The prevalence and adaptive impact of introgression

Nathaniel Edelman*+ and James Mallet*

* Department of Organismic and Evolutionary Biology, Harvard University 16 Divinity Avenue,
CAMBRIDGE MA 02138. jmallet@oeb.harvard.edu

+ Current address: School of the Environment, Yale University, 165 Prospect Street
NEW HAVEN, CT 06511. edelmannate@gmail.com

Abstract

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

Introduction

Darwin's intuition that species evolved, rather than having been created by God, required that they emerged somewhat gradually by diverging from other species (32). However, even Thomas Henry Huxley, "Darwin's bulldog," objected that Darwin had not solved the problem of the origin of hybrid incompatibility between species (63), which had been viewed as a standard definition of species (23). Mules are typically sterile, for example, and so the horse and donkey parents were therefore clearly species. In "The Origin" chapter 8 "Hybridism," Darwin (32) 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 incompatibilities, 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, claiming discipleship of Darwin, nevertheless attempted to argue that hybrid incompatibilities were advantageous, and evolved via a process he called "physiological selection" (133). In the 20th Century, these "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 (28, 34, 98).

Nonetheless, many species are known to hybridize occasionally in captivity and in the wild. Zoologists tended to belittle this trickle of hybridization, which was interpreted to have minimal effects on natural populations (98). In contrast, botanists pointed towards data that 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 20th Century, cytological studies had also shown that a substantial fraction of flowering plant speciation events involved polyploid hybrids of divergent parent species (54). More recently, data on the importance of animal hybridization was beginning to accumulate (28, 53). The introduction of molecular techniques enabling substantial numbers of molecular genetic markers to be sampled across the genome, and latterly when genome sequencing became widespread, led finally to our ability to test different ideas about plant and animal speciation (1, 10, 13, 88, 129, 146). Today we have an avalanche of genomic results demonstrating that gene flow among species can be found frequently, that some of the gene transfers are adaptive, and that hybrid speciation takes place in animals as well as plants (37, 38, 41, 45-47, 78, 82, 92, 102, 115, 124, 132, 139, 151).

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, 28, 154). Yet despite such impediments, it is clear that alleles with positive impacts on fitness have been exchanged between populations, and introgressed alleles can persist for millions of years (11, 14, 117). While the fact of introgression is today broadly accepted, we still lack a general, quantitative understanding of its magnitute and long term effects. What fraction of the genome is due to introgression across the tree (or network) of life? How likely is it that introgressed fragments of the genome will be able to provide adaptive variants in spite of linked deleterious alleles? While gene flow among species has traditionally been viewed as a hindrance to speciation, how likely is it that adaptive introgression leads to hybrid speciation or to adaptive radiations? And can we identify situations that are more likely to be conducive to adaptive introgression?

Hybridization, introgression, admixture, and hybrid speciation

Hybridization is the production of offspring between divergent populations, and in the context used here, typically between recognized species. Hhybridization between divergently adapted populations is generally rather deleterious: F1 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 gene flow actually takes place among species, the term *introgressive hybridization* or merely *introgression* came into use following Edgar Anderson's pioneering work. While introgression usually has deleterious effects, *adaptive introgression* has been used to describe the acquisition of advantageous variation via introgression (59, 70). However, this term should not be taken to mean that the initial hybridization process itself was adaptive and selected for, or that all hybrid individuals themselves experience positive selection. Evidence for heterosis in 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 likely that the early generation gain in fitness is outweighed by low average fitness of later generation hybrids (15). It is usually only after a long process of selection among the hybrids that any of the remaining introgressed variation becomes "adaptive." Even after extensive backcrossing, some introgressed variation may still be selected against and be gradually lost, and so the term *admixture* has been introduced by those studying genomic data from archaic hominins to describe the introgressed fraction that remains in the genomes of modern humans over the long periods of time since the initial hybridization (55, 59).

In some cases, hybridization and introgression can lead to the origin of a novel species lineage, or *hybrid speciation*. This has been well documented for allopolyploid speciation in plants (54), but a second type of hybrid speciation that does not involve whole genome duplication, called by Edgar Anderson *recombinational speciation*, or in today's terminology *homoploid hybrid speciation*, is also known in plants, though suspected to be rare (127). There is some controversy over what processes constitute hybrid speciation, because the term has been applied rather loosely to cases where there is evidence for speciation with introgression. Part of the problem of defining hybrid speciation is that species and speciation are themselves hard to define, and can be transient. 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. However, in practice we rarely see such patterns in nature. For example several well-known hybrid species of *Helianthus* sunflowers are clearly hybrids (see Fig. 1), but typically occur in extreme environments where parental species are absent (128). We may expect this to be a general phenomenon if hybridization allows species to expand their niche through recombination of advantageous traits (93). Similarly, the homoploid hybrid butterfly species *Heliconius heurippa* overlaps with only one of its parent species, *H. melpomene* (97), so this definition would exclude many cases that have hitherto been considered hybrid speciation.

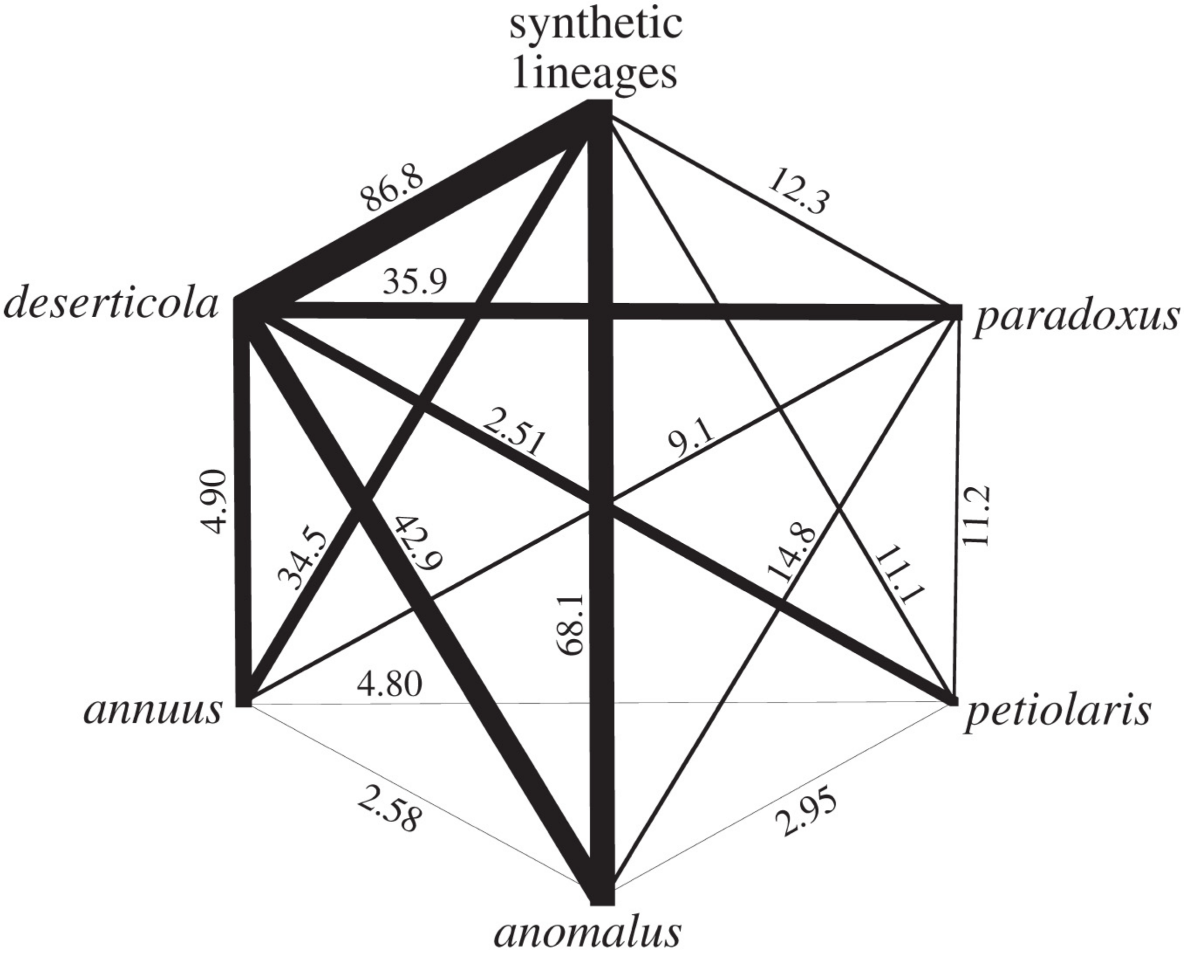

***Figure 1. Crossability of* Helianthus *sunflower species**. Percentages indicate pollen viability of first generation hybrids. The three homoploid hybrid species* H. anomalus, H. deserticola, *and* H. paradoxus, *as well as the experimentally produced "synthetic lineages," are all homoploid hybrid lineages produced by crosses between* H. annuus *and* H. petiolaris*. Line thickness is proportional to reproductive compatibility. (Reproduced from (128)).*

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. Documenting evidence for hybrid speciation requires "demonstrating that isolating mechanisms were derived from hybridization" (139). The homoploid *Helianthus* hybrid species, as well as allopolyploid hybrid species clearly qualify: they tend to be rather strongly reproductively isolated (Fig. 1), due in part to stabilized recombinant parental chromosomal arrangements that make hybridization difficult with either parent (128). The wing coloration of *Heliconius heurippa* derives from hybridization between its parents, *H. melpomene melpomene* and the *H. timareta/cydno* superspecies (9, 89). The hybrid coloration leads to pre-mating isolation between *H. heurippa* and both parents (97). However, based on genome-wide sequence data, a minority of genetic information, apart from coloration-determining genes, was inherited from *H. melpomene*, and it could therefore be argued that *H. heurippa* is merely a northern outpost of a more widespread species, *H. cydno* or the closely related *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* (49, 60, 105).

In contrast, the butterfly *Heliconius elevatus* appears to be a hybrid species that coexists with both parents (60, 135). *Heliconius elevatus* acquired colour pattern-determining loci via introgression with *H. melpomene* (159), although the great majority of its genome is much closer to that of *H. pardalinus* (60, 135). *Heliconius elevatus* today is sympatric and reproductively isolated with both parental species, and so likely obeys both of the above strict definitions of hybrid speciation, and yet, in genomic terms, this species could itself be seen as little more than an introgressed form of *H. pardalinus*.

However, the Schumer et al. definition is controversial: botanists (110), reacted against the Schumer et al. criteria (139), 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]." Especially if the hybridization that led to speciation was ancient, it will be often be very difficult to determine whether "isolating mechanisms were derived from hybridization." A different more tree-based definition, under the multispecies coalescent with introgression (MSci model), also seems reasonable: if two lineages fuse to form a third distinct lineage as part of a single speciation "event" in the past (45, 76) (see also Box 1). Regardless of whether adaptive introgression events are classified as hybrid speciation, they play an important role in evolution of many species. For the purposes of this article, we are more interested in documenting the prevalence of introgression and the factors that make introgression more or less likely, than in discuss discussing whether or not the introgression led to "hybrid speciation."

--BEGIN BOX 1---

Quantifying the prevalence of introgression in genomes

Because diploid genomes recombine each generation during meiosis, individuals contain blends of loci with unique genealogies and evolutionary histories. If introgression has occurred, some loci will have ancestors that belonged to the donor species, and genealogical, or “gene tree” information can be used to make evolutionary inferences (45, 56, 86, 92, 145). A number of tests have been devised to estimate the prevalence of introgressed loci, or genomic regions with a history of inter-specific gene flow. Some methods, such as the widely used *D* statistics and their extensions, use DNA site patterns in subsets of species to assess whether or not alleles are shared to an exceptional degree between non-sister species (22, 116, 119). Others use additional information from coalescent theory in such tests (37), or address the more complex problem of generating full phylogenetic networks that include hybridization edges (39). In addition to strategies for estimation, fundamental models of gene flow vary between methods. For example in two kinds of models based in coalescent theory, the Isolation with Migration (IM) framework (61) models migration for a sustained period of time, while the Multi-Species Coalescent with Introgression (MSci) framework models various forms of a pulse of migration at one particular time point (Fig. 2) (45, 162). Each of these estimation strategies requires researchers to compare models with different sets of parameters, and it can often be difficult to choose between options, as well as computationally challenging. The choices can be so difficult, in fact, that some introgression researchers select a wide range of models, and then compare the likelihoods of the data given those models in a variety of ways (83, 87).

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 assumptions of neutrality; in other words, it is assumed that the vast majority of informative sites are neutral. Detecting adaptive introgression in the genome requires a separate 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, 33, 71, 142). These kinds of techniques have been adapted to apply to models of evolution that include introgression, although the same processes are impacted by introgression itself, making inference more challenging (106, 142). One promising avenue of research is analysis of genomic clines (50). This framework identifies introgressed alleles that exist at unexpected frequencies, given the hybrid makeup of a population. Adaptive introgression is therefore inferred if, for example, introgressed alleles are at high frequencies, even though the population as a whole is not broadly admixed (50).

As genome sequencing technology has improved over the years, methods have evolved, using more SNP data and more complex models to identify subtle adaptive effect in population. New techniques are now arising using long-read or linked-read sequencing that leverage both population level allele frequency and haplotype frequency (103). Indirect measures of haplotype frequency based on allele frequency (40, 136, 158), as well as inferred haplotypes based on known pedigrees and parental genotypes (i.e. QTL mapping, reviewed in (144). Directly sequencing haplotypes will reduce the need for error-prone inference, and yield more confident insights into the strength of selection, timing of sweeps, and geographic structure around selected regions of the genome (Meier 2020).

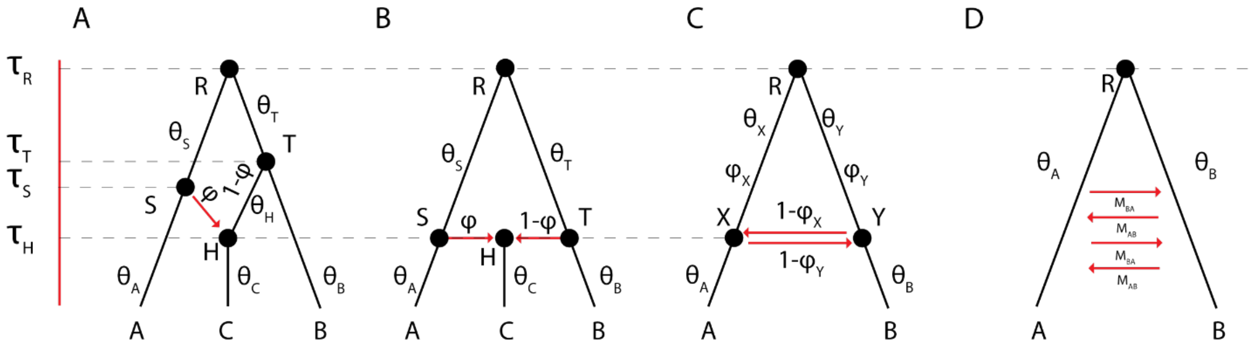

Figure 2. Models of introgression. *Genealogical models used to estimate introgression differ in their assumptions. Here are shown four models that differ in their hypotheses and therefore model parameters.* ***A.*** *Intogression, in which an ancestor of species* A*, which diverged from* A *at time* 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 **A** and **C** represent classical models of introgression, while model **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 A, B, and C are all models within the Multi-Species Coalescent with Introgression* (MSci) *framework, while model D is within the Isolation with Migration (IM) framework. (Adapted from (31, 45)).*

--END BOX 1---

Patterns and prevalence of non-adaptive and adaptive introgression

Methods for detecting and quantifying introgression with genomic data have been recently reviewed elsewhere, and are briefly summarized in Box 1 (39, 62). Using these varied methods, it has become clear that hybridization contributes substantial genomic variation to many groups of species across the Tree of Life (92, 152). The proportion of the genome that introgressed ranges over an enormous range - from around 2% in the snowshoe hare to over 70% in *Anopheles* mosquitoes (46, 66). In addition to learning that introgressed ancestry may be common within a particular genome, we have also found that introgression is common among species. The best evidence of this comes from broad phylogenetic studies, where species are not specifically chosen because 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 (150). Similarly, in an analysis of 40 *Heliconius* genomes at least 12 instances of gene flow were inferred, involving all major clades (74). In fact, phylogenies with no evidence of gene flow seem to be the exception rather than the rule. Clades as diverse as fossil and living elephants (115) darters (85), tomatoes (118), and yeast (36) all show strong evidence of introgression throughout their history.

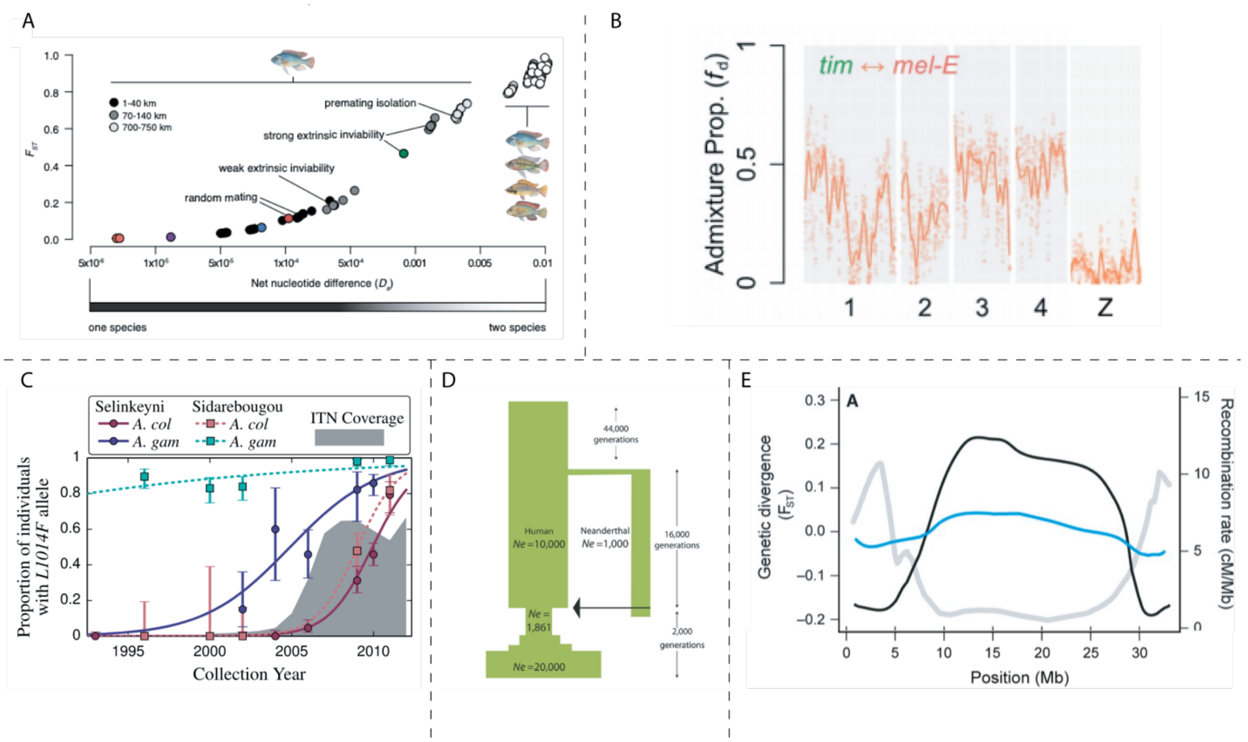

***Figure 3 Factors in determining extent of introgression**. **A.** Genetic divergence. Pairs of populations, such as these cichlids, are more likely to hybridize if they are more closely related (161). **B.** Selection against deleterious alleles. Across many hybridizing species, including* Heliconius timareta *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 because genes that contribute to hybrid incompatibility appear to be more common on sex chromosomes (95). Only four of the 20 autosomes are shown due to space constraints, but the pattern is consistent across all 20 autosomes. **C.** Selection for beneficial alleles. Increase in the use of insecticide-treated bed nets (ITN) led first to an increase in frequency of the insecticide resistance allele L1014F in* Anopheles gambiae, *and a later increase in frequency in* A. coluzzii *after introgression from the former species (111). **D.** Demography. Low population sizes of species like Neanderthals may lead to incrased frequencies of segregating deleterious alleles. When they are introgressed into larger population species like modern humans, they may contribute to fitness declines (57). **E.** Recombination. In three-spined sticklebacks, as in many other species, regions of the genome with high rates of recombination (grey line) allow deleterious introgressed alleles to become decoupled from neighboring loci. This may allow more gene flow, as detected by patterns of* F_{ST} *between multiple pairs of hybridizing species increasing in regions of low recombination (blue and black lines, (131).*

Even in groups where introgression is common, it can vary greatly. Different pairs of species exchange different fractions of their genome. One simple explanation for variation in introgressed ancestry is variation in divergence between hybridizing species. On average, we expect the extent of genetic incompatibility to increase as species diverge and the incidence of hybridization (and introgression) to decline as species diverge (Figure 3A) (27, 52, 114). This is in part due to epistatic interactions between alleles from different species. Known as Dobzhansky-Muller incompatibilities, substitutions that arise in each lineage can be neutral or beneficial in their parental population, but interact negatively with derived alleles in the other population (34, 108). Data from natural and experimental hybridization between species and subspecies generally conform to this expectation: hybrid incompatibilities increase and number of hybrids decrease with divergence time of parents (26, 52, 88, 91, 96, 107). As the time since the common ancestor increases, the number of two-locus negative epistatic interactions between alleles that have arisen in each diverging population is expected to increase quadratically, leading to a “snowballing" effect (114). Multilocus incompatibilitiess (121) can accelerate even faster than quadratic. Nonetheless, it is unclear whether actual declines in hybrid fitness are linear or accelerate due to a snowball effect, but the relationship between percent divergence and hybrid compatibility is highly variable, even among species with similar genetic divergence (27, 52).

There is little doubt that the fraction of the genome that introgressed as a function of time since divergence does not fully explain observed quantities of introgressed variation, and natural selection on introgressed alleles may play a part in the discrepancy (Figure 3B,C). Although adaptive introgression is often thought of with respect to a single trait or single locus, we must expand our search image to include all instances where hybridization can improve fitness. Adaptive introgression likely depends on the degree of genetic similarity, gene flow among populations within species, and the fitness of each population in its environment. For example, in species that are closely related or hybridize often, introgression will increase effective population size (N_e) across much of the genome (120). Introgression may be beneficial for species with small populations such as endangered species. Natural selection in a diploid population is ineffective if the coefficient of selection, s, is less than than $\sim 1/(4N_e)$ (58, 163). Alleles with negative effects can persist or be fixed stochastically in small populations. A larger effective population size leads to: (1) greater efficiency of natural selection, allowing better use of weakly advantageous alleles, and better purging of weakly deleterious alleles; (2) a supply of novel genetic variation on which selection can act; and (3) increased heterozygosity that can rescue populations from inbreeding depression (3, 4). Alleles that cross the species boundary may provide adaptive benefits regardless of their selective effect in the source population (29, 48, 143). As one example, genomic regions that show evidence of a lack of introgression between the butterflies *Heliconius pardalinus* and *H. elevatus* in the Amazon have around half the levels of polymorphism compared to regions in which gene flow is pervasive, demonstrating that increased variation is a widespread result of hybridization in these species (75). In Trinidadian guppies, an influx of migration from a large downstream population into a smaller upstream population helped to increase fitness and genetic variation (44). While conspecific, these populations had adapted to different ecological conditions, and gene flow did not swamp locally adaptive alleles in the recipient population, as has been suggested in other cases (153). Many evolutionary biologists who favour a reproductive isolation concept species concept also view "completion" of speciation (i.e. to achieve zero gene flow) as almost a kind of goal of speciation. Yet because of the effect on reduction of effective population size, and resulting reduced efficiency of natural selection, completion of speciation may be unfavourable for the population (16). While it is likely that separately adapted species are likely often individually selected to minimize hybridization to avoid unfit offspring, their "mistakes" may aid the survival of their populations. However, the relationship between small population sizes and increased genetic load is complex, and adding even globally beneficial foreign genetic variation to a low diversity population can result in a crash in population size (77) (see discussion on demography below).

In more divergent species, or those with fewer opportunities to interbreed, genes may not pass as freely among hybridizing populations. However, even here, on must not only look to large-effect loci for adaptive introgression. Analysis of genomic variation has revealed cases of introgressed loci that segregate at frequencies higher than expected under a neutral or slightly deleterious model (43, 51, 126, 137, 160). This provides evidence for adaptive introgression, even if putative advantageous traits have not yet been associated with introgressed loci. In Europe, hybridization between *Mus musculus musculus* and *M. m. domesticus* has resulted in approximately 3-18% of the genome with a history of introgression, even far from the narrow hybrid zone (149). Greater than expected frequencies of introgressed loci suggested that they were advantageous and underwent 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 (100). Across several independent hybrid zones, there was 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. Specific functions of these high-frequency alleles are still unknown, but functional categories such as transport of toxic compounds were over-represented among introgressed loci. This could be indicative of polygenic selection on particular traits, or of multiple different traits that are all being selected for in hybrid trout populations.

In cases where populations are highly divergent, only alleles with strongly beneficial effects are likely to introgress because of widespread, strong genetic incompatibilities (2, 122). For example, adaptive responses to extreme anthropogenic selective pressures, such as rodenticide resistance transferred from *Mus spretus* to *M. mus domesticus* (147) or pesticide resistance from *Anopheles gambiae* to *A. coluzzii* mosquitoes (111) involve single loci with very strong selective advantages (lower bound s=0.28 and 0.13, respectively). Another pesticide resistance allele was recently identified as adaptively introgressed from the moth *Helicoverpa armigera* into *H. zea* (155), and although no selective coefficient was estimated in that study, the frequency of the introgressed allele rose from 0% to 70% in just 4 years, implying very strong selection. *Heliconius* butterflies experience strong selection for local mimetic color patterns (20, 79, 90). Across an *H. erato* color pattern cline in Peru, average selection coefficients for three pattern-determining loci were ~0.22 (90, 134). These large-effect color pattern switch loci have also been passed among related species within the genus through introgression (60, 106, 159). Similarly, populations of snowshoe hare (*Lepus americanus*) acquired an allele through introgression from the black-tailed jackrabbit (*L. californicus*) that regulates the expression of the pigmentation gene agouti, resulting in a winter brown as opposed to winter white coat (66). This phenotype, which is advantageous in the relatively temperate Pacific Northwest, has a selective coefficient estimated between 0.027 and 0.049 (67).

Effects of demography and recombination

Some introgressed loci are globally or locally beneficial, others globally or locally deleterious, and still others neutral. However, these alleles do not exist in isolation, and cannot be considered independently. Instead, one must interpret their impacts in the context of factors that tie them together. Two such factors have been studied in depth: recombination determines the rate at which introgressed alleles at two or more loci become dissociated, and demography affects the effectiveness of natural selection on introgressed alleles.

Recombination and introgression prevalence

In species across the tree of life, regions of the genome with high recombination rates tend to be more permissive to introgression than regions with low recombination rates (Figure 3D) (2, 69, 109). This is in part due to the effects of selection on sites linked to the selected site ("linked selection") (18, 19, 24, 30). If a particular genomic region has positive ("selective sweep") or negative ("background selection") effect, both the region itself and neighboring variants will be swept into or out of the population, which will tend to reduce the variation around the selected site. The effects of linked selection varies locally depending on recombination rate, but the process has a global impact across the genome. In humans, the allele frequencies of a majority of base pairs in the genome are impacted by background selection or selective sweeps (123). 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 (130), while in others, like *Heliconius* butterflies, recombination is higher in the center and lower at the ends (95, 148). 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 lower 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 in order to rise to high frequency in recipient populations. Low recombination regions of the genome can harbor multiple divergently advantageous alleles, aiding a more stable polymorphism due to divergent selection (25, 72, 73). Interestingly, although inversion polymorphisms are more resistant to introgression because they inhibit recombination, introgression can also transfer inversions as cassettes of globally adaptive alleles between populations (64). Conversely, in regions of high recombination, relatively 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 an allele of interest, aggregate genome-wide recombination rate contributes to population-level variation in introgressed ancestry (156). 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, as much of this mixing is accomplished through independent assortment (157). In species with high global recombination, deleterious introgressed ancestry will be quickly distributed among all members of a population, meaning that each individual in the population will experience similar fitness deficits due to similar deleterious introgressed ancestry, and natural selection will only purge them at a slow rate. Simulations using human (n=23) and *Drosophila* (n=4) recombination maps show that "*Drosophila* purges as much introgressed DNA in 13 generations as humans do in 2,000 generations " (156). Consistent with this argument, *Heliconius* butterflies show a much stronger correlation between chromosome size and introgression than between local recombination rate and introgression (37). Because *Heliconius* chromosomes experience approximately one crossover per meiosis (94), the probability that any two loci on a short chromosome will recombine is much higher than that in long chromosomes. 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 leads to an unequal rate of purging of introgressed ancestry and, in turn, may lead to chromosome size being strongly correlated with introgression (156).

Demography

If deleterious alleles introgress into larger populations and the selective effects remain constant, they individuals that carry them will have lower fitness, regardless of epistasis between introgressed and non-introgressed alleles. This scenario is exemplified by recent models of Neanderthal-modern human gene flow (68)(Figure 3E). In these models, Neanderthals are imagined to interbreed freely with modern humans, the latter having a historical N_e of ~10X that of Neanderthals. Hybrids with Neanderthal alleles suffer a fitness cost simply due to the negative selective effect of the alleles themselves, leading to a gradual reduction Neanderthal ancestry to about 2% of modern non-African human genomes. Combining this phenomenon with the role of recombination results in the previously discussed positive correlation between recombination rate in introgressed ancestry. In fact, such a correlation has been observed in humans (140).

On the other hand, 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 practised in the conservation community (80). In brook trout, where large N_e domesticated individuals hybridized with a small N_e wild population, introduced domesticated ancestry has become more common in genomic regions of low recombination rate (81).

Discussion

We have examined the prevalence of introgressed ancestry in genomes, the ways in which introgressed alleles can be adaptive, and demographic factors that determine introgression probability, but we have not answered the overarching question: how important is adaptive introgression in evolution? To address that question requires an investigation as to how often adaptation of any sort depends on introgressed alleles, or how often species divergence of any sort is mediated by hybridization. Those questions are yet to be answered, though they have begun to be asked in specific groups (104). A more productive and 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 that at least some hybrid offspring will be fertile. In addition, although recombinant hybrids are expected mostly to be unfit, the adaptive landscape must be such that some hybrid individuals are of high fitness. One instance where both of these conditions are likely met is in rapid adaptive radiations, where due to key innovations or ecological opportunity, novel populations are able to expand into new niches (93, 138, 141). Genomic introgression is a feature of many rapid radiations that have been studied at genomic scale, including cichlid fish, *Heliconius* butterflies, Darwin's finches, and *Ctenotus* skinks (37, 60, 74, 78, 101, 125, 151). This introgression is not simply due to neutral variants passing between sister species; it includes adaptive alleles that have undergone inter-specific sweeps (106). In African Great Lake cichlids, likely sparks for adaptive radiation arose in two different lineages that came into contact and hybridized, leading to highly successful recombinant lineages that spawned many new species (93, 101, 151).

In general, introgression may provide beneficial variation in any situation where species enter novel environments. Many studies of the demographic impacts on adaptive introgression, as well as our own discussion above, generally assume that selective coefficients of particular alleles remain unchanged when they are transferred from one population to another. This is clearly likely in some cases, as in mosquito insecticide resistance genes (111). As long as species have conserved pathways on which the insecticide acts, alleles that confer resistance in one species will have a similar effect in the other. However, it is not clear that this is a general phenomenon. In yeast, exactly the same mutations have varying fitness effects depending on the genomic and fitness background of each particular strain (65), and, in humans, disease alleles identified by GWAS in one population do not necessarily have the same effect in another (99). Theory helps to explain these variable effects. Under a multidimensional model of quantitative adaptation towards a new optimum based on the Fisher/Orr geometric model (42, 112, 113), it is expected that alleles fixed early in the process will tend to have large fitness effects, while later alleles will fix smaller fitness effects, leading to an approximately exponential distribution of fitness effects. Recombinant hybrid genotypess between divergently adapted populations, generally far from a fitness peak, will therefore tend to show low average but highly variable fitnesses mainly due to combinations of large-effect alleles. Selection among these genotypes can then result in higher fitness introgressed populations or hybrid species (15). This effect may contribute to dynamics at range edges, in invasive species, and in populations adapting to changing environments. In all three of those situations, evidence is mounting that hybridization is indeed a catalyst for evolution. Contrary to the prediction that hybridization would swamp the effects of locally adapted alleles (98), hybrid offspring of differently adapted species in groups such as *Mimulus* rapidly accumulate combinations of traits and alleles that are most 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 hybridize (35, 120). In a genomic population structure study of the agriculturally important tetraploid switchgrass, adaptive alleles found to be beneficial in post-glaciation expansion to northern latitudes were found to have a history of introgression from other cold-adapted populations of the same species (84).

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 beneficial effects, but 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 difficulties of identifying genomic introgression (Box 1), recent studies have made clear that it is a prevalent force and can often contribute large proportions of genetic variation to extant species. These empirical findings tend to suggest that hybrid outcomes depend more strongly on long-term rather than short-term consequences, such as early generation hybrid unfitness. The novel combinations of alleles apparently provide a jolt for evolution, generating more fitness variance in a population on which natural selection can act to pull out previously untested beneficial combinations of alleles. In changing or novel conditions, this jolt 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. What we call these populations semantic. The outstanding question is 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, and this may be particularly true of species adapting to novel environments in the context of climate change. In those situations, future studies should identify traits under recent selection, and independently identify regions of the genome that were introgressed. Long-read and linked-read sequencing will help with this effort, illuminating the timing of selection and precisely which populations exchanged genes. This knowledge will, practically, help conservation managers determine which populations to preserve, and theoretically open our eyes to the true mechanisms of adaptation in wild populations.

Works Cited

1. Abbott R, Albach D, Ansell S, Arntzen JW, Baird SJE, et al. 2013. Hybridization and speciation. *Journal of Evolutionary Biology* 26: 229-46
2. Aeschbacher S, Selby JP, Willis JH, Coop G. 2017. Population-genomic inference of the strength and timing of selection against gene flow. *Proceedings of the National Academy of Sciences, USA* 114: 7061-66
3. Allendorf FW, Hohenlohe PA, Luikart G. 2010. Genomics and the future of conservation genetics. *Nature Reviews Genetics* 11: 697-709
4. Allendorf FW, Luikhart G. 2007. *Conservation and the Genetics of Populations*. Malden, Mass., USA: Blackwell Publishing. 641 pp.
5. Anderson E. 1953. Introgressive hybridization. *Biological Reviews* 28: 280-307
6. Anderson E, Stebbins GL. 1954. Hybridization as an evolutionary stimulus. *Evolution* 8: 378-88
7. Angert AL, Bontrager MG, Ågren J. 2020. What do we really know about adaptation at range edges? *Annual Review of Ecology, Evolution, and Systematics* 51: 341-61
8. Angert AL, Bradshaw HD, Schemske DW. 2008. Using experimental evolution to investigate geographic range limits in monkeyflowers. *Evolution* 62: 2660-75, 16
9. Arias CF, Giraldo N, McMillan WO, Lamas G, Jiggins CD, Salazar C. 2017. A new subspecies in a *Heliconius* butterfly adaptive radiation (Lepidoptera: Nymphalidae). *Zoological Journal of the Linnean Society* 180: 805-18
10. Arnold ML. 1992. Natural hybridization as an evolutionary process. *Annual Review of Ecology and Systematics* 23: 237-61
11. Arnold ML. 2004. Transfer and origin of adaptations through natural hybridization: were Anderson and Stebbins right? *Plant Cell* 16: 1-9
12. Arnold ML, Hodges SA. 1995. Are natural hybrids fit or unfit relative to their parents? *Trends in Ecology and Evolution* 10: 67-71

13. Arnold ML, Sapir Y, Martin NH. 2008. Genetic exchange and the origin of adaptations: prokaryotes to primates. *Philosophical Transactions of the Royal Society B: Biological Sciences* 363: 2813-20
14. Baack EJ, Rieseberg LH. 2007. A genomic view of introgression and hybrid speciation. *Current Opinion in Genetics and Development* 17: 513-18
15. Barton NH. 2001. The role of hybridization in evolution. *Molecular Ecology* 10: 551-68
16. Barton NH. 2020. On the completion of speciation. *Philosophical Transactions of the Royal Society B: Biological Sciences* 375: 20190530
17. Bay RA, Taylor EB, Schluter D. 2019. Parallel introgression and selection on introduced alleles in a native species. *Molecular Ecology* 28: 2802-13
18. Begun DJ, Aquadro CF. 1992. Levels of naturally occurring DNA polymorphism correlate with recombination rates in D. melanogaster. *Nature* 356: 519-20
19. Begun DJ, Aquadro CF. 1993. African and North American populations of *Drosophila melanogaster* are very different at the DNA level. *Nature (London)* 365: 548-50
20. Benson WW. 1972. Natural selection for Müllerian mimicry in *Heliconius erato* in Costa Rica. *Science* 176: 936-39
21. Berg JJ, Coop G. 2014. A population genetic signal of polygenic adaptation. *PLOS Genetics* 10: e1004412
22. Blischak PD, Chifman J, Wolfe AD, Kubatko LS. 2018. HyDe: a python package for genome-scale hybridization detection. *Systematic Biology* 67: 821-29
23. Buffon (Comte de) G-LL. 1753. Description de la partie du Cabinet qui a rapport à l'histoire naturelle du cheval. L'asne. In *Histoire Naturelle, Générale et Particuliére, avec la Description du Cabinet du Roy, Vol. 4*, pp. 377-403. Paris
24. Burri R. 2017. Interpreting differentiation landscapes in the light of long-term linked selection. *Evolution Letters* 1: 118-31
25. Charlesworth B, Barton NH. 2018. The spread of an inversion with migration and selection. *Genetics* 208: 377-82
26. Coyne JA, Orr HA. 1989. Patterns of speciation in *Drosophila*. *Evolution* 43: 362-81
27. Coyne JA, Orr HA. 1997. "Patterns of speciation in *Drosophila*" revisited. *Evolution* 51: 295-303
28. Coyne JA, Orr HA. 2004. *Speciation*. Sunderland, Mass.: Sinauer Associates. xiii + 545 pp.
29. Crow JF. 1948. Alternative hypotheses of hybrid vigor. *Genetics* 33: 477-87
30. Cutter AD, Payseur BA. 2013. Genomic signatures of selection at linked sites: unifying the disparity among species. *Nature Reviews Genetics* 14: 262-74
31. Dalquen D, Zhu T, Yang Z. 2017. Maximum likelihood implementation of an isolation-with-migration model for three species. *Systematic Biology* 66: 379-98
32. Darwin CR. 1859. *On the Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life*. London: John Murray. x + 502 pp.
33. DeGiorgio M, Huber CD, Hubisz MJ, Hellmann I, Nielsen R. 2016. SWEEPFINDER 2: increased sensitivity, robustness and flexibility. *Bioinformatics* 32: 1895-97
34. Dobzhansky T. 1937. *Genetics and the Origin of Species*. New York: Columbia Univ. Press. xvi + 364 pp.

35. Drake JM. 2006. Heterosis, the catapult effect and establishment success of a colonizing bird. *Biology Letters* 2: 304-07
36. Eberlein C, Hénault M, Fijarczyk A, Charron G, Bouvier M, et al. 2019. Hybridization is a recurrent evolutionary stimulus in wild yeast speciation. *Nature Communications* 10: 923
37. Edelman NB, Frandsen PB, Miyagi M, Clavijo B, Davey J, et al. 2019. Genomic architecture and introgression shape a butterfly radiation. *Science* 366: 594-99
38. Ellegren H. 2014. Genome sequencing and population genomics in non-model organisms. *Trends in Ecology & Evolution* 29: 51-63
39. Elworth RAL, Ogilvie HA, Zhu J, Nakhleh L. 2019. Advances in computational methods for phylogenetic networks in the presence of hybridization. In *Bioinformatics and Phylogenetics*, ed. T Warnow, pp. 317-60: Berlin
40. Field Y, Boyle EA, Telis N, Gao Z, Gaulton KJ, et al. 2016. Detection of human adaptation during the past 2000 years. *Science* 354: 760-64
41. Figueiró HV, Li G, Trindade FJ, Assis J, Pais F, et al. 2017. Genome-wide signatures of complex introgression and adaptive evolution in the big cats. *Science Advances* 3: e1700299
42. Fisher RA. 1930. *The Genetical Theory of Natural Selection*. Oxford: Clarendon Press. - pp.
43. Fitzpatrick BM, Johnson JR, Kump DK, Smith JJ, Voss SR, Shaffer HB. 2010. Rapid spread of invasive genes into a threatened native species. *Proceedings of the National Academy of Sciences* 107: 3606-10
44. Fitzpatrick SW, Bradburd GS, Kremer CT, Salerno PE, Angeloni LM, Funk WC. 2020. Genomic and fitness consequences of genetic rescue in wild populations. *Current Biology* 30: 517-22
45. Flouri T, Jiao X, Rannala B, Yang Z. 2019. A Bayesian implementation of the multispecies coalescent model with introgression for phylogenomic analysis. *Molecular Biology and Evolution* 37: 1211-23
46. Fontaine MC, Pease JB, Steele A, Waterhouse RM, Neafsey DE, et al. 2015. Extensive introgression in a malaria vector species complex revealed by phylogenomics. *Science* 347: 1258524
47. Foote AD, Martin MD, Louis M, Pacheco G, Robertson KM, et al. 2019. Killer whale genomes reveal a complex history of recurrent admixture and vicariance. *Molecular Ecology* 28: 3427-44
48. Frankham R, Ballou JD, Eldridge MDB, Lacy RC, Ralls K, et al. 2011. Predicting the probability of outbreeding depression. *Conservation Biology* 25: 465-75
49. Giraldo N, Salazar C, Jiggins CD, Bermingham E, Linares M. 2008. Two sisters in the same dress: *Heliconius* cryptic species. *BMC Evolutionary Biology* 8: 324
50. Gompert Z, Buerkle CA. 2011. Bayesian estimation of genomic clines. *Molecular Ecology* 20: 2111-27
51. Gompert Z, Lucas LK, Nice CC, Buerkle CA. 2013. Genome divergence and the genetic architecture of barriers to gene flow between *Lycaeides idas* and *L. melissa*. *Evolution* 67: 2498-514
52. Gourbière S, Mallet J. 2010. Are species real? The shape of the species boundary with exponential failure, reinforcement, and the "missing snowball". *Evolution* 64: 1-24
53. Grant PR, Grant BR. 1992. Hybridization of bird species. *Science* 256: 193-97

54. Grant V. 1971. *Plant Speciation*. New York: Columbia Univ. Press. - pp.
55. Green RE, Krause J, Briggs AW, Maricic T, Stenzel U, et al. 2010. A draft sequence of the Neandertal genome. *Science* 328: 710-22
56. Hahn MW, Nakhleh L. 2016. Irrational exuberance for resolved species trees. *Evolution* 70: 7-17
57. Harris K, Nielsen R. 2016. The genetic cost of Neanderthal introgression. *Genetics* 203: 881-91
58. Hartl DL, Clark AG. 2007. *Principles of Population Genetics. Fourth Edition*. Sunderland, Mass.: Sinauer. - pp.
59. Hawks J, Cochran G. 2006. Dynamics of adaptive introgression from archaic to modern humans. *PalaeoAnthropology* 2006: 101-15
60. *Heliconius* Genome Consortium. 2012. Butterfly genome reveals promiscuous exchange of mimicry adaptations among species. *Nature (London)* 487: 94-98
61. Hey J. 2010. Isolation with migration models for more than two populations. *Molecular Biology and Evolution* 27: 905-20
62. Hibbins MS, Hahn MW. 2021. Phylogenomic approaches to detecting and characterizing introgression. *EcoEvoRxiv*: 10.32942/osf.io/uahd8
63. Huxley TH. 1860. The origin of species. pp. 22-79. London: Macmillan & Co., Ltd.
64. Jay P, Whibley A, Frézal L, de Cara MÁR, Nowell RW, et al. 2018. Supergene evolution triggered by the introgression of a chromosomal inversion. *Current Biology* 28: 1839-45
65. Johnson MS, Martsul A, Kryazhimskiy S, Desai MM. 2019. Higher-fitness yeast genotypes are less robust to deleterious mutations. *Science* 366: 490-93
66. Jones MR, Mills LS, Alves PC, Callahan CM, Alves JM, et al. 2018. Adaptive introgression underlies polymorphic seasonal camouflage in snowshoe hares. *Science* 360: 1355-58
67. Jones MR, Mills LS, Jensen JD, Good JM. 2020. The origin and spread of locally adaptive seasonal camouflage in snowshoe hares. *The American Naturalist* 196: 316-32
68. Juric I, Aeschbacher S, Coop G. 2015. The strength of selection against Neanderthal introgression. *bioRxiv*
69. Kim BY, Huber CD, Lohmueller KE. 2018. Deleterious variation shapes the genomic landscape of introgression. *PLoS Genetics* 14: e1007741
70. Kim SC, Rieseberg LH. 1999. Genetic architecture of species differences in annual sunflowers: implications for adaptive trait introgression. *Genetics* 153: 965-77
71. Kim Y, Stephan W. 2002. Detecting a local signature of genetic hitchhiking along a recombining chromosome. *Genetics* 160: 765-77
72. Kirkpatrick M, Barton N. 2006. Chromosome inversions, local adaptation and speciation. *Genetics* 173: 419-34
73. Kirkpatrick M, Barton NH. 2018. Chromosome inversions, local adaptation and speciation. Corrigendum. *Genetics* 208: 433-33
74. Kozak KM, McMillan O, Joron M, Jiggins CD. 2018. Genome-wide admixture is common across the *Heliconius* radiation. *bioRxiv*: 414201
75. Kryvokhyzha D. 2014. *Whole-genome resequencing of Heliconius butterflies revolutionizes our view of the level of admixture between species*. Uppsala Universitët, Uppsala, Sweden. 21 pp pp.

76. Kubatko LS. 2009. Identifying hybridization events in the presence of coalescence via model selection. *Systematic Biology* 58: 478-88
77. Kyriazis CC, Wayne RK, Lohmueller KE. 2020. Strongly deleterious mutations are a primary determinant of extinction risk due to inbreeding depression. *bioRxiv*: 678524
78. Lamichhaney S, Berglund J, Almen MS, Maqbool K, Grabherr M, et al. 2015. Evolution of Darwin's finches and their beaks revealed by genome sequencing. *Nature* 518: 371-75
79. Langham GM. 2004. Specialized avian predators repeatedly attack novel colour morphs of *Heliconius* butterflies. *Evolution* 58: 2783-87
80. Leitwein M, Cayuela H, Ferchaud A-L, Normandeau É, Gagnaire P-A, Bernatchez L. 2019. The role of recombination on genome-wide patterns of local ancestry exemplified by supplemented brook charr populations. *Molecular Ecology* 28: 4755-69
81. Leitwein M, Duranton M, Rougemont Q, Gagnaire P-A, Bernatchez L. 2020. Using haplotype information for conservation genomics. *Trends in Ecology & Evolution* 35: 245-58
82. Li G, Figueiró HV, Eizirik E, Murphy WJ. 2019. Recombination-aware phylogenomics reveals the structured genomic landscape of hybridizing cat species. *Molecular Biology and Evolution* 36: 2111-26
83. Lopes JS, Beaumont MA. 2010. ABC: A useful Bayesian tool for the analysis of population data. *Infection, Genetics and Evolution* 10: 825-32
84. Lovell JT, MacQueen AH, Mamidi S, Bonnette J, Jenkins J, et al. 2021. Genomic mechanisms of climate adaptation in polyploid bioenergy switchgrass. *Nature*
85. MacGuigan DJ, Near TJ. 2018. Phylogenomic signatures of ancient introgression in a rogue lineage of darters (Teleostei: Percidae). *Systematic Biology* 68: 329-46
86. Maddison WP. 1997. Gene trees in species trees. *Systematic Biology* 46: 523-36
87. Mailund T, Halager AE, Westergaard M, Dutheil JY, Munch K, et al. 2012. A new isolation with migration model along complete genomes infers very different divergence processes among closely related great ape species. *PLoS Genetics* 8: e1003125
88. Mallet J. 2005. Hybridization as an invasion of the genome. *Trends in Ecology and Evolution* 20: 229-37
89. Mallet J. 2009. Rapid speciation, hybridization and adaptive radiation in the *Heliconius melpomene* group. ed. RK Butlin, D Schluter, JR Bridle, pp. 177-94. Cambridge: Cambridge University Press
90. Mallet J, Barton NH. 1989. Strong natural selection in a warning color hybrid zone. *Evolution* 43: 421-31
91. Mallet J, Beltrán M, Neukirchen W, Linares M. 2007. Natural hybridization in heliconiine butterflies: the species boundary as a continuum. *BMC Evolutionary Biology* 7: 28
92. Mallet J, Besansky N, Hahn MW. 2016. How reticulated are species? *BioEssays* 38: 140-49
93. Marques DA, Meier JI, Seehausen O. 2019. A combinatorial view on speciation and adaptive radiation. *Trends in Ecology & Evolution*

94. Martin SH, Davey J, Salazar C, Jiggins C. 2018. Recombination rate variation shapes barriers to introgression across butterfly genomes. *bioRxiv*

95. Martin SH, Davey JW, Salazar C, Jiggins CD. 2019. Recombination rate variation shapes barriers to introgression across butterfly genomes. *PLoS Biology* 17: e2006288

96. Matute DR, Butler IA, Turissini DA, Coyne JA. 2010. A test of the snowball theory for the rate of evolution of hybrid incompatibilities. *Science* 329: 1518-21

97. Mavárez J, Salazar C, Bermingham E, Salcedo C, Jiggins CD, Linares M. 2006. Speciation by hybridization in *Heliconius* butterflies. *Nature (London)* 441: 868-71

98. Mayr E. 1963. *Animal Species and Evolution*. Cambridge, Mass.: Harvard University Press. xiv + 797 pp.

99. McClellan J, King M-C. 2010. Genetic heterogeneity in human disease. *Cell* 141: 210-17

100. McKelvey KS, Young MK, Wilcox TM, Bingham DM, Pilgrim KL, Schwartz MK. 2016. Patterns of hybridization among cutthroat trout and rainbow trout in northern Rocky Mountain streams. *Ecology and Evolution* 6: 688-706

101. Meier JI, Marques DA, Mwaiko S, Wagner CE, Excoffier L, Seehausen O. 2017. Ancient hybridization fuels rapid cichlid fish adaptive radiations. *Nature Communications* 8: 14363

102. Meier JI, Marques DA, Wagner CE, Excoffier L, Seehausen O. 2018. Genomics of parallel ecological speciation in Lake Victoria cichlids. *Molecular Biology and Evolution*: msy051-msy51

103. Meier JI, Salazar PA, Kučka M, Davies RW, Dréau A, et al. 2020. Haplotype tagging reveals parallel formation of hybrid races in two butterfly species. *bioRxiv*: 2020.05.25.113688

104. Menon M, Bagley JC, Page GFM, Whipple AV, Schoettle AW, et al. 2021. Adaptive evolution in a conifer hybrid zone is driven by a mosaic of recently introgressed and background genetic variants. *Communications Biology* 4: 160

105. Mérot C, Mavárez J, Evin A, Dasmahapatra KK, Mallet J, et al. 2013. Genetic differentiation without mimicry shift in a pair of hybridizing *Heliconius* species (Lepidoptera: Nymphalidae). *Biological Journal of the Linnean Society* 109: 830-47

106. Moest M, Van Belleghem SM, James JE, Salazar C, Martin SH, et al. 2020. Selective sweeps on novel and introgressed variation shape mimicry loci in a butterfly adaptive radiation. *PLoS Biology* 18: e3000597

107. Moyle LC, Nakazato T. 2010. Hybrid incompatibility "snowballs" between *Solanum* species. *Science* 329: 1521-23

108. Muller HJ. 1942. Isolating mechanisms, evolution and temperature. In *Biological Symposia Volume 6. Temperature and evolution. Isolating mechanisms. Genetic control of Embryonic development*, ed. T Dobzhansky, pp. 71-125. Lancaster, Pennsylvania: Jacques Cattell Press

109. Nachman MW, Payseur BA. 2012. Recombination rate variation and speciation: theoretical predictions and empirical results from rabbits and mice. *Philosophical Transactions of the Royal Society B: Biological Sciences* 367: 409-21

110. Nieto Feliner G, Alvarez I, Fuertes-Aguilar J, Heuertz M, Marques I, et al. 2017. Is homoploid hybrid speciation that rare? An empiricist's view. *Heredity* xxx

111. Norris LC, Main BJ, Lee Y, Collier TC, Fofana A, et al. 2015. Adaptive introgression in an African malaria mosquito coincident with the increased usage of insecticide-treated bed nets. *Proceedings of the National Academy of Sciences* 112: 815-20
112. Orr HA. 1998. The population genetics of adaptation: the distribution of factors fixed during adaptive evolution. *Evolution* 52: 935-49
113. Orr HA. 2000. Adaptation and the cost of complexity. *Evolution* 54: 13-20
114. Orr HA, Turelli M. 2001. The evolution of postzygotic isolation: accumulating Dobzhansky-Muller incompatibilities. *Evolution* 55: 1085-94
115. Palkopoulou E, Lipson M, Mallick S, Nielsen S, Rohland N, et al. 2018. A comprehensive genomic history of extinct and living elephants. *Proceedings of the National Academy of Sciences* 115: E2566-E74
116. Patterson NJ, Moorjani P, Luo Y, Mallick S, Rohland N, et al. 2012. Ancient admixture in human history. *Genetics* 192: 1065-93
117. Payseur BA, Rieseberg LH. 2016. A genomic perspective on hybridization and speciation. *Molecular Ecology* 25: 2337-60
118. Pease JB, Haak DC, Hahn MW, Moyle LC. 2016. Phylogenomics reveals three sources of adaptive variation during a rapid radiation. *PLoS Biology* 14: e1002379
119. Peter BM. 2016. Admixture, population structure, and *F*-statistics. *Genetics* 202: 1485-501
120. Pfennig KS, Kelly AL, Pierce AA. 2016. Hybridization as a facilitator of species range expansion. *Proceedings of the Royal Society B: Biological Sciences* 283: 000-00
121. Phadnis N. 2011. Genetic architecture of male sterility and segregation distortion in *Drosophila pseudoobscura* Bogota-USA Hybrids. *Genetics* 189: 1001-09
122. Piálek J, Barton NH. 1997. The spread of an advantageous allele across a barrier: the effects of random drift and selection against heterozygotes. *Genetics* 145: 493-504
123. Pouyet F, Aeschbacher S, Thiéry A, Excoffier L. 2018. Background selection and biased gene conversion affect more than 95% of the human genome and bias demographic inferences. *eLife* 7: e36317
124. Pulido-Santacruz P, Aleixo A, Weir JT. 2020. Genomic data reveal a protracted window of introgression during the diversification of a Neotropical woodcreeper radiation. *Evolution* 74: 842-58
125. Rabosky DL, Hutchinson MN, Donnellan SC, Talaba AL, Lovette IJ. 2014. Phylogenetic disassembly of species boundaries in a widespread group of Australian skinks (Scincidae: *Ctenotus*). *Molecular Phylogenetics and Evolution* 77: 71-82
126. Racimo F, Sankararaman S, Nielsen R, Huerta-Sánchez E. 2015. Evidence for archaic adaptive introgression in humans. *Nature Reviews Genetics* 16: 350-71
127. Rieseberg LH. 1997. Hybrid origins of plant species. *Annual Review of Ecology and Systematics* 28: 359-89
128. Rieseberg LH. 2006. Hybrid speciation in wild sunflowers. *Annals of the Missouri Botanical Garden* 93: 34-48, 15
129. Rieseberg LH, Soltis DE, Palmer JD. 1988. A molecular reexamination of introgression between *Helianthus annuus* and *H. bolanderi* (Compositae). *Evolution* 42: 227-38
130. Roesti M, Hendry AP, Salzburger W, Berner D. 2012. Genome divergence during evolutionary diversification as revealed in replicate lake–stream stickleback population pairs. *Molecular Ecology* 21: 2852-62

131. Roesti M, Moser D, Berner D. 2013. Recombination in the threespine stickleback genome -- patterns and consequences. *Molecular Ecology* 22: 3014-27
132. Rogers J, Raveendran M, Harris RA, Mailund T, Leppälä K, et al. 2019. The comparative genomics and complex population history of *Papio* baboons. *Science Advances* 5: eaau6947
133. Romanes GJ. 1886. Physiological selection; an additional suggestion on the origin of species. *Journal of the Linnean Society of London (Zoology)* 19: 337-411
134. Rosser N, Dasmahapatra KK, Mallet J. 2014. Stable *Heliconius* butterfly hybrid zones are correlated with a local rainfall peak at the edge of the Amazon basin [contrary to one prediction of Pleistocene Refugium theory]. *Evolution* 68: 3470-84
135. Rosser N, Queste L, Cama B, Edelman N, Mann F, et al. 2019. Geographic contrasts between pre- and post-zygotic barriers are consistent with reinforcement in *Heliconius* butterflies. *Evolution* 73: 1821-38
136. Sabeti PC, Reich DE, Higgins JM, Levine HZP, Richter DJ, et al. 2002. Detecting recent positive selection in the human genome from haplotype structure. *Nature (London)* 419: 832-37
137. Schield DR, Adams RH, Card DC, Perry BW, Pasquesi GM, et al. 2017. Insight into the roles of selection in speciation from genomic patterns of divergence and introgression in secondary contact in venomous rattlesnakes. *Ecology and evolution* 7: 3951-66
138. Schluter D. 2000. *The Ecology of Adaptive Radiation*. New York: Oxford University Press. - pp.
139. Schumer M, Rosenthal G, Andolfatto P. 2014. How common is homoploid hybrid speciation? *Evolution* 68: 1553-60
140. Schumer M, Xu C, Powell DL, Durvasula A, Skov L, et al. 2018. Natural selection interacts with recombination to shape the evolution of hybrid genomes. *Science* 360: 656-60
141. Seehausen O. 2004. Hybridization and adaptive radiation. *Trends in Ecology and Evolution* 19: 198-207
142. Setter D, Mousset S, Cheng X, Nielsen R, DeGiorgio M, Hermisson J. 2020. VolcanoFinder: genomic scans for adaptive introgression. *PLoS Genetics* 16: e1008867
143. Shull GH. 1952. Beginnings of the heterosis concept. In *Heterosis. A Record of Researches Directed Toward Explaining and Utilizing the Vigor of Hybrids*, ed. JW Gowen, pp. 14-48. Ames, Iowa: Iowa State College Press
144. Slate J. 2005. Quantitative trait locus mapping in natural populations: progress, caveats and future directions. *Molecular Ecology* 14: 363-79
145. Slowinski JB, Page RDM. 1999. How should species phylogenies be inferred from sequence data? *Systematic Biology* 48: 814-25
146. Soltis PS, Soltis DE. 2009. The role of hybridization in plant speciation. *Annual Review of Plant Biology* 60: 561-88
147. Song Y, Endepols S, Klemann N, Richter D, Matuschka FR, et al. 2011. Adaptive introgression of anticoagulant rodent poison resistance by hybridization between Old World mice. *Current Biology* 21: 1296-301

148. Stapley J, Feulner PGD, Johnston SE, Santure AW, Smadja CM. 2017. Variation in recombination frequency and distribution across eukaryotes: patterns and processes. *Philosophical Transactions of the Royal Society B: Biological Sciences* 372
149. Staubach F, Lorenc A, Messer PW, Tang K, Petrov DA, Tautz D. 2012. Genome patterns of selection and introgression of haplotypes in natural populations of the house mouse (*Mus musculus*). *PLoS Genetics* 8: e1002891
150. Suvorov A, Kim BY, Wang J, Armstrong EE, Peede D, et al. 2021. Widespread introgression across a phylogeny of 155 *Drosophila* genomes. *bioRxiv*: 2020.12.14.422758
151. Svardal H, Quah FX, Malinsky M, Ngatunga BP, Miska EA, et al. 2019. Ancestral hybridisation facilitated species diversification in the Lake Malawi cichlid fish adaptive radiation. *Molecular Biology and Evolution*
152. Taylor SA, Larson EL. 2019. Insights from genomes into the evolutionary importance and prevalence of hybridization in nature. *Nature Ecology & Evolution* 3: 170-77
153. Todesco M, Pascual MA, Owens GL, Ostevik KL, Moyers BT, et al. 2016. Hybridization and extinction. *Evolutionary Applications* 9: 892-908
154. Turelli M, Lipkowitz JR, Brandvain Y. 2014. On the Coyne and Orr-igin of species: effects of intrinsic postzygotic isolation, ecological differentiation, X chromosome size, and sympatry on *Drosophila* speciation. *Evolution* 68: 1176-87
155. Valencia-Montoya WA, Elfekih S, North HL, Meier JI, Warren IA, et al. 2020. Adaptive introgression across semipermeable species boundaries between local *Helicoverpa zea* and invasive *Helicoverpa armigera* moths. *Molecular Biology and Evolution* 37: 2568-83
156. Veller C, Edelman NB, Muralidhar P, Nowak MA. 2019. Recombination, variance in genetic relatedness, and selection against introgressed DNA. *bioRxiv*: 846147
157. Veller C, Kleckner N, Nowak MA. 2019. A rigorous measure of genome-wide genetic shuffling that takes into account crossover positions and Mendel's second law. *Proceedings of the National Academy of Sciences* 116: 1659-68
158. Voight BF, Kudaravalli S, Wen X, Pritchard JK. 2006. A map of recent positive selection in the human genome. *PLoS Biology* 4: e72
159. Wallbank RWR, Baxter SW, Pardo-Diaz C, Hanly JJ, Martin SH, et al. 2016. Evolutionary novelty in a butterfly wing pattern through enhancer shuffling. *PLoS Biology* 14: e1002353
160. Walsh J, Kovach AI, Olsen BJ, Shriver WG, Lovette IJ. 2018. Bidirectional adaptive introgression between two ecologically divergent sparrow species. *Evolution* 72: 2076-89
161. Weber AA-T, Rajkov J, Smailus K, Egger B, Salzburger W. 2021. Diversification dynamics and (non-)parallel evolution along an ecological gradient in African cichlid fishes. *bioRxiv*: 2021.01.12.426414
162. Wen D, Nakhleh L. 2018. Coestimating reticulate phylogenies and gene trees from multilocus sequence data. *Systematic Biology* 67: 439-57
163. Wright S. 1931. Evolution in Mendelian populations. *Genetics* 10: 97-159