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Prevalence and Adaptive Impact of Introgression

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Abstract

Alleles that introgressed between species can influence the evolutionary and ecological fate of species exposed to novel environments. Hybrid offspring of different species are often unfit, and yet it has long been argued that introgression can be a potent force in evolution, especially in plants. Over the last two decades, genomic data have increasingly provided evidence that introgression is a critically important source of genetic variation and that this additional variation can be useful in adaptive evolution of both animals and plants. Here, we review factors that influence the probability that foreign genetic variants provide long-term benefits (so-called adaptive introgression) and discuss their potential benefits. We find that introgression plays an important role in adaptive evolution, particularly when a species is far from its fitness optimum, such as when they expand their range or are subject to changing environments.

INTRODUCTION

Darwin's (33) intuition that species evolved, rather than having been created by God, required that they emerged somewhat gradually by diverging from other species. However, even Thomas Henry Huxley, known as Darwin's bulldog, objected that Darwin had not solved the problem of the origin of hybrid incompatibility between species (65), which had been viewed as a standard definition of species (24). For example, mules are typically sterile, and so the horse and donkey parents were considered clearly different species. In "Hybridism," Chapter 8 of *On the Origin of Species*, Darwin (33) instead argued that while hybrid sterility and inviability are correlated with what we mean by species in taxonomy, the correlation is loose: Many clearly demarcated species lack hybrid incompatibility, and incompatibilities often also occur within taxa we consider to be species. Darwin suggested that incompatibilities evolved as incidental by-products of divergence and were not, therefore, useful as a definition or essence of speciation. The weakness of the correlation between hybrid incompatibility and what we mean by species, especially in intermediate cases ("doubtful species"), strengthened Darwin's gradualist view of speciation. Soon after Darwin's death, George Romanes (135), claiming discipleship of Darwin, nevertheless attempted to argue that hybrid incompatibilities were advantageous and evolved via a process he called physiological selection. In the twentieth century, physiological and mating incompatibilities were seen as isolating mechanisms between species, and this led to a renewal of opinion among today's evolutionary biologists that species are best defined by reproductive isolation, an idea known as the biological species concept (29, 36, 100).

Nonetheless, many species are known to hybridize occasionally in captivity and in the wild. Zoologists belittled this trickle of hybridization, which was interpreted to have minimal effects on natural populations (100). In contrast, botanists emphasized the importance of hybridization, introgression (the acquisition of genetic variation from another species), and recombinational speciation (today known as homoploid hybrid speciation) (5, 6). By the mid-twentieth century, cytological studies had also shown that a substantial fraction of flowering plant speciation events involved polyploid hybrids of divergent parent species (56). More recently, data on the importance of animal hybridization were beginning to accumulate (29, 55). The introduction of techniques enabling substantial numbers of molecular genetic markers to be sampled across the genome, and, more recently, genome sequencing led to greatly improved power to test different ideas about plant and animal speciation (1, 10, 13, 89, 131, 149). Today, an avalanche of genomic results demonstrate both frequent gene flow among species, some of which is adaptive, and that hybrid speciation occurs in animals as well as plants (39, 40, 43, 48–49, 79, 83, 94, 104, 117, 126, 134, 141, 154).

A great deal of attention has been paid to the immediate, negative consequences of hybridization, including hybrid sterility and hybrid inviability of early generation hybrids (15, 29, 157). Yet despite such impediments, it is becoming clear that alleles with positive impacts on fitness have been exchanged between populations, and that introgressed alleles can persist for millions of years (11, 14, 119). While the fact of introgression is today broadly accepted, we still lack an understanding of its magnitude and long-term effects. What fraction of the genome is due to introgression across the tree (or network) of life? How likely are introgressed fragments of the genome to aid adaptation in spite of linked deleterious alleles? Gene flow among species was traditionally viewed as a hindrance to speciation, but how likely is it that adaptive introgression leads to hybrid speciation or to adaptive radiation? Can we identify scenarios that are more conducive to adaptive introgression?

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HYBRIDIZATION, INTROGRESSION, ADMIXTURE, AND HYBRID SPECIATION

Hybridization is the production of offspring between divergent populations, and in the present context, we mean between recognized species. Hybridization between divergently adapted populations is generally rather deleterious: First-generation hybrids and early generation backcrosses are often inviable or sterile, and so there is no guarantee that hybridization will lead to gene flow in the longer term. For cases where genes are successfully transferred among species, the term introgressive hybridization, or merely introgression, came into use following Edgar Anderson's (5) pioneering work. While hybridization is largely deleterious, the phrase adaptive introgression describes the acquisition of advantageous variation via introgression (62, 72). This term should not be taken to mean that the initial hybridization process itself was adaptive and selected for or that most hybrids are fitter. Heterosis of first-generation hybrids between species has been used to suggest that hybridization itself is often adaptive (12). However, heterosis depends on the likely mode of adaptation and dominance, and it is probable that any initial gain in fitness is greatly outweighed by low average fitness of later generation hybrids (15). It is usually only after a long process of selection among hybrids that any of the remaining introgressed variation becomes adaptive. Even after extensive backcrossing, introgressed variation may still be selected against and be gradually lost. The term admixture has been used to describe the introgressed fraction that remains in the genomes of modern humans thousands of generations since hybridization with archaic hominins such as Neanderthals (57, 62).

Hybridization and introgression can also lead to the origin of a novel species lineage, or hybrid speciation. This has been well documented for allopolyploid hybrid speciation in plants (56), but a second type of hybrid speciation that does not involve whole-genome duplication, recombinational speciation, or, in today's terminology, homoploid hybrid speciation, is also known in plants, though suspected to be rare (129). Controversy exists about the meaning of hybrid speciation because the term has been applied rather loosely to cases where there is evidence for speciation as well as introgression in the same lineages. Part of the problem of defining hybrid speciation is that species and speciation are themselves hard to define.

A strict definition of hybrid speciation might require a novel hybrid species to coexist and overlap spatially with both parents, which would prove that all three are good species. In practice we rarely see such patterns in nature. For example, several well-known hybrid species of *Helianthus* sunflowers are clearly hybrids (see **Figure 1**) but normally occupy extreme environments where parental species are absent: *Helianthus anomalus* is found in sand dune habitats; *Helianthus deserticola* is a xerophytic species found in sand/clay deserts; and *Helianthus paradoxus* is a specialist on high salinity soils. Both parents (*Helianthus annuus*, *Helianthus petiolaris*) are found mainly in more mesic habitats (130). This may be a general phenomenon if hybridization allows species to expand their niches through recombination of advantageous traits (90, 95, 129). Similarly, the homoploid hybrid butterfly species *Heliconius heurippa* overlaps with only one of its parent species, *Heliconius melpomene* (98). Therefore, this definition would exclude many cases that have hitherto been considered hybrid speciation.

An alternative strict definition of hybrid speciation is that reproductive isolation is required and has been produced as a direct result of hybridization that led to the emergence of the new species. Proving hybrid speciation requires "demonstrating that isolating mechanisms were derived from hybridization" (141, p. 1556). The homoploid *Helianthus* hybrid species, as well as allopolyploid hybrid species, clearly qualify: They tend to be rather strongly reproductively isolated (**Figure 1**), due in part to stabilized recombinant parental chromosomal arrangements that make hybridization difficult with either parent (130). The wing coloration of *H. heurippa* derives

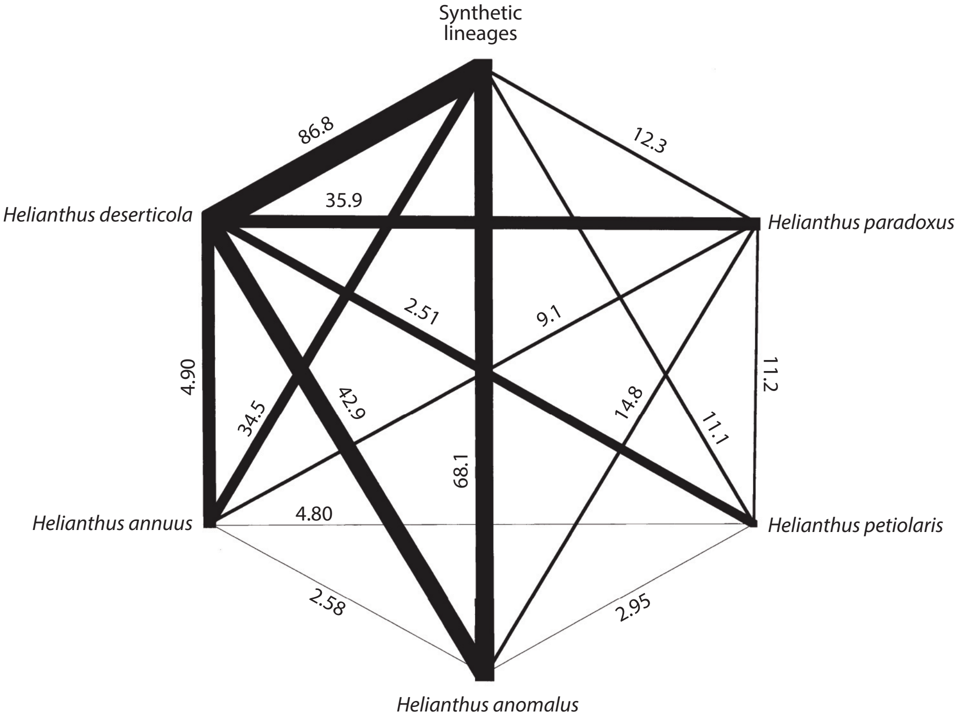


Figure 1

Crossability of *Helianthus* sunflower species. Percentages indicate pollen viability of first-generation hybrids. The three homoploid hybrid species *Helianthus anomalus*, *Helianthus deserticola*, and *Helianthus paradoxus*, as well as the experimentally produced synthetic lineages, are all homoploid hybrid lineages produced by crosses between *Helianthus annuus* and *Helianthus petiolaris*. Line thickness is proportional to reproductive compatibility. Figure reproduced with permission from Reference 130.

from hybridization between its parents, *H. melpomene melpomene* and the *Heliconius timareta/cydno* superspecies (9, 91). The red and yellow hybrid coloration leads to premating isolation between *H. heurippa* and *H. melpomene* and weaker assortative mate choice between *H. heurippa* and *H. cydno* (98). The case for coloration-led premating isolation, however, is now weakened by the discovery of a data analysis error in the original paper (99). The case of hybrid origin of color pattern is clear, but its involvement in reproductive isolation between *H. timareta/cydno* and *H. heurippa* is now in doubt. Nonetheless, *H. cydno* and *H. timareta* remain partially isolated from *H. heurippa*, in part due to color pattern but also perhaps due to pheromonal communication, in experimental tests (61, 98, 99). In addition, based on genome-wide sequence data, little genetic information, apart from coloration-determining genes, was inherited from *H. melpomene*, and it could therefore be argued that the lack of sympatry of *H. heurippa* and *H. timareta/H. cydno* is more simply explained if *H. heurippa* is a subspecies of a more widespread species, *H. timareta*, that has undergone introgression from *H. melpomene*. Like *H. heurippa*, most of the more southern forms of the same *H. timareta* lineage have also clearly acquired adaptive coloration, used in Müllerian mimicry, from various other local forms of *H. melpomene* (34, 51, 107).

In contrast, the butterfly *Heliconius elevatus* appears to be a hybrid species that coexists widely with both parents across most of the Amazon basin (34, 137). *H. elevatus* acquired color-pattern-determining loci via introgression with *H. melpomene* (34, 162), although its ancestor and the majority of its genome were much closer to *Heliconius pardalinus* (34, 137). *H. elevatus* today is sympatric with and reproductively isolated from both parental species and so likely obeys both of the above strict definitions of hybrid speciation. Yet, based on genomic data, *H. elevatus* could be viewed as little more than an introgressed sister species of *H. pardalinus*.

However, this second strict definition is controversial: Botanists reacted against the Schumer et al. criteria (141), arguing, "We think that if there is evidence that a hybridization event has given rise to an established, persistent, morphologically and ecologically distinct hybrid lineage, the recognition of this fact should not be compromised by whether or not we can demonstrate that hybridization was directly the cause of [reproductive isolation]" (112, p. 514). Especially if the hybridization that led to speciation was ancient, it is often very difficult to determine whether "isolating mechanisms were derived from hybridization" (141, p. 1556). A different, more tree-based definition, under the multispecies-coalescent-with-introgression (MSci) model, also seems reasonable: Two lineages fuse to form a third distinct lineage in a single speciation event (47, 77) (see also the section below titled Assessing Prevalence of Introgression). Regardless of whether adaptive introgression events are classified as hybrid speciation, they can play an important role in the adaptive divergence of many species. For the purposes of the rest of this article, we concentrate more on documenting introgression, the factors that make it more or less likely, and its adaptive consequences than on discussing the semantic issue of whether introgression led to hybrid speciation.

ASSESSING PREVALENCE OF INTROGRESSION

Methods for detecting and quantifying introgression with genomic data have been recently reviewed elsewhere (41, 64), and we summarize them only briefly. Because diploid genomes recombine each generation during meiosis, individuals contain blends of loci with unique genealogies and evolutionary histories. If introgression occurred, each part of the genome may have different ancestors, and genealogical or gene tree information can be used to make evolutionary inferences (47, 58, 87, 94, 147). A number of tests have been devised to estimate the prevalence of introgressed loci or genomic regions with a history of interspecific gene flow. Some methods, such as the widely used D statistics and their extensions, use DNA site patterns in subsets of species to test the null hypothesis that alleles are shared between nonsister species due to incomplete lineage sorting; a bias toward nonsister sharing implies introgression (23, 118, 121). Others use gene tree branch length information and coalescent theory in such tests (39) or address the more complex problem of generating full phylogenetic networks that include hybridization edges (22, 41, 148). Underlying models of gene flow vary between network estimation methods. For example, in models based in coalescent theory, isolation-with-migration (IM) models assume migration for a sustained period of time (63) while MSci models assume pulses of gene flow at particular times (47, 165) (**Figure 2**). These strategies estimate models with different sets of parameters, and it can often be difficult, as well as computationally challenging, to choose among options. The choices can be so difficult, in fact, that some introgression researchers select a wide range of models and then compare likelihoods of the data from those models in a variety of ways (84, 88).

Methods that estimate the probability that loci across the genome have a history of introgression are widely accessible and widely used. Nonetheless, they are based mostly on an assumption of neutrality: that the vast majority of informative sites are neutral. Detecting adaptive introgression in the genome requires an additional test for positive selection, which typically requires population-level sampling. Powerful methods to identify selection on a genome-wide scale have been developed based on expected patterns of heterozygosity and expected changes in the coalescent process around selected sites (21, 35, 73, 144). These techniques have recently been adapted

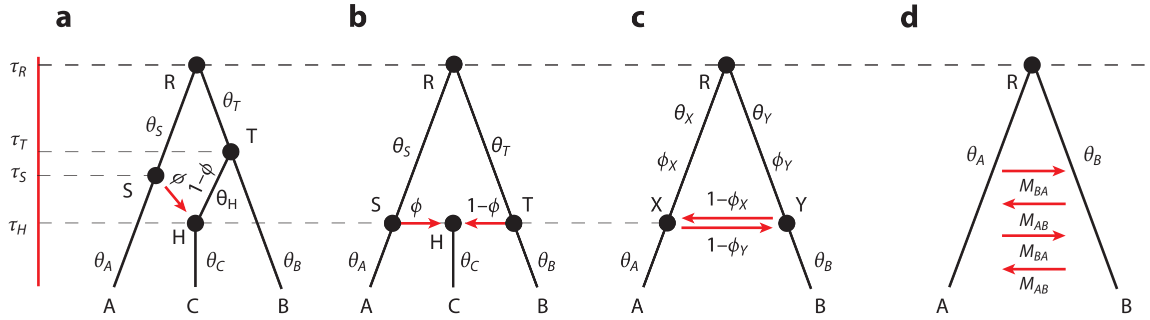


Figure 2

Models of introgression. Genealogical models used to estimate introgression differ in their assumptions. We here show four models that differ in their hypotheses and, therefore, in model parameters. (*a*) Introgression, in which an ancestor of species A, which diverged from A at time τ_S, contributed genetic material to the ancestor of species C at time τ_H. (*b*) Ancestors of species A and B both contribute genetic material to an ancestor of species C at the same time, τ_H. (*c*) Bidirectional, instantaneous gene flow. Models in panels *a* and *c* represent classical models of introgression, while the model in panel *b* in a phylogenetic sense represents hybrid speciation. In each model, populations have a population size designated by θ and probability of genetic contribution designated by ϕ. (*d*) Species A and B contribute genetic material to each other at a constant rate, starting at their divergence. Models in panels *a*, *b*, and *c* are alternatives within the MSci framework, while the model in panel *d* is within the isolation-with-migration (IM) framework (47). Figure adapted with permission from References 32 (panel *d*) and 47 (panels *a–c*).

to models of evolution that include introgression (108, 144). One promising avenue is analysis of genomic clines (52). This framework identifies introgressed alleles that are present at unexpected frequencies, given the average hybrid makeup of a population. Adaptive introgression is inferred if, for example, introgressed alleles are at high frequencies, even though the genome as a whole is not broadly admixed (52).

As genome sequencing technology has improved, methods have evolved, using genome-wide single-nucleotide polymorphism (SNP) data and more complex models to identify subtle adaptive effects in populations. New analytical techniques are also currently being developed to take advantage of phased haplotype information in diploids, revealed by long-read or linked-read sequence data (105). Indirect measures of haplotype frequency based on allele frequency (42, 138, 161), as well as inferred haplotypes based on known pedigrees and parental genotypes [i.e., quantitative trait locus (QTL) mapping (reviewed in 146)], are widely used and have proved effective. However, direct sequencing of haplotypes will reduce the need for error-prone inference and yield more confident assessments of the strength of selection, timing of sweeps, and geographic population structure of selected regions of the genome (105).

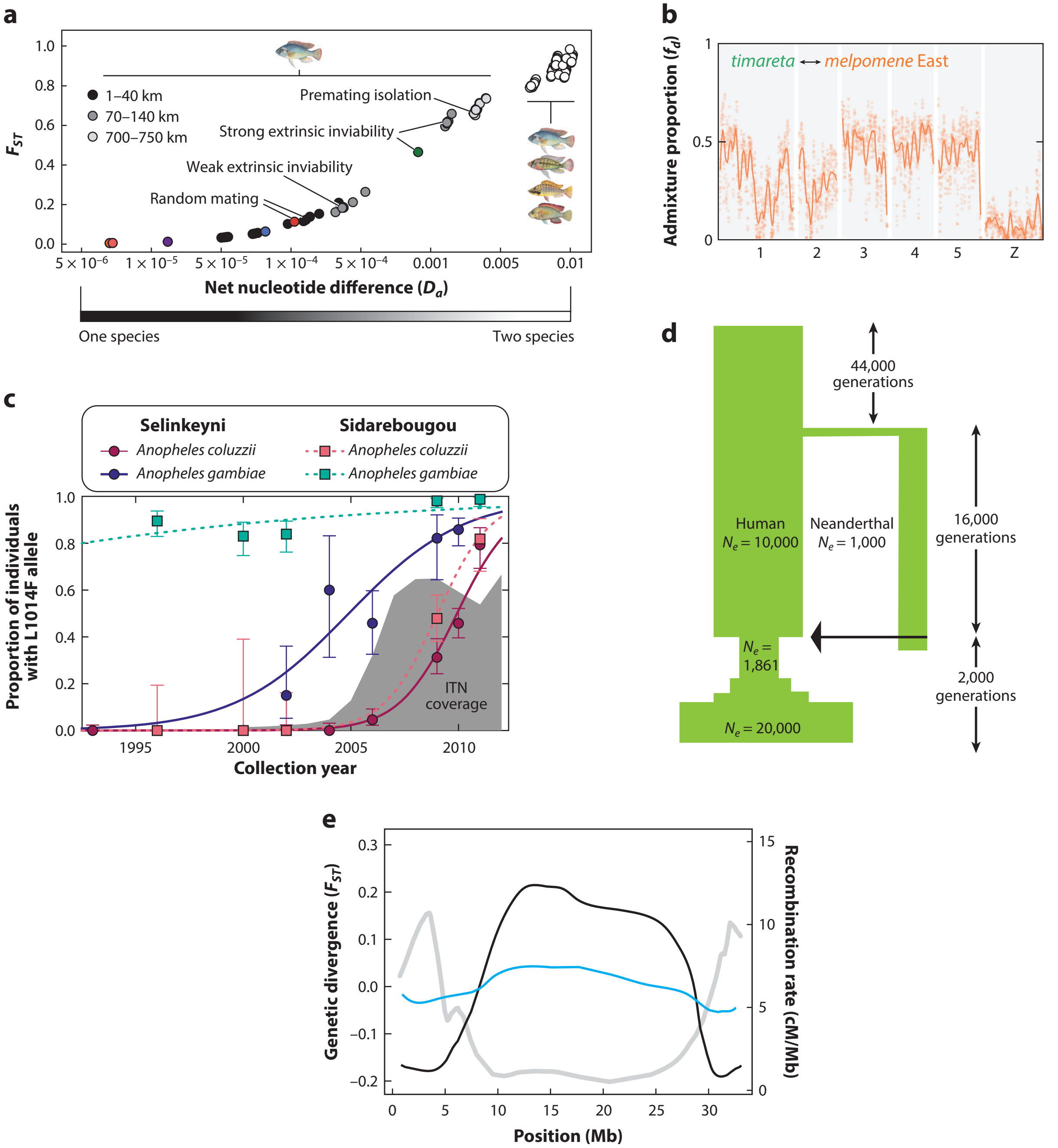
NONADAPTIVE AND ADAPTIVE INTROGRESSION

The various methods reviewed above (41, 64) have shown that hybridization contributes substantial genomic variation to many groups of species across the tree of life (94, 155). The fraction of the genome that introgressed has an enormous range—from around 2% in the snowshoe hare to over 70% in *Anopheles* mosquitoes (48, 68). In addition to learning that introgressed ancestry may be abundant within a particular genome, we have also found introgression to be common among species. The best evidence for this comes from broad phylogenetic studies where species were not chosen on the basis of known hybridization. For example, a recent study of 155 species of *Drosophila* and related genera divided the clade into nine broad monophyletic groups and identified evidence of introgression in eight of them (153). Similarly, in an analysis of 40 *Heliconius* genomes, at least 12 instances of gene flow were inferred, involving all major clades (75). Rather than forming a preponderance of cases, phylogenies with no evidence of gene flow are beginning to seem like the exception rather than the rule. Clades as diverse as fossil and living elephants (117), darters (86), tomatoes (120), and yeast (38) all show strong evidence of introgression throughout their history.

Even in groups where introgression is common, its prevalence can vary. Different pairs of species exchange different fractions of their genome. A simple explanation for variation in introgressed ancestry is variation in divergence between hybridizing species. On average, as species diverge, we find that genetic incompatibility increases and the incidence of hybridization (and introgression) declines, although the relationship is often noisy (27, 28, 54, 89, 93, 97, 109, 116) (**Figure 3*a***). The correlation between divergence and incompatibility is in part due to the evolution of epistatic interactions, known as Dobzhansky-Muller incompatibilities, between alleles from different species: Substitutions in one lineage can be neutral or beneficial but will sometimes interact negatively with derived alleles in another lineage (36, 110). As the time since the common ancestor and the number of divergent substitutions increase, the number of two-locus negative epistatic interactions between a pair of isolated populations is expected to increase quadratically, leading to a snowballing effect with time (116); multilocus incompatibilities (123) can accelerate even faster. Whether declines in hybrid fitness do conform to a snowball effect in nature is still unclear; in any case, the relationship between percent divergence and hybrid compatibility is highly variable, even among species with similar genetic divergence (28, 54).

There is little doubt that the fraction of the genome that introgressed as a function of time since divergence does not fully explain observed levels of admixture or its heterogeneity across the genome: Natural selection on introgressed alleles almost certainly plays a part (**Figure 3*b*,*c***). Adaptive introgression is often envisaged to involve single traits or loci, but there are a number of additional ways whereby hybridization can lead to improved fitness. Adaptive introgression likely depends on degree of genetic similarity, gene flow among populations within species, and the fitness of each population in its own and novel environments. For example, in pairs of species that are closely related or hybridize often, introgression can increase effective population size (N_e) across much of the genome (122). Introgression may sometimes prove beneficial for species with small populations, such as endangered species, because natural selection in a diploid population is ineffective if the coefficient of selection on an allele, s, is less than $\sim 1/(4N_e)$ (60, 166). Weakly deleterious alleles will more readily persist and be fixed stochastically in small populations. A larger effective population size leads to (*a*) greater efficiency of natural selection that will improve the use of weakly advantageous alleles and more successfully purge weakly deleterious alleles; (*b*) a supply of novel genetic variation on which selection can act; and (*c*) increased heterozygosity that can rescue populations from inbreeding depression (3, 4).

Alleles that cross the species boundary may provide adaptive benefits other than their selective effect in the source population (30, 50, 145). As one example, genomic regions that fail to introgress between the butterflies *H. pardalinus* and *H. elevatus* in the Amazon have around half of the levels of polymorphism compared to levels in regions in which gene flow is pervasive, demonstrating that increased variation is a widespread result of hybridization in these species (76). In Trinidadian guppies, an influx of migrants from a large downstream population into a smaller upstream population helped to increase fitness and genetic variation (46). These conspecific populations had adapted to different ecological conditions, but gene flow did not swamp locally adaptive alleles in the recipient population, as has been suggested in other cases (156). Evolutionary biologists tend to view an absence of gene flow as a positive outcome of speciation. Yet, because of the effect on the reduction of effective population size and the resulting reduced efficiency of natural selection, completion of speciation may prove unfavorable (16). Individuals of divergently adapted species may be mostly selected to minimize hybridization to avoid unfit offspring, but their mistakes may aid the ultimate survival of the populations to which they belong. However, the relationship between small population sizes and increased genetic load is complex, and adding foreign genetic



(Caption appears on following page)

Figure 3 (*Figure appears on preceding page*)

Factors determining the extent of introgression. (*a*) Genetic divergence (measured by fixation index, F_{ST}). Pairs of populations, such as these cichlids, are more likely to hybridize if they are closely related (164). Panel *a* adapted from Reference 164; CC BY 4.0. (*b*) Selection against deleterious alleles. Across many pairs of hybridizing species, including *Heliconius timareta* and *Heliconius melpomene* (*mel*-E) butterflies shown here, the proportion of introgressed variants is reduced on the sex chromosome. This is hypothesized to be due partly to deleterious recessive alleles being expressed in the heterogametic sex and partly to the fact that genes that contribute to hybrid incompatibility appear to be more common on sex chromosomes (96). Only 5 of the 20 autosomes are shown due to space constraints, but the pattern is consistent across all 20 autosomes. Panel *b* adapted with permission from Reference 96; CC BY 4.0. (*c*) Selection for beneficial alleles. An increase in the use of insecticide-treated bed nets (ITNs) led first to an increase in frequency of the *kdr* pyrethroid resistance allele L1014F in *Anopheles gambiae*, and a later increase in frequency in *Anopheles coluzzii* after introgression from the former species (113). Panel *c* adapted with permission from Reference 113. (*d*) Demography. Low effective population sizes (N_e) of species like Neanderthals may lead to increased frequencies of segregating deleterious alleles. When these alleles introgress into larger population species like modern humans, they may contribute to fitness decline (59). Panel *d* adapted with permission from Reference 59 (*e*) Recombination. In three-spined sticklebacks, as in many other species, regions of the genome with low rates of recombination (*gray line*) prevent deleterious introgressed alleles from becoming decoupled from neighboring loci. This may prevent gene flow, resulting in higher levels of divergence (F_{ST}) in regions of low recombination (*blue* and *black lines*) (133). Panel *e* adapted with permission from Reference 133.

variation from a population with large effective size to a small population can sometimes result in a crash in population size (78) (see the section below titled Demography).

In more divergent species, or those with fewer opportunities to interbreed, genes may not travel very freely among hybridizing populations. However, even here, one must not look only to large-effect loci for adaptive introgression. Analysis of genomic variation has revealed cases of introgressed alleles that segregate at frequencies higher than expected under a neutral or slightly deleterious model (45, 53, 128, 139, 163). This provides evidence for adaptive introgression, even if the advantages of introgressed alleles are yet to be identified. In Europe, hybridization between *Mus musculus musculus* and *M. musculus domesticus* has resulted in a history of introgression in approximately 3–18% of the genome, even far from the narrow hybrid zone (152). Introgressed alleles at greater than expected frequencies were inferred to be advantageous and to have undergone selective sweeps, although selective coefficients were not estimated. In the northern Rocky Mountains of the United States, recently introduced rainbow trout hybridize with westslope cutthroat trout in mountain streams (102). Across several independent hybrid zones, there is an overrepresentation of certain rainbow trout alleles relative to neutral expectations (17). Selective coefficients as large as 0.05 are needed to explain the frequencies of these alleles in hybrid populations, which are consistent across zones. The specific functions of these high-frequency alleles are still unknown, but functional categories such as transport of toxic compounds were overrepresented among introgressed loci. This could be indicative of polygenic selection on particular traits or on multiple different traits in hybrid trout populations.

Only alleles with strongly beneficial effects are likely to introgress between highly divergent populations or species, because of widespread genetic incompatibilities (2, 124). For example, adaptive responses to extreme anthropogenic selective pressures, such as rodenticide resistance transferred from *Mus spretus* to *M. musculus domesticus* (150) or *kdr* insecticide resistance from *Anopheles gambiae* to *Anopheles coluzzii* mosquitoes (113), involve single loci with very strong selective advantages (lower-bound selection coefficient $s = 0.28$ and 0.13, respectively). Another insecticide resistance allele was recently identified as adaptively introgressed from the moth *Helicoverpa armigera* into *Helicoverpa zea*: Although no selective coefficient was estimated, the frequency of the introgressed allele rose from 0% to 70% in just 4 years, implying very strong selection (158). *Heliconius* butterflies experience strong selection for local mimetic color patterns (20, 80, 92). Across a *Heliconius erato* color pattern cline in Peru, the average selection coefficients for three pattern-determining loci were ~0.22 (92, 136). These large-effect color pattern switch loci have also been passed between hybridizing species within the genus through introgression (34, 108, 162). Similarly, the allele regulating expression of the *AGOUTI* pigmentation gene, resulting in a winter brown as opposed to a winter white coat, arose in the black-tailed jackrabbit (*Lepus californicus*) and was transferred to populations of snowshoe hare (*Lepus americanus*) (68). This phenotype, which is adaptive in the relatively temperate Pacific Northwest, had a selective advantage of between 0.027 and 0.049 (69).

EFFECTS OF DEMOGRAPHY AND RECOMBINATION

Some introgressed alleles are globally or locally beneficial, others are globally or locally deleterious, and still others will be effectively neutral. However, introgressed alleles may not act independently of other loci. Instead, one must interpret their impacts in the context of interactions among loci. Two factors that influence non-independence have been studied in depth: Recombination determines the rate at which introgressed alleles at two or more loci become dissociated, and demography influences the effectiveness of natural selection on linked introgressed alleles.

Recombination

Regions of the genome with high recombination rates tend to be more permissive to introgression than regions with lower recombination rates (2, 71, 111) (**Figure 3*d***). This is in part due to the effects of selection on sites linked to introgressed alleles (i.e., linked selection) (18, 19, 25, 31). If a particular genomic region has positive (i.e., selective sweep) or negative (i.e., background selection) effects, both the region itself and neighboring variants will be swept into or out of the population, which will tend to reduce variation around the selected site. The effects of linked selection vary locally depending on recombination rate, but the process has a global impact across the genome. In humans, allele frequencies of a majority of SNPs in the genome are impacted by background selection or selective sweeps (125). Recombination is also heterogeneous across the genome—in many species, such as three-spined sticklebacks, recombination rate is high at the ends of chromosomes and low in the center, especially near centromeres (132), while in others, like *Heliconius* butterflies, recombination is higher in the center and lower at the ends (96, 151). These patterns mean that the probability of introgression for loci with a given selective advantage or disadvantage varies depending on physical location in the genome. Within low recombination regions, introgressed loci are effectively linked to a larger number of deleterious alleles. Beneficial alleles must have high selective coefficients to overcome the combined effects of negative linked selection against their neighbors and rise to high frequency in recipient populations. Low recombination regions of the genome can harbor multiple divergently advantageous alleles, aiding stable polymorphisms among ecotypes or among species due to divergent selection (26, 74). Interestingly, although fixed inversions are more resistant to introgression because they inhibit recombination, introgression can also transfer inversions as cassettes of globally adaptive alleles between populations (66). Conversely, in regions of high recombination, mildly advantageous alleles can recombine away from deleterious alleles and escape the effects of linked negative selection.

In addition to the effects of local recombination rate and selection around a locus of interest, aggregate genome-wide recombination rate contributes to population-level variation in introgressed ancestry (159). This aggregate rate, or the probability that any two loci in the genome recombine in each meiosis, is largely driven by the haploid number of chromosomes because the majority of this mixing is accomplished through independent assortment (160). In species with high global recombination, deleterious introgressed ancestry will be distributed rapidly among all members of a population. Such populations will have a low variance in fitness, due to similar proportions of deleterious introgressed ancestry among individuals, and natural selection will purge deleterious alleles at a low rate. Simulations assuming high (human, $n = 23$) and low (*Drosophila*, $n = 4$) aggregate recombination rates show that "*Drosophila* purges as much introgressed DNA in 13 generations as humans do in 2,000 generations " (159, p. 10). Consistent with this argument, *Heliconius* butterflies show a much stronger correlation between chromosome size and introgression than between local recombination rate and introgression (39). Because each *Heliconius* chromosome has approximately one crossover per meiosis (96), the probability that linked loci recombine on a short chromosome is higher than on a long chromosome. Introgressed variation on shorter chromosomes, therefore, may equilibrate across the population more quickly than that on longer chromosomes, while that on long chromosomes will remain more heterogeneous, with larger blocks of introgressed and non-introgressed regions. This led to an unequal rate of purging of introgressed ancestry and the strong observed negative correlation between chromosome size and fraction of loci introgressed (159).

Demography

When deleterious alleles introgress into larger populations and the selective effects remain constant, individuals that carry them will have lower fitness, regardless of epistasis between introgressed and nonintrogressed alleles. This scenario is exemplified by recent models of Neanderthal–modern human gene flow (70) (**Figure 3*e***). In these models, Neanderthals interbreed freely with modern humans, the latter having a historical N_e of approximately 10 times that of Neanderthals. Hybrids with Neanderthals likely suffered a fitness cost simply due to deleterious effects of Neanderthal alleles, leading to a gradual loss of Neanderthal ancestry in modern humans to about 2% of today's non-African human genomes. This deleterious effect of hybridization led to an inverse correlation between recombination rate and introgressed ancestry (142), as expected from theory (159).

Alternatively, introgression from large populations into small ones can reverse the correlation between gene flow and recombination. If a large population sends migrants into a small population, individuals with hybrid ancestry may have fewer deleterious alleles. In addition, if the population is so small as to have appreciable levels of inbreeding, introgression may contribute needed heterozygosity to rescue individuals from inbreeding depression. This is the basis for hybrid rescue practiced in the conservation community (81). In brook trout, where domesticated individuals with a large N_e hybridized with wild individuals with a small N_e, introduced domesticated ancestry has become more common in genomic regions with low recombination rates (82).

DISCUSSION

We have examined the prevalence of introgressed ancestry in genomes, the ways in which introgressed alleles can be adaptive, and the demographic factors that determine introgression probability. However, we have yet to answer the overarching question: How important is adaptive introgression in evolution? To address that question requires an investigation of how often adaptation of any sort depends on introgressed alleles, or how often species divergence of any sort is accompanied or aided by introgression. While still unanswered, these questions have begun to be asked in specific groups (106). A more tractable question given current data might be, When do we expect hybridization to be of most importance? For introgression to take place, two species must have overlapping geographic ranges and must be sufficiently closely related so that at least some hybrid offspring are fertile. In addition, although most hybrids are expected to be unfit, the adaptive landscape must be such that some recombinant hybrids have high fitness. One instance where both conditions are likely met is in rapid adaptive radiations: Novel populations are able to expand into new niches due to key innovations or ecological opportunity (95, 140, 143). Genomic introgression is a feature of many rapid radiations studied at a genomic scale, including in cichlid fish, *Heliconius* butterflies, Darwin's finches, and *Ctenotus* skinks (34, 39, 75, 79, 103, 127, 154). This introgression is not simply due to neutral variants passing between sister species; it includes adaptive alleles that have undergone interspecific sweeps (108). In African Great Lake cichlids, likely triggers for adaptive radiation arose in different lineages that came into contact and hybridized. The resulting hybrid population led to highly successful recombinant lineages that spawned many new species (95, 103, 154).

Introgression has the potential to provide beneficial variation in any situation where species enter novel environments. Many studies of the demographic impact of adaptive introgression (including much of our own discussion above) tacitly assume that selective coefficients of alleles remain unchanged when transferred from one population to another. This is perhaps true in some cases, such as target site insecticide resistance in mosquitoes (113). Provided the pathways of insecticide action are conserved, alleles that confer resistance in one species will likely have a similar effect in the other. However, this independence of genomic background may not be true in general. In yeast, the same mutations have varying fitness effects depending on the genomic and fitness background of each particular strain (67), and, in humans, disease alleles identified by genome-wide association study in one population do not necessarily have the same effect in another (101).

Theory helps to explain these variable effects. In the Fisher–Orr geometric model of quantitative adaptation toward a new optimum (44, 114, 115), alleles fixed early in the process are expected to have the largest fitness effects, while later evolving alleles will have smaller effects, leading to an approximately exponential distribution of fitness effects. Recombinant hybrid genotypes between divergently adapted populations will tend to be far from a fitness peak and will have low average fitness with a high variance mainly due to combinations of large-effect alleles. Selection among these genotypes can then ultimately result in higher fitness of introgressed populations or hybrid species (15, 90). These effects may contribute to rapid adaptation at range edges, in invasive species, and in other populations subject to changing environments. Evidence is mounting that hybridization is indeed a catalyst for evolution in all three of these situations. Contrary to the prediction that hybridization always swamps the effects of locally adapted alleles (100), hybrid offspring of differently adapted species in groups such as *Mimulus* rapidly accumulate combinations of traits and alleles that are highly beneficial in their current environment (7, 8). Similarly, invasive species that hybridize can be more likely to establish in a new environment than those that do not (37, 122). In the agriculturally important tetraploid switchgrass, alleles beneficial in postglacial expansion to northern latitudes also showed a history of introgression among independently cold-adapted populations of the same species (85).

CONCLUSION

The probability that two populations will hybridize, and that hybridization will result in introgression, depends in a complex way on reduced compatibility due to divergence, positive and negative selection, recombination, and demography. Adaptive introgression of an allele depends not only on its beneficial effects but also on where that allele is located in the genome, how it impacts fitness in the recipient population, and the recent history of the introgressed population. Despite the difficulty of identifying genomic introgression (see the section titled Assessing Prevalence of Introgression), recent studies have made clear that it is widespread and can often contribute large fractions of the genome in extant species. These empirical findings suggest that hybrid outcomes depend more strongly on long-term rather than short-term consequences, such as early generation hybrid unfitness. Novel combinations of alleles apparently provide a catalyst for evolution, generating high fitness variance in a population from which natural selection can pull out previously untested beneficial combinations of alleles. In changing or novel conditions, this catalytic process appears to allow populations to cross fitness valleys and provide new avenues along which populations can evolve and persist. The question of whether hybrid populations should be categorized as hybrid species is somewhat moot—it is clear that hybridization can kick-start ecological divergence, yielding species that interact with their environments in different ways than their parents. Whether we call these hybrid species is semantic.

Remaining questions include the one we started with: How important is adaptive introgression in evolution? We predict that researchers investigating both plants and animals will continue to find evidence for adaptation aided by introgression, particularly in species adapting to novel environments such as in the context of climate change. In these situations, future studies should identify traits under recent selection, and independently identify introgressed regions of the genome. Long-read and linked-read sequencing will help with this effort, illuminating the timing of selection and the identities of populations that exchanged genes. This knowledge promises to be helpful in conservation to decide which populations are most valuable and of theoretical interest by more fully elucidating mechanisms of adaptation and speciation in natural populations.

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