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Facultative Mate Choice Drives Adaptive Hybridization

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Mating with another species (hybridization) is often maladaptive. Consequently, females typically avoid heterospecifics as mates. Contrary to these expectations, female spadefoot toads were more likely to choose heterospecific males when exposed to environmental conditions that favor hybridization. Indeed, those females with phenotypic characteristics for which hybridization is most favorable were most likely to switch from choosing conspecifics to heterospecifics. Moreover, environmentally dependent mate choice has evolved only in populations and species that risk engaging in, and can potentially benefit from, hybridization. Thus, when the benefits of mate choice vary, females may radically alter their mate selection in response to their own phenotype and their environment, even to the point of choosing males of other species.

Mating between species typically results in no, few, or poor-quality offspring (1). Consequently, females generally prefer to mate with males of their own species (1–3). When hybridization does occur, it is often ascribed to mistakes during, or constraints on, female mate choice (4–7). Yet, hybridization can sometimes be beneficial (8), and females might facultatively adjust their choice of conspecific versus heterospecific mates depending on the fitness consequences of hybridization (9–12). Such facultative switches in female mate choice may thereby mediate adaptive hybridization and could explain patterns of hybridization observed in many species (8).

Spadefoot toads, *Spea bombifrons* and *Spea multiplicata*, risk hybridizing where they co-occur in the southwestern United States across ~20% of *S. bombifrons*' range (13, 14). Hybrid offspring are viable and can reproduce, albeit with reduced fertility: Hybrid males can be sterile (15) [although the frequency of sterility among hybrid males is unknown (16)], and female hybrids produce fewer eggs than pure-species females (15). Hybridization between these species has historically been spatially variable, with hybrid frequency ranging from 0 to 40% across

populations (14). Hybridization is most common in small ponds that tend to be shallow and highly ephemeral, with *S. bombifrons* females hybridizing more often than *S. multiplicata* females (14).

These observed patterns of hybridization may be explained if *S. bombifrons* females can benefit from hybridization. Spadefoots breed in ephemeral pools (Fig. 1, A and B), and their tadpoles often fail to metamorphose before ponds dry (17). *S. multiplicata* develop more rapidly than *S. bombifrons*, and hybrid tadpoles metamorphose sooner than pure *S. bombifrons* tadpoles (14). Thus, for *S. bombifrons* females, hybridization may enhance offspring survival.

As further evidence that hybridization may be beneficial for *S. bombifrons* females, hybrid offspring of *S. bombifrons* females ("BM" tadpoles) developed significantly faster than did pure *S. bombifrons* tadpoles ("BB" tadpoles) when reared in the lab for 16 days (18) [mean difference in Gosner developmental stage, BB – BM = -0.75 ± 0.28 (SEM), $t_{97} = -2.67$, $P = 0.009$]. Additionally, for tadpoles reared in naturally drying artificial pools in the field (14, 18), the likelihood that all tadpoles metamorphosed in a given replicate was higher for BM tadpoles (likelihood ratio $\chi_1^2 = 8.15$, $P = 0.004$) and increased with maternal condition ($\chi_1^2 = 4.70$, $P = 0.03$). Similarly, the proportion of tadpoles in a replicate that metamorphosed (18) was higher for BM

tadpoles ($F_{1,53} = 11.76$, $P = 0.001$) and increased with maternal condition ($F_{1,53} = 3.98$, $P = 0.05$).

Hybridization by *S. bombifrons* females therefore results in a trade-off: Hybrid offspring may have lower fertility and fecundity, but they can develop faster than pure *S. bombifrons* offspring and may therefore be more likely to escape a drying pool. Consequently, the fitness effects of hybridization depend on the habitat in which offspring develop. Because pond duration depends largely on initial pond size and depth [deeper ponds generally outlast shallow ones (17)], in deep (long-lasting) ponds, pure *S. bombifrons* offspring can metamorphose before the ponds dry (14). Thus, in such ponds, *S. bombifrons* females would have higher fitness by mating with conspecifics. In contrast, in shallow (rapidly drying) ponds, hybridization may be beneficial for *S. bombifrons* females because hybrids are more likely than pure *S. bombifrons* offspring to escape and therefore to survive. Furthermore, a given pond's depth (and longevity) can vary dramatically with the amount of yearly rainfall (Fig. 1, A and B). Thus, because *S. bombifrons* females may encounter year-to-year variation in pond longevity, they may facultatively adjust their choice for conspecific versus heterospecific mates, depending on the depth of their breeding pond.

To evaluate this hypothesis, I tested two predictions by performing controlled mate-choice tests in the lab (18). First, I predicted that *S. bombifrons* females would more likely choose *S. multiplicata* males in shallow ponds than in deep ponds. Second, because maternal condition predicts the likelihood that offspring will metamorphose, I predicted that *S. bombifrons* females in relatively poor condition would be more apt than those in good condition to alter their choice for conspecifics depending on water level.

S. bombifrons females were presented with calls of conspecific versus heterospecific (*S. multiplicata*) males under conditions simulating a deep (long-duration) pond versus a shallow (short-duration) pond (18). When females were tested three times in a deep pool (18), they showed a significant preference for conspecific calls versus heterospecific calls (Wilcoxon signed rank = 245,

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$n = 52$ females, $P = 0.009$) (Fig. 1C). In these deep water trials, individual females were significantly consistent in their choice: females chose the same stimulus, on average, $87.5 \pm 2.5\%$ (SEM) of the time (Wilcoxon signed rank = 345.5, $n = 52$, $P < 0.001$; 34 out of 52 females chose the same stimulus in all three trials). When these same females were tested four times in a shallow pool (18), as a group, they showed no preference for conspecific calls (Wilcoxon signed rank = -84, $n = 52$, $P = 0.24$) (Fig. 1C). Indeed, the frequency with which females chose conspecifics was higher in deep versus shallow water ($t_{51} = 3.16$, $P = 0.003$) (Fig. 1C). Although females as a group were not significantly more likely to choose one stimulus over the other in shallow water, individual females

were significantly consistent in their preference: females chose the same stimulus, on average, $76.4 \pm 2.8\%$ (SEM) of the time (Wilcoxon signed rank = 390, $n = 52$, $P < 0.001$; 19 out of 52 females chose the same stimulus in all four trials, and 30 out of 52 females chose the same stimulus in at least three of the four trials). Thus, *S. bombifrons* females, as a group, were more likely to choose *S. multiplicata* males in shallow ponds than in deep ponds, as predicted.

Also as predicted, whether an individual female switched from choosing conspecifics in deep water to heterospecifics in shallow water depended on the female's condition. Females in relatively poor condition were most likely to make such a switch (Fig. 2A). Poor-condition females may be

more prone to switch because, as noted above, they can potentially benefit more by hybridizing. Indeed, when bred with conspecific males (18), females with a higher propensity to switch their choice from conspecifics in deep water to heterospecifics in shallow water produced tadpoles that developed more slowly than those produced by females with a lower propensity to switch (Fig. 2B). Thus, females' responses to changes in the water level depended on their condition and the developmental rate of their offspring in pure-species pairings, suggesting that female mate choice results from an interplay of a female's own phenotype and the specific ecological circumstances in which her offspring develop.

The tendency to switch patterns of mate choice in response to water level appears to have evolved only in populations and species that risk engaging in, and can potentially benefit from, hybridization. In three mate-choice trials [two in deep water and one in shallow water (18)], allopatric females (females from populations where *S. multiplicata* does not occur) did not discriminate between conspecific and heterospecific calls (first deep water trial: 9 chose conspecific calls, 16 chose heterospecific calls, $\chi_1^2 = 1.99$, $P = 0.16$; second deep water trial: 17 chose conspecific calls, 12 chose heterospecific calls, $\chi_1^2 = 0.87$, $P = 0.35$; shallow water trial: 14 chose conspecific calls, 12 chose heterospecific calls, $\chi_1^2 = 0.15$, $P = 0.69$). These responses were not significantly different among the three trials ($\chi_1^2 = 3.01$, $P = 0.22$). Thus, contrary to sympatric *S. bombifrons* females, allopatric *S. bombifrons* females did not vary their choice depending on water level.

Moreover, switches in patterns of mate choice are not generalized responses of sympatric *Spea* females to shallow water: Sympatric *S. multiplicata* from the same populations as the sympatric *S. bombifrons* used in the experiments above significantly preferred conspecific calls, regardless of water level (deep water: 43 chose conspecific calls, 22 chose heterospecific calls, $\chi_1^2 = 6.91$, $P = 0.009$; shallow water: 47 chose conspecific calls, 29 chose heterospecific calls,

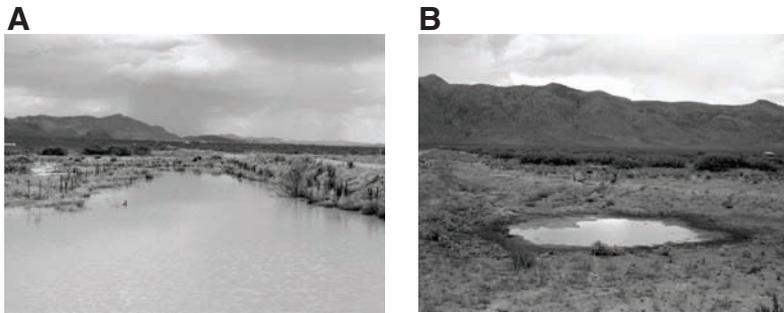
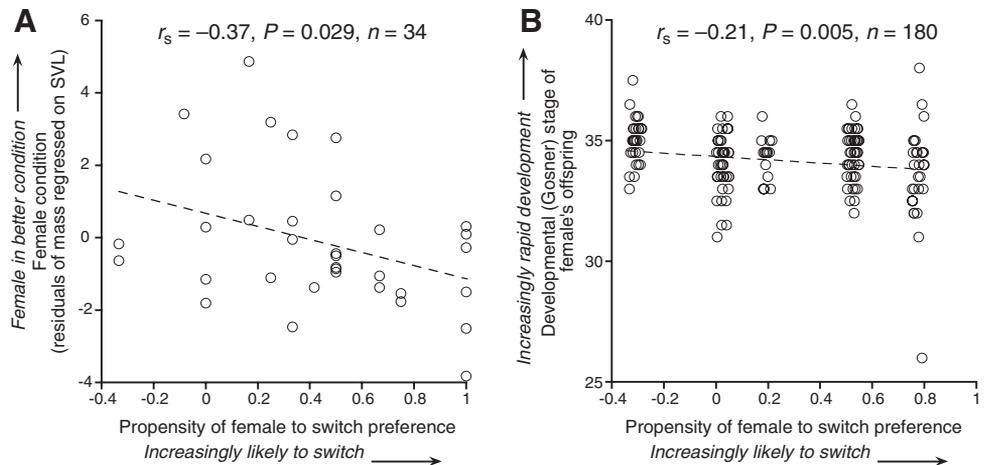


Fig. 1. (A and B) *S. bombifrons* breeding ponds vary in depth (2 to 66 cm) and longevity (7 days to several months; longevity is positively correlated with depth) in different years, depending on the amount of rainfall. (A) and (B) show the same pond in different years. (C) Solid circles represent the mean percent \pm SEM (error bars) of times that conspecific calls were chosen by sympatric *S. bombifrons* females in repeated tests of preference for conspecific versus heterospecific calls (18). The dashed line illustrates a random expectation of 50%. In deep water, females significantly chose conspecific calls more frequently than random (as indicated by the asterisk) and more frequently than they did in shallow water. In shallow water, females as a group showed no preference for conspecific calls.

Fig. 2. (A) Female condition as a function of female propensity to switch from choosing conspecific calls in deep water to choosing heterospecific calls in shallow water (18). (B) Development rate of a female's offspring (from pure *S. bombifrons* pairings) as a function of that female's propensity to switch from choosing conspecific calls in deep water to choosing heterospecific calls in shallow water (18). Each point represents the mean of two tadpoles from a given replicate; there were 15 replicates for each of the 12 females (18). Data are jittered (by adding small random values to the original data along the x axis for presentation only). Each panel shows the results of a nonparametric Spearman rank-order correlation analysis that is not sensitive to outliers (18). Least-squares regression (dashed) lines are shown for illustration only. r_s , Spearman rank correlation coefficient; SVL, snout-to-vent length.



$\chi_1^2 = 4.30$, $P = 0.038$). Mate choice of *S. multiplicata* females did not differ significantly between water-depth treatments ($\chi_1^2 = 0.28$, $P = 0.60$). Thus, because *S. multiplicata* females do not benefit by hybridizing with *S. bombifrons* males (14), the fact that they chose conspecific mates regardless of water level supports the hypothesis that switches in mate choice should evolve only when hybridization is potentially adaptive.

In deep-water trials, sympatric *S. bombifrons* chose conspecific calls significantly more often than did allopatric females (Wilcoxon normal approximation: z score = -2.15 , $P = 0.03$, $n = 81$). The fact that sympatric *S. bombifrons* females discriminated against heterospecifics when hybridization was not favorable (i.e., in deep water) suggests that behaviors that minimize hybridization have evolved in sympatry. Such differences between allopatry and sympatry are expected if selection favors mating behaviors that promote reproductive isolation between species (1, 2, 19–22). Thus, sympatric females have apparently evolved the ability to modify their discrimination against heterospecifics, depending on the fitness consequences of hybridization.

These findings suggest that facultative switches in female mate-choice behavior contribute to adaptive hybridization and explain localized hybridization in habitats where hybrids may have higher fitness (8, 14). In addition, these results suggest how hybrids may persist in the face of a general pattern of selection against them. Generally, when hybrids are disfavored, selection should promote the evolution of behaviors in sympatry that preclude hybridization (i.e., reinforcement) (1, 2, 19–22). As expected, *S. bombifrons* females in sympatry, but not allopatry, discriminate against heterospecifics when hybridization is costly. If, however, females facultatively hybridize when it is beneficial, hybridization may persist locally in the face of a global pattern of reinforcement. The presence of hybrids in systems that have seemingly undergone reinforcement is often attributed to mistakes in mate choice, constraints on female choice, or forced copulation by males (4–7). However, facultative adaptive hybridization potentially explains the persistence of hybrids despite the prediction that reinforcement should eventually eliminate hybridization (19, 23–25).

Generally, whenever fitness is reversed in different habitats, facultative switches in mating behavior may evolve if females routinely experience different habitats and can assess environmental cues that reliably predict offspring fitness (26, 27). Because the fitness consequences of mate choice may often depend on the females' own phenotype or the habitat in which their offspring develop (10, 12, 28), context-dependent female mate choice may be common (9–12). Explaining such variation in mate choice is important, because it can dramatically affect the outcome of sexual selection and, ultimately, speciation.

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Materials and Methods

Fig. S1

Audio S1 and S2

References

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Bypass of DNA Lesions Generated During Anticancer Treatment with Cisplatin by DNA Polymerase η

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DNA polymerase η (Pol η) is a eukaryotic lesion bypass polymerase that helps organisms to survive exposure to ultraviolet (UV) radiation, and tumor cells to gain resistance against cisplatin-based chemotherapy. It allows cells to replicate across cross-link lesions such as 1,2-d(GpG) cisplatin adducts (Pt-GG) and UV-induced *cis-syn* thymine dimers. We present structural and biochemical analysis of how Pol η copies Pt-GG-containing DNA. The damaged DNA is bound in an open DNA binding rim. Nucleotidyl transfer requires the DNA to rotate into an active conformation, driven by hydrogen bonding of the templating base to the dNTP. For the 3'dG of the Pt-GG, this step is accomplished by a Watson-Crick base pair to dCTP and is biochemically efficient and accurate. In contrast, bypass of the 5'dG of the Pt-GG is less efficient and promiscuous for dCTP and dATP as a result of the presence of the rigid Pt cross-link. Our analysis reveals the set of structural features that enable Pol η to replicate across strongly distorting DNA lesions.

All three kingdoms of life possess special Y-family DNA polymerases (1, 2). These enzymes share with high-fidelity DNA polymerases the basic nucleotidyl transfer mechanism and the right-hand-like structure, but

the potential DNA duplex binding surface is increased by a polymerase-associated domain (PAD, also denoted "little finger" for its role in template binding) found only in Y-family polymerases (3). DNA polymerase η (Pol η) in eukaryotes is able to replicate through UV-induced cyclobutane pyrimidine dimers (CPDs) (4–6), or cisplatin-induced 1,2-d(GpG) adducts (Pt-GGs) (7) formed in a typical anticancer therapy with cisplatin (8). Bypass of such cross-links is particularly difficult because two adjacent coding bases are simultaneously damaged. To reveal the mechanism for this poorly understood lesion

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