Ancestral recombination graphs

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Computational biology

Genealogy

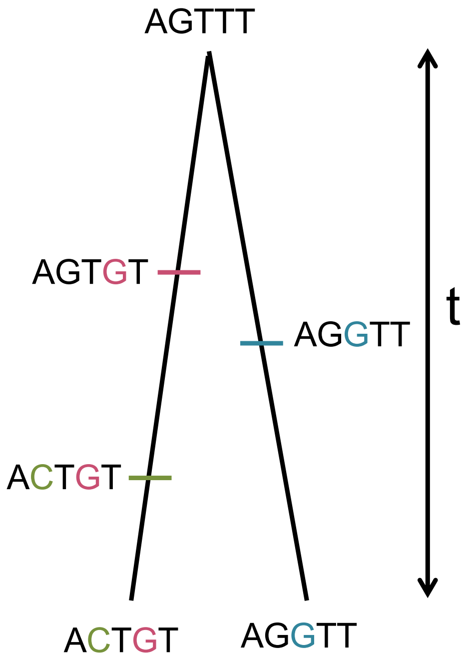


Figure 1: From Graham Coop's book

Genealogy Y-chromosome

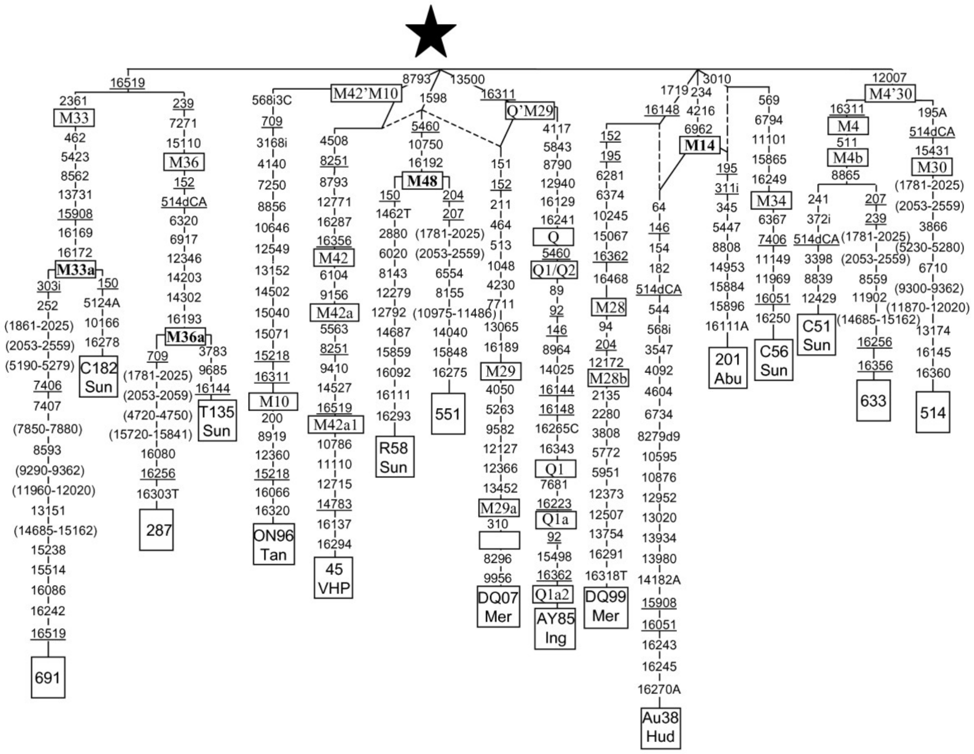
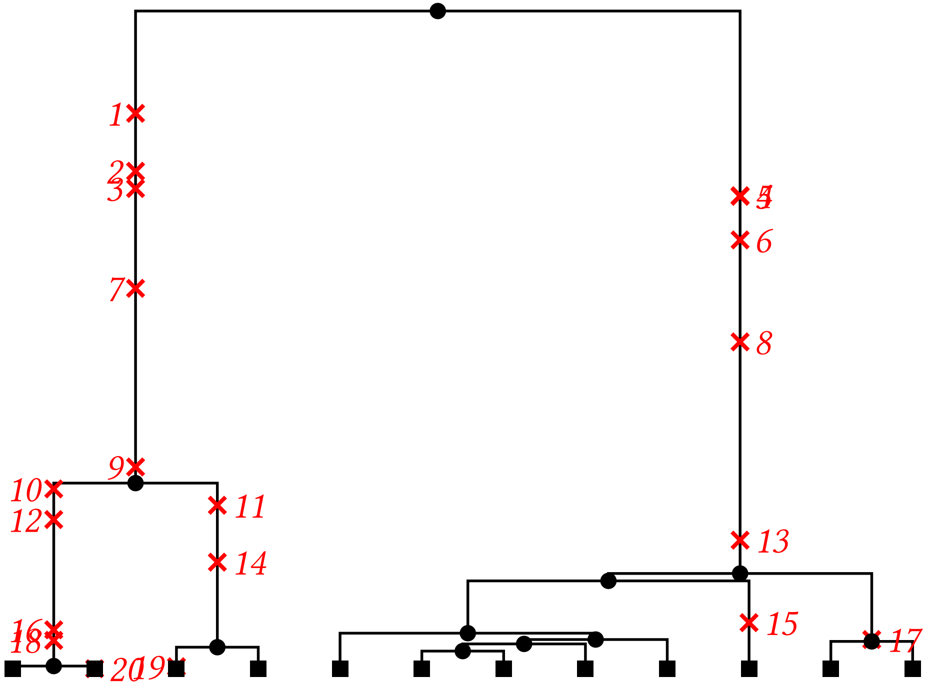


Figure 2: From wikipedia

Mutations



Primer in coalescence theory

- How populations’ genetic variation evolves.
- Developed independently in the 1980s by John Kingman, Fumio Tajima and Richard Hudson.
- A model (backwards in time) of how samples originate from a common ancestor.

Wright-Fisher population

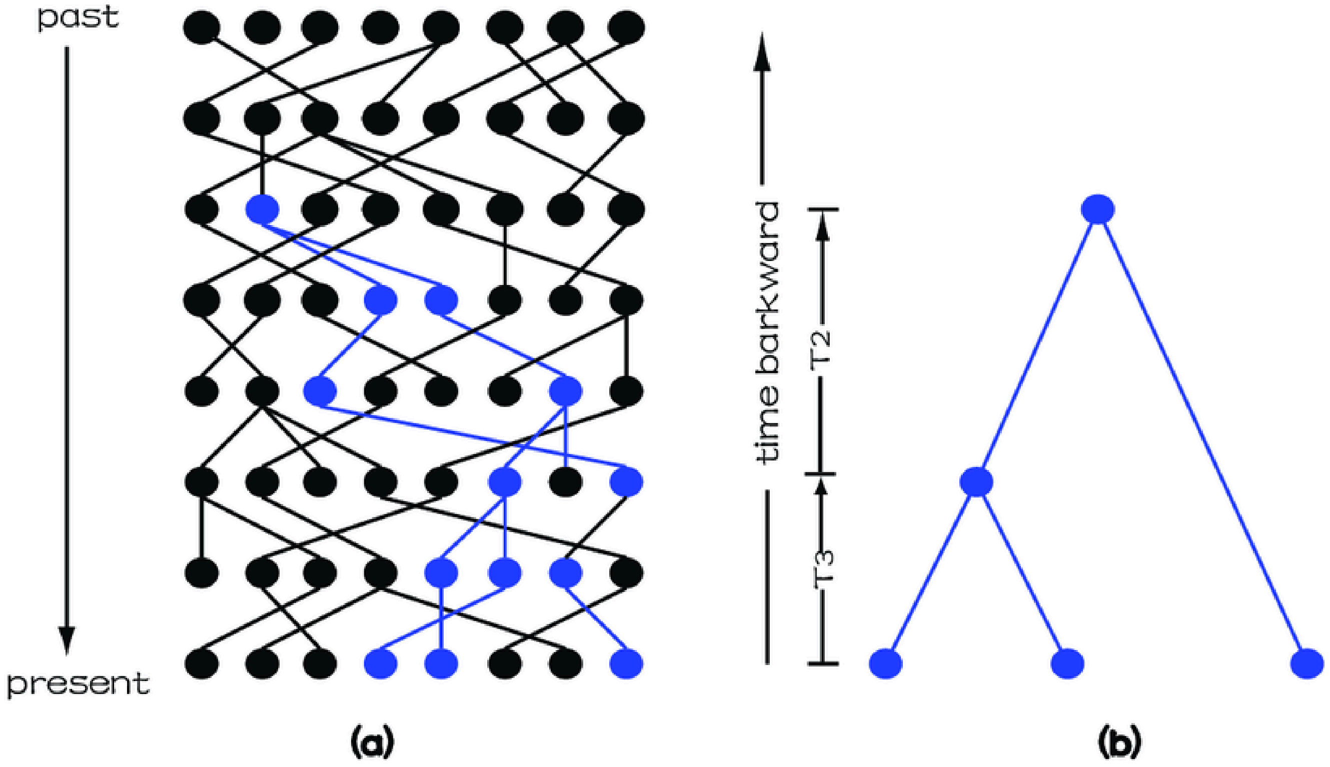


Figure 4: From Rosenberg and Nordborg (2002)

Coalescence of two lineages

The probability that two genes are copies of the same gene (i.e. they coalesce) in the previous generation is

$$\frac{1}{N}$$

i.e. the population size is the inverse of the *rate at which coalescence events* take place but only in the simplest cases!

Coalescence of k lineages

The probability that any pair of k genes coalesce in the previous generation is

$$\binom{k}{2}\frac{1}{N}$$

For $k = 3$, this is

$$\binom{3}{2}\frac{1}{N} = \frac{3}{N}$$

Waiting times

When $k \ll N$, waiting times are **exponentially** distributed with rate

$$\lambda = \frac{\binom{k}{2}}{N}$$

At any point in the genealogy, the probability that the next coalescence event occurs in time $t + \Delta t$ is

$$p(\Delta t) = \exp(-\Delta t \cdot \lambda) \times \lambda$$

What about recombination?

parent 1

parent 2

sibling 1

sibling 2

Ancestral recombination graphs

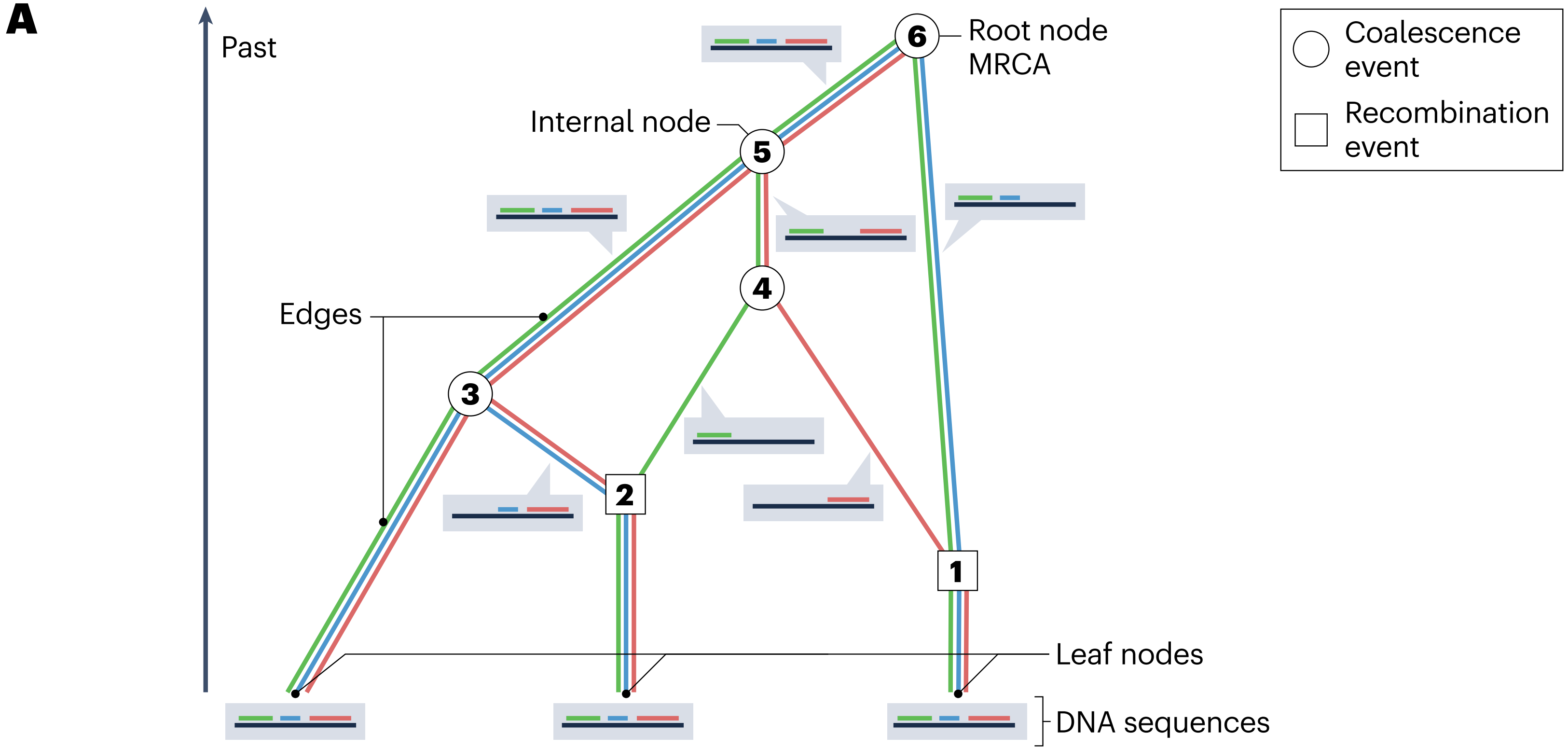


Figure 6: From Nielsen *et. al.* 2025

Sequence of trees

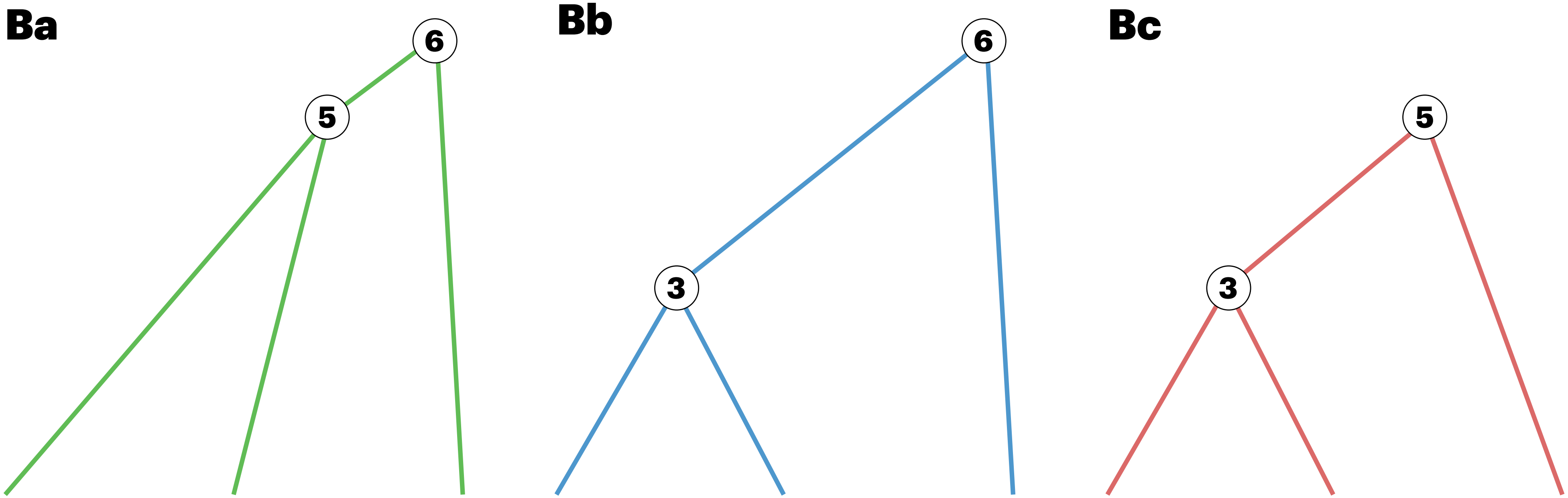


Figure 7: From Nielsen *et. al.* 2025

Succinct tree sequences

Figure 8: Storage, manipulation and analysis of genomes with `tskit`

ARGs as data structures

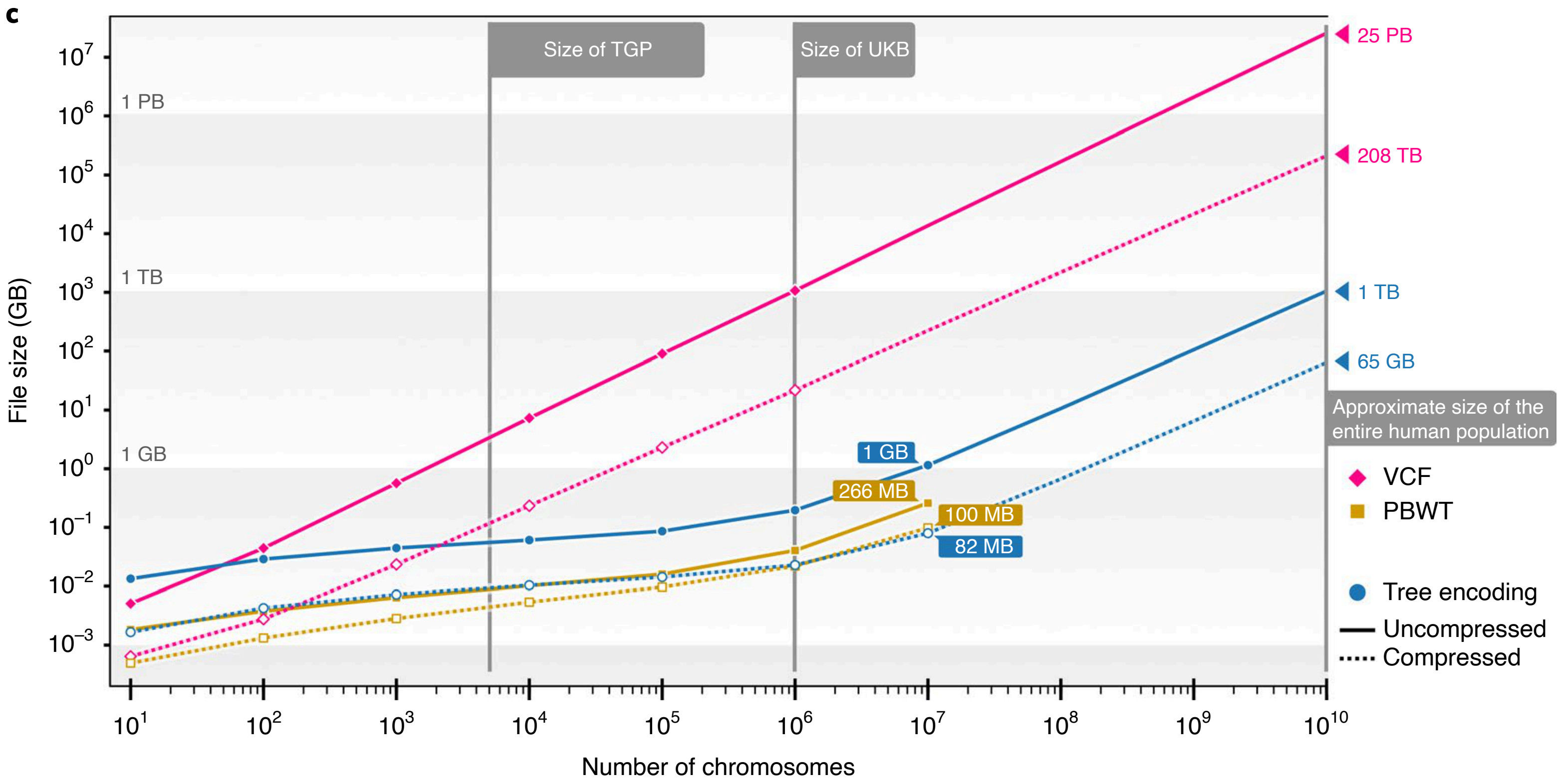


Figure 9: From Kelleher *et. al.* (2019)

Interactive demo?

Visit www.argscape.com

Play with four key parameters:

- Population size
- Number of lineages
- Recombination rate
- Mutation rate

Applications (more to come)

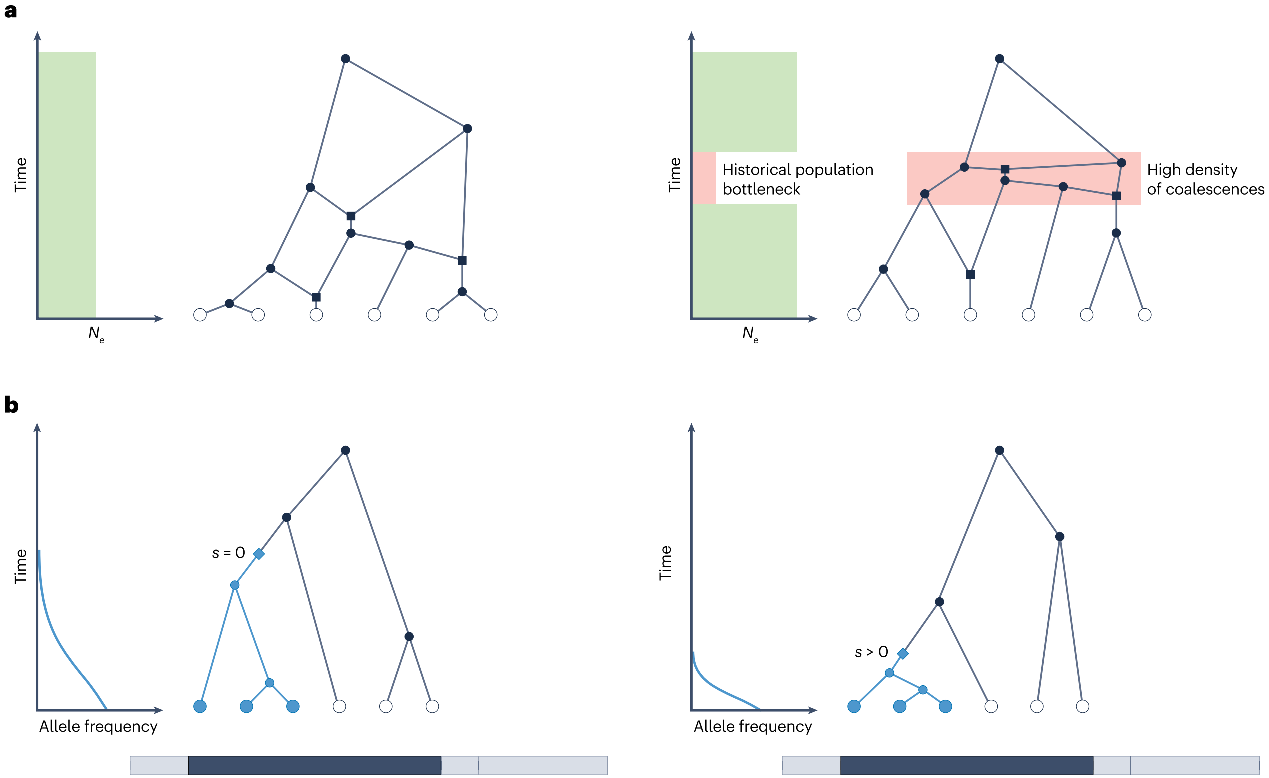


Figure 10: From Nielsen 2025

Contact information

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In the next section

> Now, in the first place I deny that the mathematical theory of population genetics is at all impressive, at least to a mathematician. … Our mathematics may impress zoologists but do not greatly impress mathematicians.
>
> — Haldane (1964)

> Well, that was true in the past, but not anymore.
>
> — Arthur (today)