Q&A: Genetic Lineages

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Abstract

Genetic lineages are key to understanding evolution in complex scenarios and the evolution of genetic systems. However, they are often misunderstood; for example, confused with alleles or pedigrees. Here, we provide an accessible introduction to genetic lineages in question and answer format, from their definition as a physical object in space-time to their empirical characterization through ancestral recombination graphs. We then illustrate how lineages are essential to a clear understanding of several cutting-edge problems, for which more classical population genetic techniques are inadequate.

Keywords: evolvability; bet-hedging; evolution of mutation rate; evolution of recombination rate; incomplete lineage sorting; invasion fitness; social evolution

Q. What is a genetic lineage?

Consider a single DNA base pair in the genome of one haploid individual (or one copy in a diploid or polyploid individual) within a population. When that individual produces an offspring, suppose further that a new mutation arises at the location of that base pair; i.e., the nucleotide in the offspring has a different base from the one in the parent from which that stretch of DNA was inherited. When the mutated individual reproduces, this mutation can be inherited by its offspring and beyond. In this Q&A, we define a (genetic) **lineage** as the set of all copies at this DNA position that descend from the original mutation (each lineage is shown by a different color in Fig. 1). We thus only discuss genetic lineages, noting that the word lineage is also sometimes used to discuss relationships by descent of organisms, species, or cells (Hull 1980; Nunney 1999; Neto 2019; Suárez and Haber 2025; Weinreich 2026).

“Descent” involves the physical process of copying DNA from a template, making the lineage a concrete object in space-time, rather than merely an abstraction. Since lineage members are

copies from a template, we can see that the lineage can expand not only via vertical inheritance, but also via other processes like horizontal gene transfer and gene conversion.

Q. How is a lineage different from an allele?

Both alleles and lineages describe something about a nucleotide or a longer non-recombining stretch of DNA. However, if exactly the same mutation occurs twice, it gives rise to two lineages, each encoding the same allele (Fig. 1A; triangles represent the same derived allele arising independently in several lineages, which together constitute a soft sweep through the population). The sameness of the allele is based on its information content rather than its evolutionary history. (This is the same distinction as between identical by descent in genetics versus identical by state (Lynch and Walsh 1998: 132; Rousset 2002)).

If one mutation creates a lineage, and later a second mutation either reverses this back to the first allele, or creates a third allele, then that second mutation creates a **sublineage** (Fig. 2, nested circles). Because members of this sublineage are still directly descended from the original mutation, the entire sublineage is a subset of the first lineage, despite containing multiple alleles.

Q. How long does a lineage last?

Most mutations die out due to random genetic drift (Fig. 1A: purple, dark blue, and orange triangles); some eventually take over the population; either outcome might be enhanced or impeded by selection. When a lineage becomes fixed, it lasts until it is replaced by gene flow from a different population, until the population itself goes extinct, or until a deletion at that site becomes fixed. Non-deletion mutations at the same nucleotide position do not extinguish parental lineage identity; they instead found sublineages that are also part of the lineage of the original founding mutation. Lineages that spread into many individuals over long periods of time are most prone to spawn sublineages. Some lineages, e.g. those underlying core innovations of the translational machinery, have persisted and diversified such that they now encompass all extant cellular life (Bowman et al. 2020).

Q. Why a single nucleotide - isn't a haplotype a kind of lineage?

A genetic lineage describes a genetic unit that recombination does not divide, a condition that is met automatically for single base pairs. One can also define lineages for longer stretches of DNA, corresponding to haplotypes in which no recombination has occurred. In this case, not just mutation but also recombination within the stretch can found a new lineage.

Q. What does recombination do to lineages?

Recombination shortens the stretch of nucleotides that share the same lineage history. Recombination can also be mutagenic (Halldorsson et al. 2019), in which case each recombination-associated mutation creates new lineages at the mutated sites. Lineages can also track the influence of population structure in space (King et al. 2026).

Q. What defines a new lineage?

In principle, we could choose a nucleotide and start tracking a lineage for no reason at all. In practice, a sublineage isn't interesting when nothing happened to make it different from its parent lineage. A mutation to a site or recombination changing a haplotype can make a lineage worth tracking. So could a horizontal transfer event into a new population or species. Similarly, recombination or chromosomal rearrangement could make a lineage even at a single nucleotide site worth tracking when the implications of a particular allele depend on its chromosomal neighborhood.

Q. How is a genetic lineage different from a pedigree?

A pedigree (or family tree) describes the history of which whole ***organisms*** are descended from which, while the structure of a genetic lineage describes the history of relatedness for just a small, unrecombined stretch of DNA, potentially even as short as a single base pair. The term "gene genealogy" in population genetics (Takahata and Nei 1985) and coalescent theory (Hudson 1990; Wakeley 2009) means the same thing as genetic lineage, whereas "genealogy" on its own generally means pedigree.

In a completely asexual species, the organismal pedigree will be identical to the lineage of each of its genes. Both segregation of chromosomes and recombination within chromosomes cause different genetic lineages to follow different paths back through the pedigree. Horizontal gene transfer similarly causes the transferred gene to have a different lineage from either the donor or the recipient organism. Gene duplication also causes the two to differ, creating an additional branching event in the lineage that is not found in the pedigree. Gene conversion similarly differentiates lineages in a manner not reflected in the pedigree.

Q. How do you use lineages empirically?

The **coalescent** is a mathematical model of the structure of lineages. The coalescent ignores extinct lineages, instead describing only how genes in the present "coalesce" in the past due to inheritance from a common parent (Kingman 1982a; Kingman 1982b). Fig. 1B shows the coalescent subset of the lineages in Fig. 1A.

Different genes within the same species can have different lineage (coalescent) histories. The term "incomplete lineage sorting" (DeMarais et al. 1992; Maddison 1997) came to be used to describe genes whose lineage history differs from the usual history that tracks that of the species (Fig. 3A). This occurs when a polymorphism persists through multiple speciation events, and then different alleles (Fig. 3A, teal and purple lineages) are retained in different species (Avise et al. 1983; Tajima 1983).

Traditional coalescence methods assume that all DNA sites share the same history, ignoring recombination. Recent advances in "ancestral recombination graphs" (Lewanski et al. 2024) now allow the history of recombination to be included, giving a more nuanced view of how different portions of the sequence have different lineage histories (Fig. 3B). For example, ancestral recombination graphs reveal that the SARS-CoV-2 XBB Omicron lineage, which rose in frequency in late 2022, arose from recombination between two BA.2 lineages, BJ.1 and BM.1.1.1 (Tamura et al. 2023).

Gene-tree species-tree differences can also arise from horizontal transfer, and from gene duplication and loss. New phylogenetic methods that recognize gene-tree species-tree differences, and explicitly model gene duplication, transfer and loss, are achieving superior outcomes in inferring gene trees and species trees (Morel et al. 2020; Morel et al. 2022; Morel et al. 2024).

In experimental laboratory populations, lineages can be measured by tagging individual cells with unique barcodes generated in a combinatorial manner, generally 10^5 or more (Levy et al. 2015). This has been used to study the time course of many lineages defined by beneficial mutations simultaneously (Levy et al. 2015; Nguyen Ba et al. 2019), and to trace the fate of cell lineages within multicellular organisms (Wagner and Klein 2020).

Q. How does a lineage approach help us understand natural selection?

Early evolutionary theory studied selection, mutation, and drift at a single genetic locus in a single well-mixed population whose environment remained constant (e.g.: Fisher 1922; Haldane 1927; Wright 1931; Kimura 1955). The 1960s and 1970s brought investigations of how natural selection operates in more complex scenarios where genes can modify the reproduction process itself including mutation and recombination, where the environment can change randomly over time, and where individuals can interact and affect each other's fitness. Below we explain how all three of these cases were better understood by tracking the fate of lineages founded by mutations that alter the phenomena of interest.

Q. How do lineages help us understand how evolutionary processes such as mutation and recombination evolve?

An individual's germline mutation rate and recombination rate do not directly affect their fitness, but do affect the fitness of their descendants. Early work on the evolution of these rates in infinitely large, randomly mating populations argued that the rates that evolved were the ones that maximized the arithmetic mean fitness of individuals in the population at equilibrium (Kimura 1967; Karlin and McGregor 1972; Karlin and McGregor 1974). However, evolution does not always maximize arithmetic mean fitness (Moran 1964; Lewontin 1970; Feldman et al. 1996). Instead, evolution of these rates is better understood by tracking the fate of alleles at distinct "modifier" loci (Karlin and McGregor 1972; Karlin and McGregor 1974) that affect mutation rate (e.g., Leigh 1970; Karlin and McGregor 1972; Karlin and McGregor 1974) and recombination rate (e.g., Nei 1967; Feldman 1972; Feldman et al. 1980; Otto and Feldman 1997). A long-term measure of the fitness of a lineage is needed to capture which alleles tend to persist versus go extinct.

In a pioneering set of papers, Eshel (1973a; 1973b) made two innovations. First, he recognized the centrality of lineages in understanding the fate of modifier alleles. Second, he treated modifier alleles stochastically to operationalize modifier fitness in terms of the probability of establishment. Specifically, Eshel noted that the evolutionary success of these genes depends on the "long-run survival probabilities of whole, evolving lines of descendents carrying a given modifying [gene], rather than [on] the short term success of individuals in the population" (Eshel 1973a). Eshel called selection on the long-run survival of a lineage "clone selection" (Eshel 1973a; Eshel 1973b); clones are equivalent to lineages in the clonal populations considered by Eshel.

More recently, this kind of selection has been called "lineage selection" (Aboitiz 1991). (Van Valen, 1975 also uses the term "lineage selection" to mean species selection, which is not our usage here). Correspondingly, the establishment probability of the lineage captures an aspect of "lineage fitness" (Lehmann et al. 2015; Akçay and Van Cleve 2016; Lehmann et al. 2016; Van Cleve 2023; Smith et al. 2026) of the mutation defining the lineage.

Q. How do lineages help us understand evolution in variable environments?

Consider an environment that changes on the timescale of multiple generations. Because the fate of a mutant lineage depends on the fitness of descendants in different environments, a lineage perspective is needed (Graves and Weinreich 2017). Geometric mean fitness captures the idea that population growth is a multiplicative process, and thus that fitness should similarly multiply over generations, such that a single generation with fitness of zero causes extinction (Cohen 1966; Lewontin and Cohen 1969). For example, evolution might favor parents whose seeds are split between germinating in the current season versus staying dormant and available to take advantage of better conditions in the future. This is an example of a diversified bet-hedging strategy (Seger and Brockmann 1987). If evolution optimizes geometric mean fitness, then the probability of germinating evolves to become equal to the probability of a wet year (Cohen 1966; Lewontin and Cohen 1969). There is empirical evidence for the adaptive evolution of dormancy (Venable 2007; Beaumont et al. 2009; Gremer and Venable 2014; Rajon et al. 2014). This suggests that bet-hedging strategies more broadly may be adaptive, including mutational and phenotypic switching (Leigh 1970; Ishii et al. 1989; Lachmann and Jablonka 1996; Salathé et al. 2009; Carja et al. 2014), recombination (Carja et al. 2014), and other factors that increase genetic variability.

Because geometric mean fitness includes the fitness of all descendants, it is a lineage property and a measure of lineage fitness. The expected geometric growth rate of an initially rare mutant lineage is a crucial concept in evolutionary game theory (Maynard Smith and Price 1973; Taylor and Jonker 1978; Hofbauer and Sigmund 1998) and related fields like adaptive dynamics (Metz et al. 1996; Geritz et al. 1998; Dercole and Rinaldi 2008). The growth rate of a mutant lineage is called “invasion fitness” in those fields (Metz et al. 1992; Rand et al. 1994; Heino et al. 1998). By measuring the lineage fitness of a specific mutation, invasion fitness avoids the need to argue that adaptation will produce an optimal population-level solution. While both geometric mean fitness and invasion fitness capture the distribution of future environments, they ignore important stochasticity that occurs in small populations. Newer fitness measures that capture this additional stochasticity show that it can further drive rates of bet-hedging (King and Masel 2007; Weissman et al. 2025; Smith et al. 2026).

Q. How do lineages help us understand social behavior?

One of the ways that individuals can affect each other’s fitness is for one individual to expend effort that reduces their fitness in order to help another individual whose fitness increases as a result. This is called altruistic helping (Hamilton 1963), and it was the subject of considerable controversy beginning in the 1960s and continuing for many years (reviewed in Okasha 2001; and Wilson and Wilson 2007). If only the fitness of a single individual and the genes within it are considered, altruistic helping is an evolutionary conundrum. One solution to this conundrum is to

track all copies of the altruistic allele and measure their evolutionary success. One measure of this success is “inclusive fitness,” which weights the fitness consequences of interactions between individuals in a manner depending on the degree of genetic relatedness (Hamilton 1964).

Mathematical models show that a calculation of lineage invasion fitness can yield exactly the same expression as could be obtained in a calculation of inclusive fitness (Akçay and Van Cleve 2016; Lehmann et al. 2016). The choice of which one to use is colored by preconceptions as to whether fitness is better conceived as an individual versus as a lineage property. One reason we advocate for the centrality of lineages is that it provides a common conceptual and analytical framework across diverse scenarios. The fate of a modifier of mutation or recombination depends on children and grandchildren, i.e. on later members of the same lineage. The fate of modifiers of social evolution additionally depends on siblings and cousins, i.e. on concurrent members of the same lineage.

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Figures

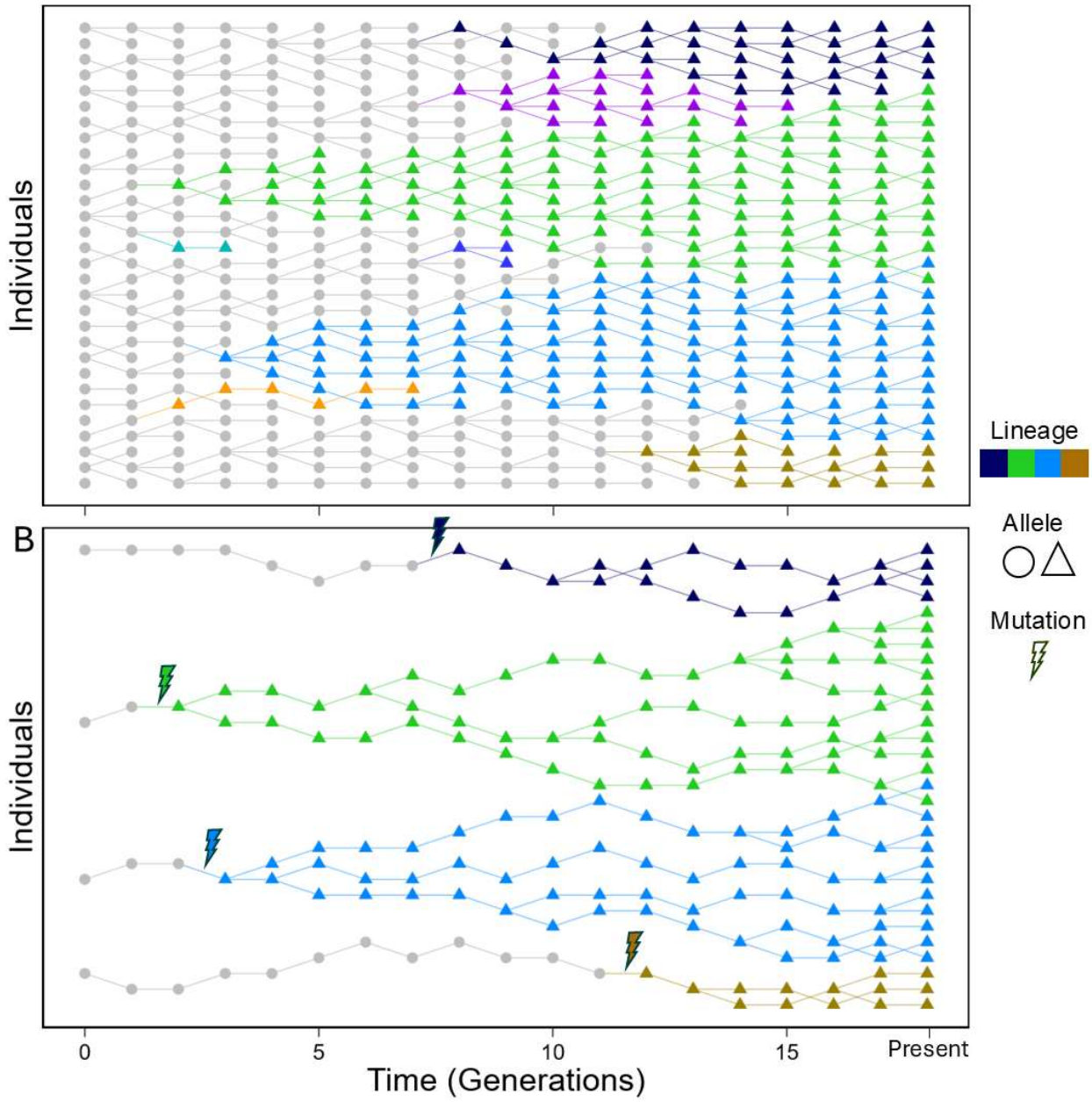

Figure 1. A simulated population illustrating the relationship between genetic lineages, alleles, and the coalescent. Each point is one individual's copy of a genetic locus, linked by descent to the copy inherited from its parent; color denotes lineage identity, with a new color marking a mutation event (lightning bolt) that founds a new lineage. Point shape denotes allelic state — circle, ancestral allele; triangle, derived allele — indicating the parallel arrival of the same allele in different lineages. (A) A soft selective sweep (Hermisson and Pennings 2005): the derived allele (triangle) arises independently in several unrelated lineages (distinct colors,

one shape), each spreading under positive selection and together driving the allele toward fixation. (B) The same population, pruned to gene copies with descendants in the present generation. The lineage structure is unchanged, but pruning reveals the coalescent from the present back to a handful of ancestors. Simulated under a discrete-generation Wright-Fisher model (haploid population size N = 30 over 18 generations; each offspring's parent is drawn from its own position or an adjacent one in the previous generation, weighted by fitness). The derived allele arises by recurrent mutation from the ancestral background (μ = 0.02 per generation) — independently, in different lineages — and confers a 2.5-fold fitness advantage.

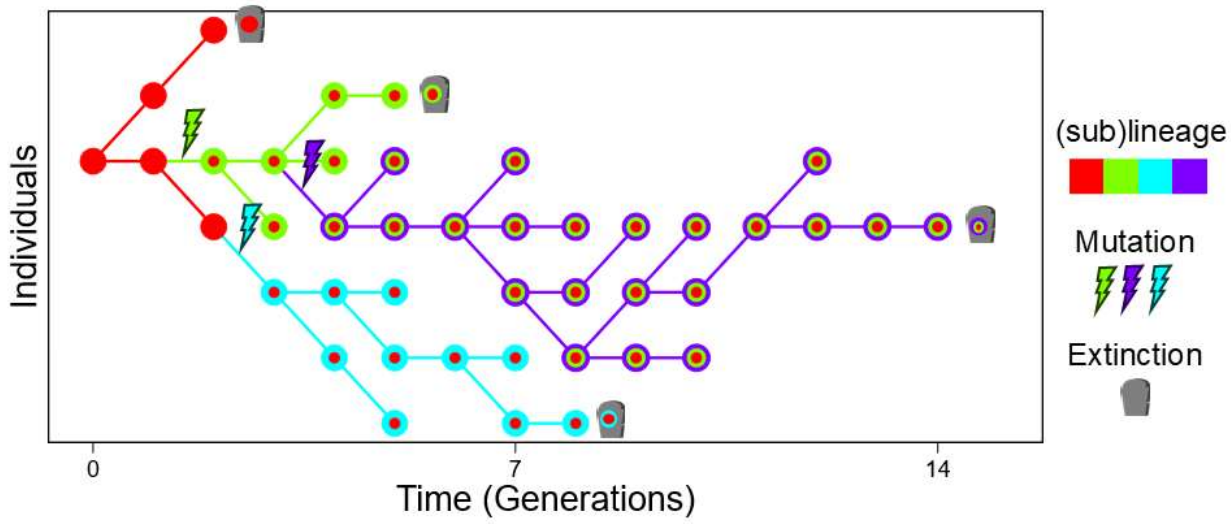

Figure 2. A simulated complete history of a lineage, including the formation of sublineages through mutation. As in Fig. 1, each point is one individual's copy of a locus, linked by descent to the copy inherited from its parent; color denotes lineage and sublineage identity, with a new color marking a mutation event (lightning bolt; probability = 0.035 per individual per generation) that founds a new sublineage nested within its parent lineage. A tombstone marks the extinction of a (sub)lineage — the point after which it leaves no further descendants. The mutations shown here are neutral. This population was simulated as a branching process — each gene copy independently leaves 0–3 descendants per generation with the expected increase from mean 1.2 being insufficient in this example to avoid chance extinction.

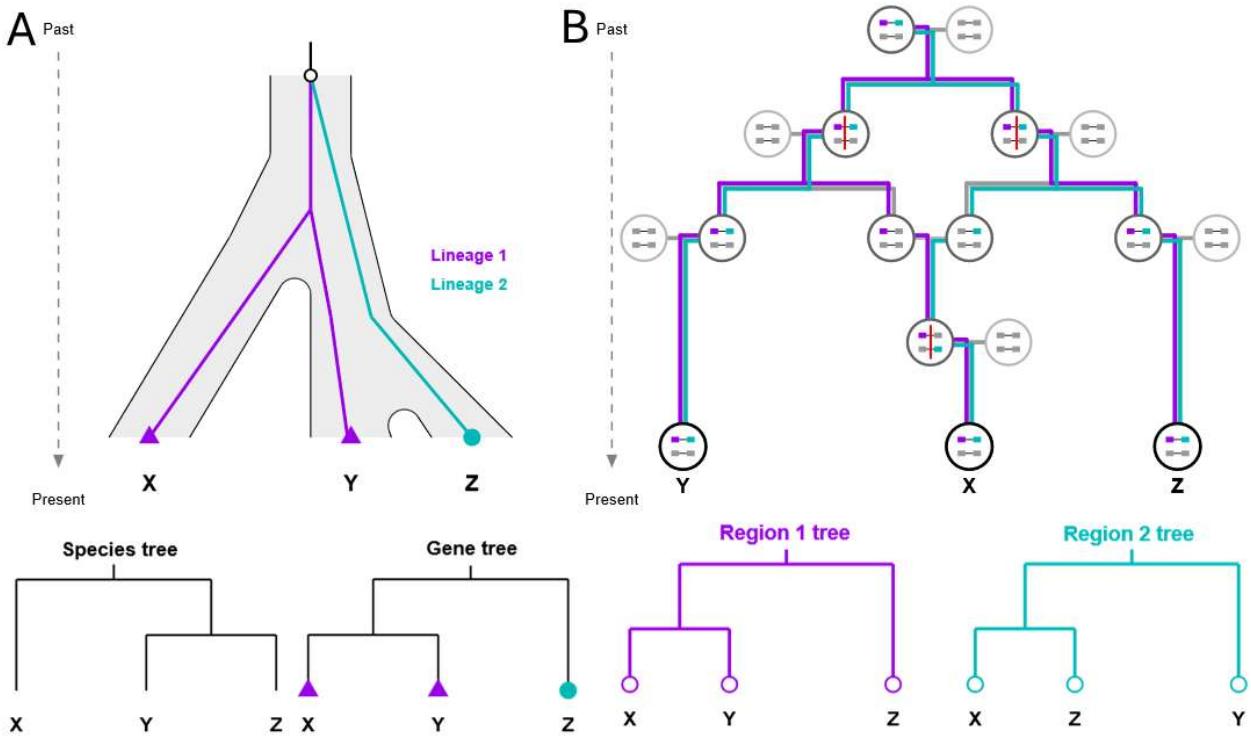

Figure 3. Both incomplete lineage sorting (A) and recombination (B) can cause different loci to have different lineage histories. (A) Two speciation events in quick succession (grey species tree) can lead to sister species (Y and Z) inheriting different alleles from a polymorphism that pre-dates an earlier speciation event (with X). The resulting gene tree does not match the species tree. (B) A lineage initiated in one gene (in purple) is twice separated by recombination (red vertical line) from another gene whose allele is shown in teal on the same chromosome. The two alleles are brought back together by a third recombination event, shown in this pedigree as taking place in the offspring of a first-cousin marriage. Despite individuals X, Y, and Z each having the same genotype, the two genes have different lineage histories.

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