions, cannot be employed except in the last stage of the predatory sequence, after capture. The consequence of the interaction for the predator is limited to a lost meal and to whatever energy and time costs are accrued during the foraging bout. Although the average consequence of losing a prey may be strong enough to drive an arms race, the predictability of this consequence for any individual predator is low (Figure 1b). A predator may capture the very next prey item, in which case the realized consequence of the first interaction is negligible. If alternative prey are available,

the predator might switch to a more profitable quarry and experience higher fitness than if it had captured the original prey. The cost of losing any individual prey will, therefore, depend on factors such as the predator's condition, its number of previously lost meals, its reproductive status, and a host of other variables. None of these factors mitigates the deadly consequence for the prey of the failure to escape.

Predators, much more than other exploiters, tend to be generalists (Thompson 1994, Vermeij 1994). Although there are exceptions, most predators are opportunistic and forage on a number of prey species. As a result of their lack of specialization, predators have ample opportunities to switch to alternative food sources if one becomes rare or difficult to capture. This ability to switch can alleviate selection by any single prey species in two ways. First, the consequence of lost meals is likely to be averaged over several prey types. As a result, the covariance between predator fitness and the phenotype of any one prey should be low (i.e., selection resulting from any one prey is weak; Figure 1b). Second, a predator can increase its individual fitness by switching to alternative prey. The ability to exploit alternative prey can alleviate the consequences experienced through interactions with one prey type, resulting again in low covariance of fitness with the traits of that prey (Figure 1c). Because the ability to exploit alternative prey is a behavioral response, it can increase an individual's fitness and circumvent the cost of losing races with other prey. The relationship between predator fitness and the ability to switch prey should be much steeper than that between fitness and the ability to exploit any single prey. The resulting difference in selection on these abilities suggests that predators will evolve prey switching when possible, thereby alleviating selection by single prey.

This pattern of selection could, in fact, underlie the lack of specialization that is typical of most predators. Specialization is commonly expected to result from coevolutionary interactions (Thompson 1994). If predators and prey are rarely caught in arms races, then the lack of spe-

cialization between predators and prey is no surprise. Similarly, this pattern of selection may explain why most foraging adaptations, even the most eccentric, are general and not specialized to individual prey types. The dangling lures of angler fish and snapping turtles, the projectile tongues of chameleons, and cooperative hunting in many canids are all examples of elaborate adaptations that increase the ability to exploit a variety of prey types rather than one specific taxon (although the same is true of some toxin-avoidance defenses of herbivores, such as the trenching behavior of cabbage loopers).

When dinner bites back— dangerous prey

There are, however, situations in which prey and predator interact intimately, and in which the consequences of interacting with prey are severe and predictable. Prey defenses can be categorized according to the phase of the predation sequence (detection, capture, or handling) in which they operate (for alternative categories, see Endler 1986). Primary defenses, such as crypsis, refuge use, and reduced activity, operate before detection by a predator. Secondary defenses, such as speed, startle behaviors, and evasive flight, function to prevent capture after detection. Successful defenses in either of these categories are unlikely to generate strong selection on predators for the reasons discussed in the previous section. Tertiary defenses halt the predation sequence after predator and prey have entered the handling phase; these defenses include mechanisms that prevent subjugation or ingestion or that repel the predator directly. When a predatory interaction proceeds to the handling phase, the degree of intimacy between victim and exploiter is high, and whatever consequences result from handling the prey are directly experienced by the predator. Thus, the predictability of consequences is expected to be high for predators interacting with prey whose main defense is a tertiary mechanism.

The consequences of tertiary defense mechanisms can vary widely. Despite the intimacy of interaction,

many tertiary defenses are unlikely to have a substantial fitness consequence for predators. For example, the shells of turtles and the repellent terpenoid secretions of “stink bugs” act to stop the subjugation stage of predation but cause little or no direct harm to most predators. In such cases, selection on predators is still weak because the slope of the relationship between fitness and prey phenotype is shallow even though the predictability of the effect is high (Figure 1c). On the other hand, some prey have spines and other morphological features that can damage a predator (e.g., porcupines, sticklebacks, and horned lizards), and others possess toxins or venoms that can harm or even kill (e.g., dendrobatid frogs, pufferfish, and scorpions). Predators that capture and handle such prey will experience a severe consequence with high predictability and therefore strong selection (Figure 1a).

It is these systems—in which predators interact with dangerous prey—that are most likely to meet the requisites for coevolution. In the same sense that hosts are “forced” into experiencing selection from their parasites, predators are forced into experiencing selection from dangerous prey. Provided that genetic variation for appropriate traits is present, this situation will lead inevitably to an evolutionary response by predators. Still, at least two alternative types of response are possible—predator fitness can be increased by either avoidance of the prey type altogether or improved exploitative ability (leading to an arms race).

Avoidance of dangerous prey

Avoidance of specific prey types is common among predators and drives the evolution of mimicry systems and aposematic signals in prey. Individual predators learn to avoid prey that have noxious qualities after an intimate experience with the prey. The unpleasant consequences of handling distasteful prey can lead a predator to avoid similar prey in the future. The encounters that lead to avoidance may be unpleasant, but they do not generally have severe fitness consequences (i.e., noxious prey are not necessarily dangerous). The ability

of individual predators to learn cues associated with the negative stimulus results in a population pattern of avoidance of noxious prey. However, learned avoidance does not represent an evolutionary response of predators to prey because each individual must go through the process itself (although the ability to learn may itself evolve). Innate avoidance of general aposematic cues (e.g., yellow and black ringed patterns) has been demonstrated in chickens (Schuler and Hesse 1985, Roper and Cook 1989), but most attempts to detect innate avoidance of specific prey or warning signals by natural predators have yielded negative results (Guilford 1990a, 1990b). This lack of evolutionary response is not surprising, given the relatively minor consequences of handling most distasteful prey.

A notable exception to this pattern is the avoidance of poisonous coral snakes by vertebrate predators (Greene and McDiarmid 1981, Pough 1988, Brodie 1993). Neotropical coral snakes possess a neurotoxic venom that can kill potential predators. The bright red, yellow, and black ringed pattern that gives coral snakes their name is shared by a wide variety of sympatric snake species that are not venomous or produce only mild toxins. Although it may seem obvious that these species are involved in a mimicry complex, wherein the undefended species are protected by their resemblance to a poisonous species, it is difficult to imagine how individual predators could possibly learn to avoid a prey type that will likely kill them during a single interaction. The tertiary defense of coral snakes includes biting and envenomation, the consequence of which is likely to be death (Brugger 1989). Surely this interaction has severe and predictable consequences, and therefore strong selection, for the predator.

Experimental evidence indicates that potential predators of coral snakes have indeed evolved in response to this selection pressure. Susan Smith's work (1975, 1977) with motmots and great kiskadees from Costa Rica—both potential predators of small snakes—demonstrates the existence of genetic avoidance of coral snakes. Naive hand-

reared birds reacted with alarm when presented with wooden dowels painted with the red, yellow, and black ringed pattern of coral snakes. Dowels painted with other colors (e.g., blue and green) presented in the same pattern, or with the same colors presented in different patterns (e.g., as stripes rather than rings), did not elicit the same response and were often attacked as potential prey. This genetic avoidance is not a basic feature of avian perception, as demonstrated by the finding that North American bird species (which are allopatric to coral snakes) did not avoid coral snake patterns (Smith 1980). Therefore, the avoidance of coral snake patterns by sympatric predators is an evolutionary response to dangerous prey. The innate avoidance of these cues by predators also generates a selective advantage to harmless snakes with similar color patterns, explaining how mimicry of potentially lethal prey can arise (Greene and McDiarmid 1981, Pough 1988, Brodie 1993).

Counteradaptation—TTX resistance in garter snakes

Evolved avoidance is one possible result of the predictable and severe consequences of interacting with dangerous prey, but it hardly represents the kind of escalating counteradaptation to prey defenses imagined for coevolutionary arms races. If an arms race-type process is occurring, extreme but matched levels of both defensive ability of the prey and exploitative ability of the predator are expected wherever the criteria of strong interspecific selection are met (as in Figure 1). Across the geographic range of the interaction, the selective environment may vary, and with it the degree of elaboration of exploitative and defensive traits (Thompson 1994, 1997). Nevertheless, the abilities of both species generally should remain matched in areas of sympatry (e.g., Berenbaum and Zangerl 1998). Finally, some historical perspective is required to know whether or not traits are, in fact, "extreme" or "elaborate."

These lines of evidence in support of an arms race type of coevolution come together in the predator-prey interaction between the toxic newt

Taricha granulosa and its garter snake predator *Thamnophis sirtalis* in western North America. Seven species of garter snakes are sympatric with one or more members of the genus *Taricha*, but only *T. sirtalis* has ever been reported to eat *Taricha* (Nussbaum et al. 1983). Early research suggested that *T. sirtalis* is the only predator that is resistant to the effects of the toxin found in *Taricha* (Brodie 1968), but more recent work has revealed that resistance varies among western populations of *T. sirtalis* (Brodie and Brodie 1991). Evolved avoidance of *Taricha* as a prey item may not have been possible for *T. sirtalis* because it feeds primarily on amphibians throughout the range of the genus *Taricha* (Wright and Wright 1957, Fitch 1965, Nussbaum et al. 1983). Prey recognition responses are a genetically correlated suite of traits that mediate foraging in snakes (Arnold 1981, 1992), so evolved avoidance of one prey type might result in avoidance of others.

The phenotypic interface of the interaction between *T. sirtalis* and *T. granulosa* revolves around the chemical defense, TTX, of the newt. TTX is one of the most potent neurotoxins known; molecules of the toxin bind to sodium channels in nerve and muscle tissue, blocking signal propagation (Hille 1992). The toxicity of newts of the genus *Taricha* results almost entirely from high amounts of TTX in the skin (Mosher et al. 1964), and this group is lethal to a wide range of potential predators (Brodie 1968). All newts of the genus *Taricha* possess TTX, but *T. granulosa* is many times more toxic than its congeners (one *T. granulosa* adult contains enough toxin to kill 25,000 white mice; Brodie et al. 1974). Although TTX is found in a variety of animals spanning at least four phyla (reviewed in Daly et al. 1984, 1987, Kodama et al. 1985), *T. granulosa* is the only TTX-possessing animal with a known resistant predator (Brodie 1968, Brodie and Brodie 1990, 1991).

The selective consequences of ingesting a TTX-bearing prey item are severe and obvious. Predators that eat *T. granulosa* virtually always die, sometimes before killing the newt itself. The garter snake *T. sirtalis* is

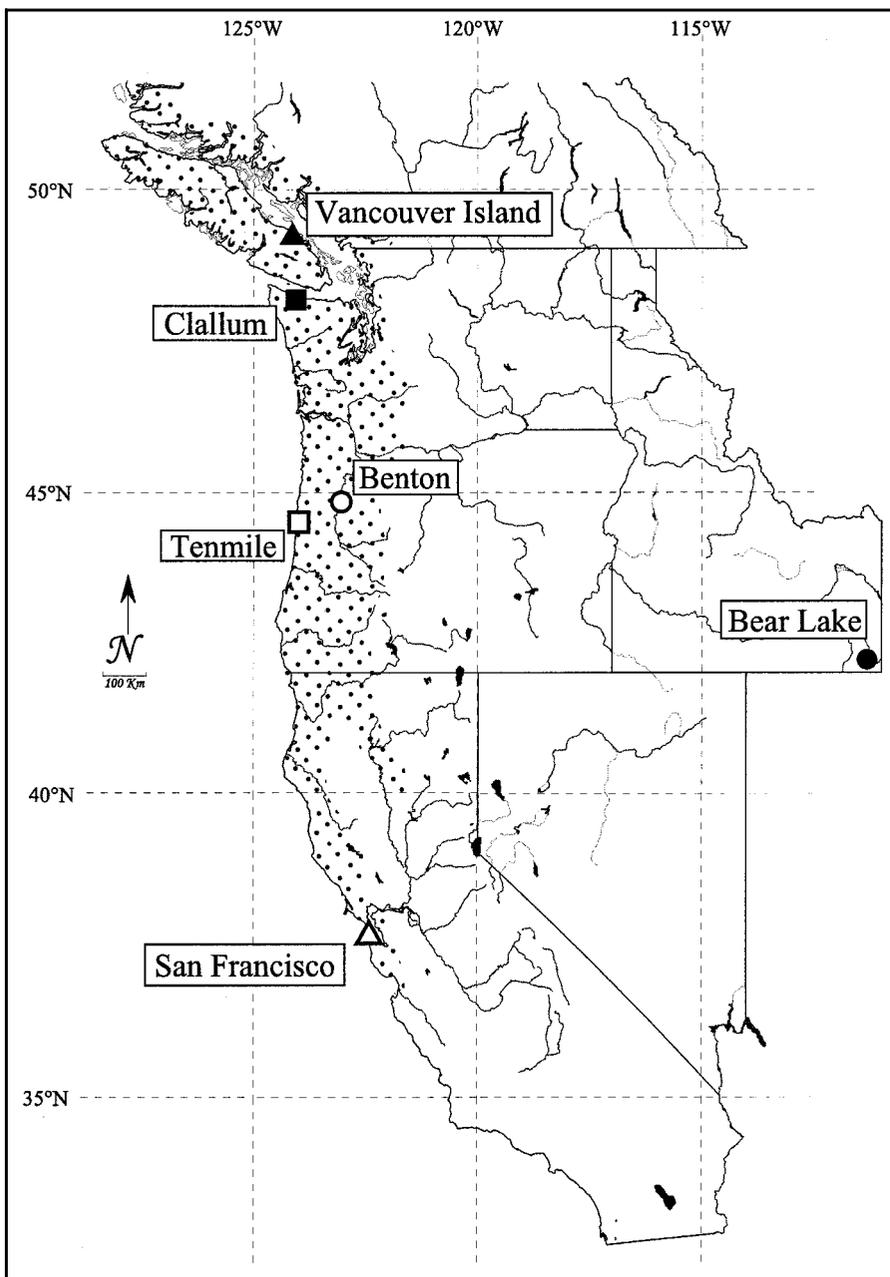


Figure 2. Geographic distribution of tetrodotoxin (TTX) resistance in the garter snake *Thamnophis sirtalis*. Open symbols indicate resistant populations, and solid symbols indicate nonresistant populations. The range of the newt *Taricha granulosa* is shown as the dotted area.

the lone exception to this rule, but even it is not unaffected after swallowing a *Taricha*. One of the first symptoms of TTX poisoning is the loss of muscle control and mobility, and some *T. sirtalis* individuals that swallow a newt and survive may be immobilized for up to 7 hours. Even this reduced effect of TTX can represent a severe consequence, because an individual that cannot move is unable to thermoregulate effectively (and may overheat and die if caught

in a sun spot for too long) or to escape predation. As with other tertiary defenses, the effects of TTX for *T. sirtalis*—or any other species, for that matter—are unavoidable once the predator has attacked the prey. Thus, TTX toxicity fits the model of a dangerous prey defense that holds a strong and predictable consequence for predators (Figure 1).

Evolutionary response of garter snakes. Understanding the evolution-

ary potential and history of a character requires some knowledge of the patterns of variation among individuals, populations, and species. To gather these data, we developed a bioassay to measure TTX resistance based on the negative effect of TTX on locomotor performance (Brodie and Brodie 1990). Individual snakes are injected with a known amount of TTX, and their maximum crawl speed is measured. The reduction in their performance is indicative of their resistance to TTX; snakes unaffected by TTX crawl at 100% of their baseline speed, whereas susceptible snakes may crawl at less than 25% of their normal speed. This technique works because TTX is a neurotoxin, and one of its first effects is to impair muscle control. The injection bioassay is powerful in that it uses small, controllable dosages, preserves individual differences in locomotor behavior, and is ecologically relevant because of the importance of locomotor performance in prey capture and escape from predators. Intraperitoneal injection of TTX produces qualitatively similar effects to ingestion, and previous experiments have demonstrated that TTX is not neutralized in the digestive system or blood of *T. sirtalis* (Edmund D. Brodie Jr., unpublished data). Using this methodology, we have begun to understand the elaboration of a character evolving in response to prey defenses.

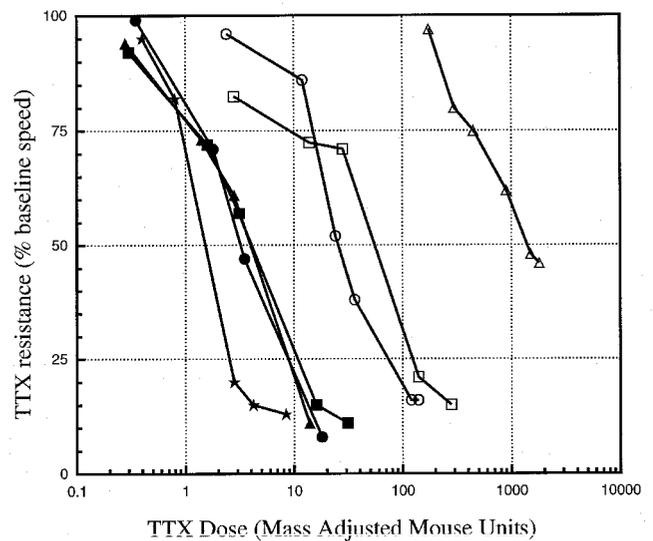
The level of TTX resistance in *T. sirtalis* is clearly a derived character. Interspecific comparisons reveal that *T. sirtalis* is the only species of garter snake that is resistant to TTX at an ecologically relevant level (i.e., sufficient to allow it feed on toxic newts), with a level of resistance 10–1000 times that of any other member of the genus *Thamnophis*. However, phylogenetic analysis also reveals the ancestral condition in the genus *Thamnophis* and its close relatives to be a 10-fold higher resistance to TTX than is found in other colubrids (Motychak et al. in press), suggesting that there may be some predisposition to TTX resistance within the lineage.

More detailed within-population analyses indicate substantial individual variation for selection to act on and ample genetic potential for

evolutionary change. TTX resistance has high heritability (h^2 ranges from 0.65 to 0.8, based on full-sib estimates of over 20 families per population) in three resistant populations studied to date (Brodie and Brodie 1990, unpublished data). Some of this genetic variation is likely controlled by one or a few genes of major effect (Edmund D. Brodie III and Edmund D. Brodie Jr., unpublished data). Environmental influences on resistance appear minimal, and experimental attempts to induce or increase resistance through repeated exposure to TTX have had no effect (Ridenhour et al. 1999). Together, these results demonstrate that TTX resistance is a genetically determined, individually variable character that has the potential to respond to selection. The presence of genes of major effect is congruous with the genetic architecture usually observed for major adaptations, especially those at the phenotypic interface of coevolutionary interactions (Turner 1985, Orr and Coyne 1992, Orr and Irving 1997).

As generally expected for adaptations, resistance to TTX in *T. sirtalis* comes with a cost—in this case, reduced locomotor performance. In three populations (including resistant and nonresistant populations) analyzed so far, we have found evidence of a tradeoff between sprint speed and resistance at both the phenotypic and genetic levels (Brodie and Brodie 1999). Individuals and families that have the greatest resistance to TTX tend to have the slowest sprint speed. The source of this tradeoff may lie in the proximate mechanism of TTX resistance. Although the mechanism is still unknown, resistance most likely results from the existence of TTX-resistant sodium channels. Sodium channels are encoded by a multigene family, and different forms have different affinities for TTX. TTX-resistant channels have been identified in many species; such channels typically exhibit lower conductance and different kinetics than TTX-susceptible channels (Weiss and Horn 1986a, 1986b, Yoshida 1994). If the mechanism of resistance in garter snakes involves the evolution of TTX-insensitive sodium channels, the tradeoff between locomotor perfor-

Figure 3. Population differences in resistance of the garter snake *Thamnophis sirtalis* to tetrodotoxin (TTX). The resistance of each population is plotted as a function of amount of TTX. The symbols for the populations correspond to the localities on the map in Figure 2; stars, Maine population (not shown on Figure 2); solid circles, Bear Lake, Idaho; solid triangles, Vancouver Island, British Columbia; solid squares, Clallum, Washington; open circles, Benton, Oregon; open squares, Tenmile, Oregon; open triangles, San Francisco. Resistance was assayed as the percentage of an individual's crawl speed 30 minutes after an injection of a known concentration of TTX. TTX dose is presented on a log₁₀ scale, in relative units known as MAMUs (mass-adjusted mouse units, or the amount of TTX required to kill 1 gram of white mouse in 10 minutes divided by the mean neonate mass of snakes from a given population). Nonresistant western populations of *T. sirtalis* (Vancouver Island, Clallum, and Bear Lake) are approximately five times more resistant to TTX than eastern populations (represented by the Maine population). Two of these nonresistant western populations (Vancouver Island and Clallum) are sympatric with *Taricha granulosa* populations that lack TTX (see Figure 4). The three resistant populations (Benton, Tenmile, and San Francisco) span an almost 100-fold range of resistance and are sympatric with newt populations known to possess TTX.

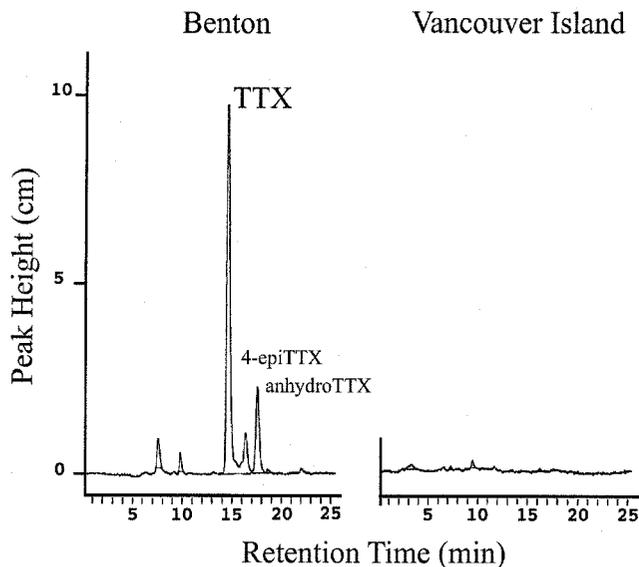


mance and resistance might stem from the altered function of these channels. Whatever the proximate source of the tradeoff, its presence may be an important factor in slowing the evolution of resistance or possibly generating the coevolutionary dynamics predicted by some models (e.g., Saloniemi 1993, Dieckmann et al. 1995, Abrams and Matsuda 1996, Gavrilets 1997).

An arms race between predator and dangerous prey? The evolutionary response of predators to dangerous prey is of course only one side of an arms race, and we are only beginning to collect the data necessary to evaluate whether reciprocal coevolution is occurring between garter snakes and newts. Nevertheless, we have identified some conspicuous patterns that suggest an arms race in action. For example, levels of toxicity of newts and snakes are matched on a coarse scale, and our studies of populations throughout western North America indicate a complex pattern of geographic variation in resistance and toxicity.

TTX resistance varies not only among species of garter snakes, but also among populations of *T. sirtalis*. Using the average percent reduction in speed after an injection of a mass-adjusted dose of TTX, we have compared the effect of TTX among populations of *T. sirtalis* (Figures 2 and 3). Unsurprisingly, populations of snakes that exist outside the range of newts are not resistant to TTX (Brodie and Brodie 1990). Because these populations are not faced with the selective pressures of encountering toxic newts, we would not expect them to have evolved resistance. What is surprising is that among the populations studied that are sympatric with newts and are known to feed on them, resistance varies over an almost 1000-fold range (Brodie and Brodie 1990, 1991). TTX resistance was originally detected in populations from Oregon that are approximately 10–30 times as resistant as allopatric *T. sirtalis* populations or other *Thamnophis* species. However, *T. sirtalis* populations from Vancouver Island and the Olympic Peninsula of Washington State that

Figure 4. Population differences in tetrodotoxin (TTX) levels of newts. Skin extracts from wild-caught *Taricha granulosa* captured in Benton, Oregon, and Vancouver Island, British Columbia, were analyzed for presence of TTX using HPLC (High-Performance Liquid Chromatography). The Benton population of newts has high concentrations of TTX, as well as small amounts of two identifiable analogs, 4-epiTTX and anhydroTTX (the small unlabelled peaks to the left are standards). Neither TTX nor the analogs are found in skin extracts from Vancouver Island newts.



are known to feed on *T. granulosa* are no more resistant than the allopatric populations. We classify these populations as “nonresistant” because their level of resistance is no greater than the ancestral *Thamnophis* condition. At the other extreme are snakes from the San Francisco Bay area (members of the endangered San Francisco garter snake, *Thamnophis sirtalis tetrataenia*) that are almost 100 times more resistant than any other population sampled. This estimate is based on zoo-bred individuals, whose history of inbreeding could affect their level of resistance; however, recent samples have revealed other natural populations with comparable levels of resistance (Edmund D. Brodie III and Edmund D. Brodie Jr., unpublished data).

If the pattern of resistance among populations is so variable, then the factors influencing the evolution of resistance must also differ (i.e., there is a “geographic mosaic” of coevolution, sensu Thompson 1994). The most obvious candidate is the selective environment. Although it has long been assumed that *T. granulosa* are toxic throughout their range and that the level of toxicity is constant within the species, recent observations suggest that both assumptions are incorrect. The presence of TTX in *T. granulosa* was initially documented in the 1960s using specimens from the Willamette Valley of Or-

egon and the San Francisco Bay area, both regions with TTX-resistant *T. sirtalis* populations (Mosher et al. 1964, Wakely et al. 1966, Brodie 1968). Subsequent experiments using skin extract from Vancouver Island newts indicated quantitatively reduced toxicity and qualitatively different symptoms of toxicity in laboratory mice, as compared to newts from the populations known to possess TTX (Brodie and Brodie 1991). This result suggests that newts from Vancouver Island have little or no TTX, which is expected from the finding that nonresistant *T. sirtalis* can feed on them.

We have recently undertaken a survey of the quantitative variation in TTX levels among populations of newts throughout their range. Using HPLC (High-Performance Liquid Chromatography) techniques, we have been able to measure individual differences in TTX concentrations among individual newts and obtain population values for some of the localities for which levels of snake resistance are known. Results indicate that *T. granulosa* populations vary in the presence or absence of TTX in skin, as well as in the amount of TTX (Figure 4; Charles T. Hanifin, Utah State University; Mari Yotsu-Yamashita, Tohoku University, Sendai, Japan; Edmund D. Brodie III; Edmund D. Brodie Jr.; and Takeshi Yasumoto, Japan Food Research Laboratories, Tokyo; unpublished data).

T. granulosa populations from Oregon, where garter snakes are resistant, have the greatest amounts of TTX. Olympic Peninsula *T. granulosa* have much lower levels of TTX, and one population even varies in presence/absence of TTX (with some individuals lacking TTX altogether). Vancouver Island (and surrounding island) *T. granulosa* populations have no TTX at all.

The emerging picture of geographic variation in TTX levels matches that of snake resistance. In the context of a covariance view of selection, the population differences in TTX levels translate to differences in the strength of selection. Where newts lack TTX, predators experience neither a severe nor a predictable consequence of feeding on newts (Figures 1c and 1d), and there is no reason to expect predators to evolve resistance. In fact, given the cost of TTX resistance in *T. sirtalis*, there may even be selection against exploitative abilities in areas where newts lack the toxin. Whether the evolution of resistance represents an arms race is still unclear at this point. The criteria of reciprocity and continued counteradaptation have not yet been demonstrated, and we have little information regarding inheritance, variation of, and selection on defense in prey, although these are all topics of our current research. However, the evolution of prey in response to predator exploitation is expected. The unique feature of the garter snake–newt system is that it demonstrates how dangerous prey can force selection on predators, thereby driving the evolution of exploitative traits.

Conclusions

Although predators and prey are often assumed to coevolve in an arms race–style interaction, both empirical evidence and theoretical expectations suggest that predator–prey interactions often do not follow arms race dynamics. Predator–prey interactions differ from other types of victim–exploiter systems in that selection on predators may frequently be weaker than on prey. The expected consequence of this asymmetry is that prey evolve more rapidly than predators, leaving predators less

able to exploit them. Using the covariance approach to selection as a heuristic, it becomes clear that two factors—the consequence of individual interactions and the predictability of the consequence—influence the strength of selection experienced by one species through interactions with another. A close inspection of these elements in predator–prey systems suggests that the asymmetry in selection is usually driven not by the classic life–dinner principle, but rather by the unpredictability of the consequence when an individual predator fails to capture a prey.

However, when interactions proceed to the handling or subjugation phase of the predation sequence, consequences are usually more predictable. At this stage, prey employ tertiary defenses, such as repellent armor or toxins, that can harm or even kill a predator. In such cases, predators are expected to experience strong selection and to respond evolutionarily. Predators might evolve innate avoidance of dangerous prey, thereby dodging the bullet of selection, or they might evolve exploitative traits that allow continued interaction with the dangerous prey. The latter scenario is exemplified by the interaction between toxic newts and their resistant garter snake predators. Historical, geographic, and intrapopulation patterns of resistance and toxicity all indicate that garter snakes are evolving in response to prey defenses, and that an arms race between predators and prey is taking place.

Acknowledgments

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