Computational Biology

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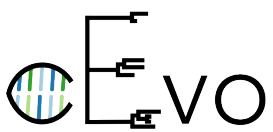
Sarah Nadeau & Marc Manceau

Computational Evolution
Department of Biosystems Science and Engineering

HS 2019



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Linkage and phylogeny
Wright-Fisher with Recombination
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Questions

- Under a structured birth-death model, how do the sub-population sizes vary (if at all) through time?

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- Suppose you perform a structured coalescent analysis on sequences collected from a relatively *unstructured* population. Would you expect the posterior migration rate to be very low or very high? Why?

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- How might the evolution of languages violate the assumptions of a substitution+birth/death phylodynamic model?

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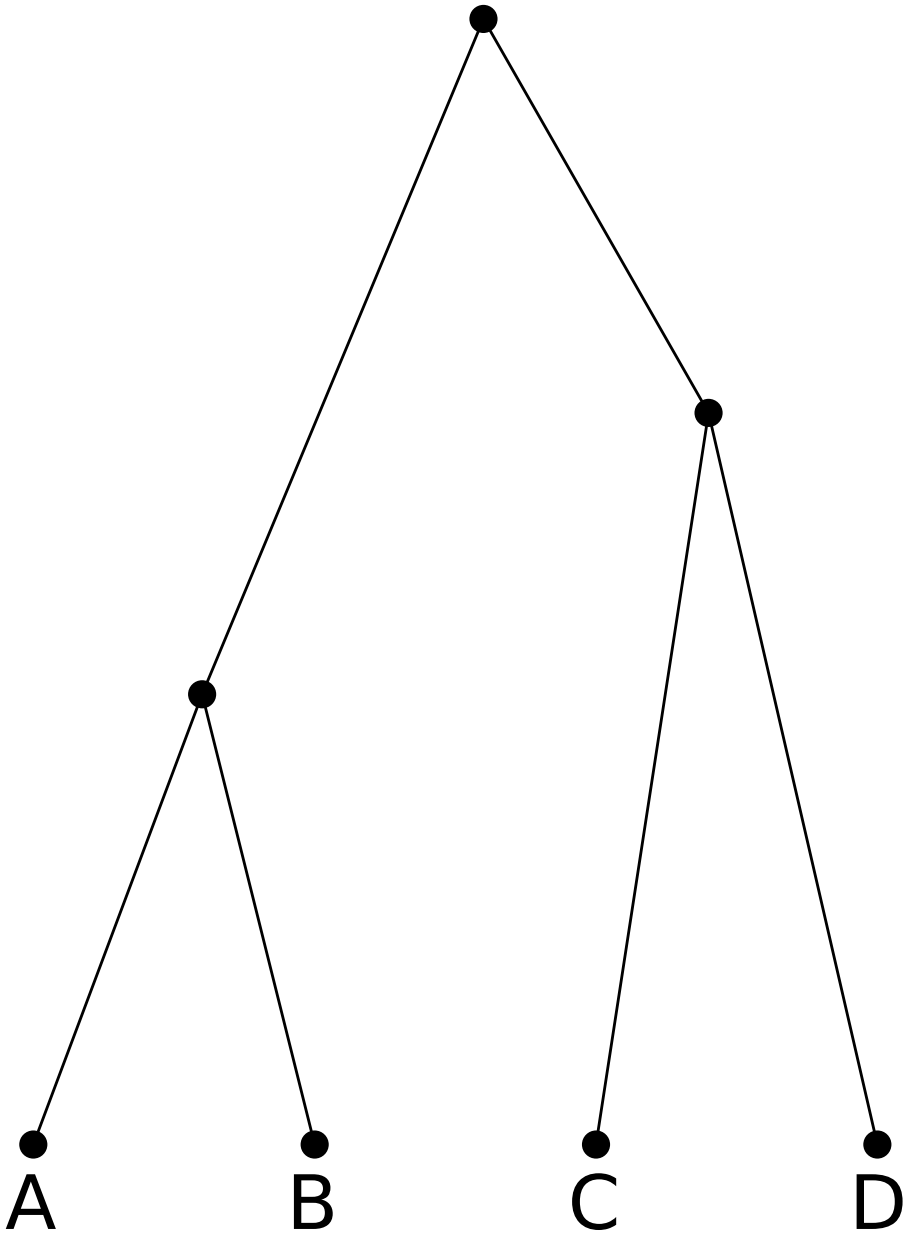
Phylogenetic Trees



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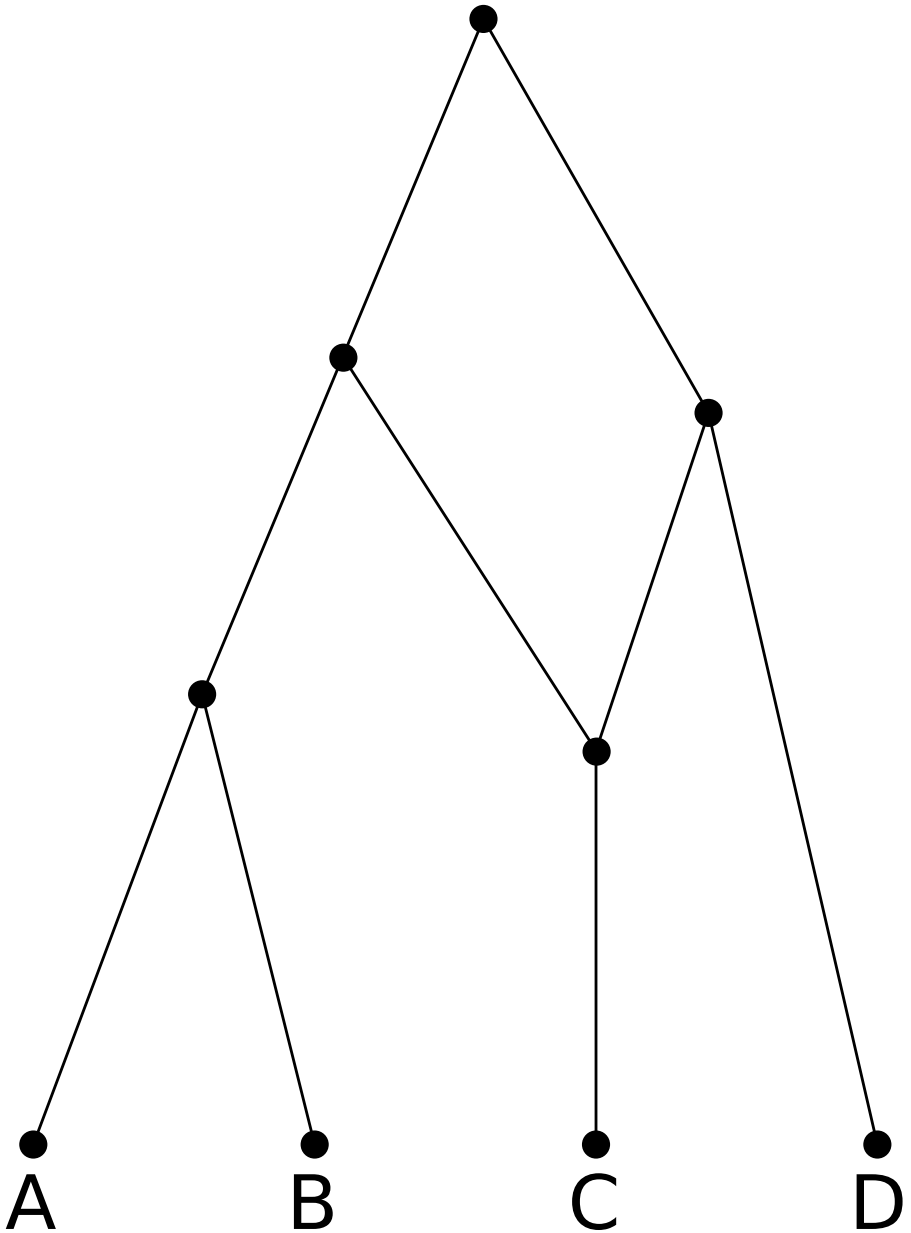

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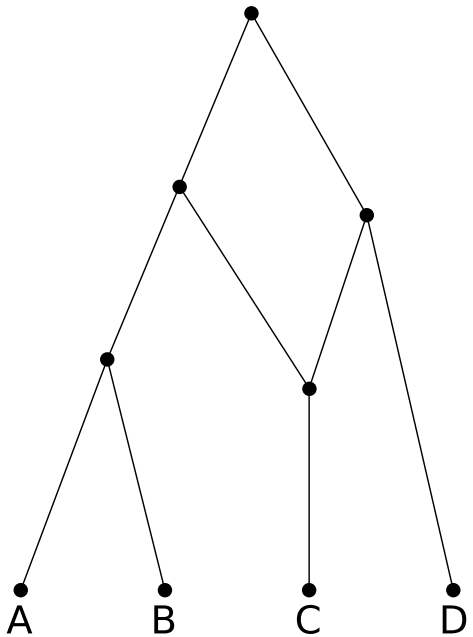
Phylogenetic Networks

Just as for trees, phylogenetic networks represent a wide range of evolutionary relationships:



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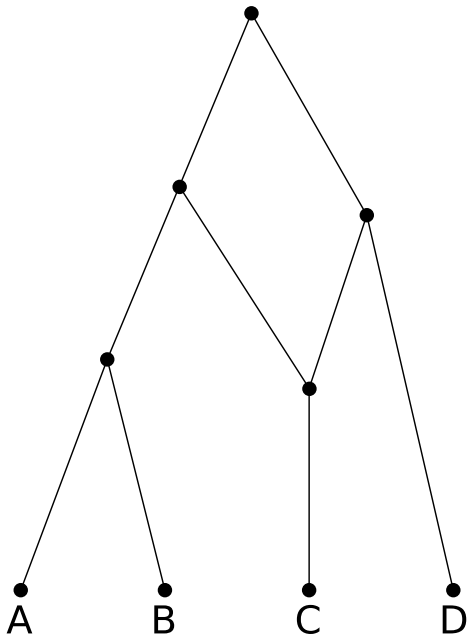
- For **species**, the network represents species ancestry and nodes with multiple parents represent hybridisation or horizontal gene transfer (HGT) events.



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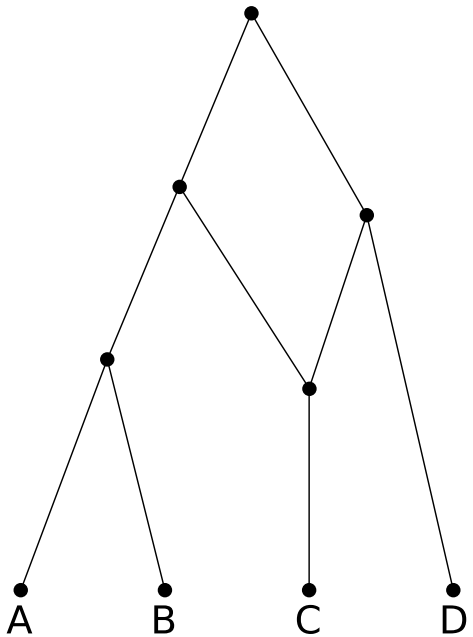
- For **individuals**, the network represents ancestry of individual lineages and nodes with multiple parents represent either hybridization, HGT or simply a node in a pedigree (family tree) of a sexually reproducing organism.



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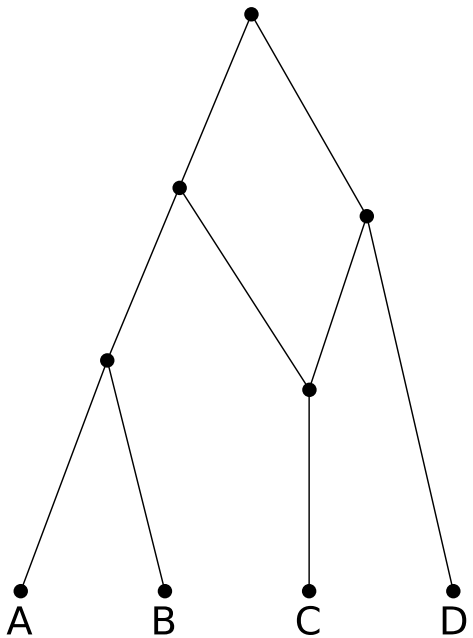
- For **genes or chromosomes**, the network represents ancestry of sequence data and nodes with multiple parents represent recombination events.



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How many networks are there?

- Consider the ancestry of 4 species. How many distinct network topologies are there?

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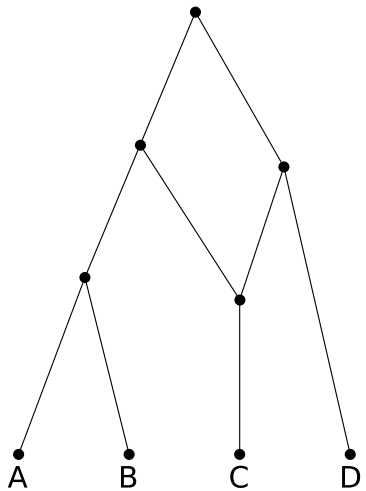

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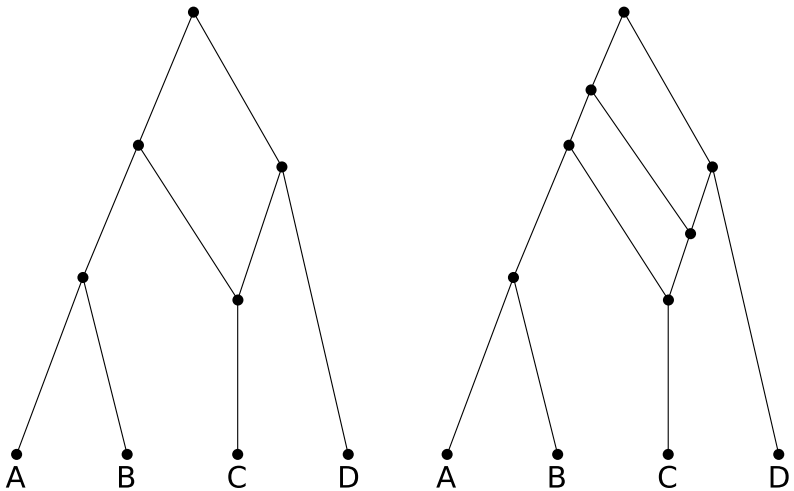

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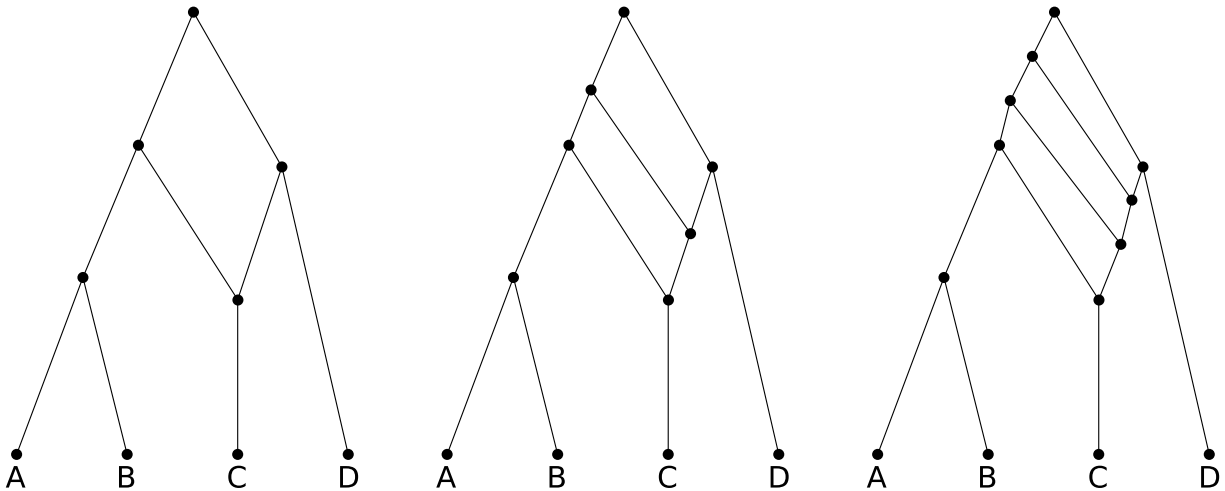

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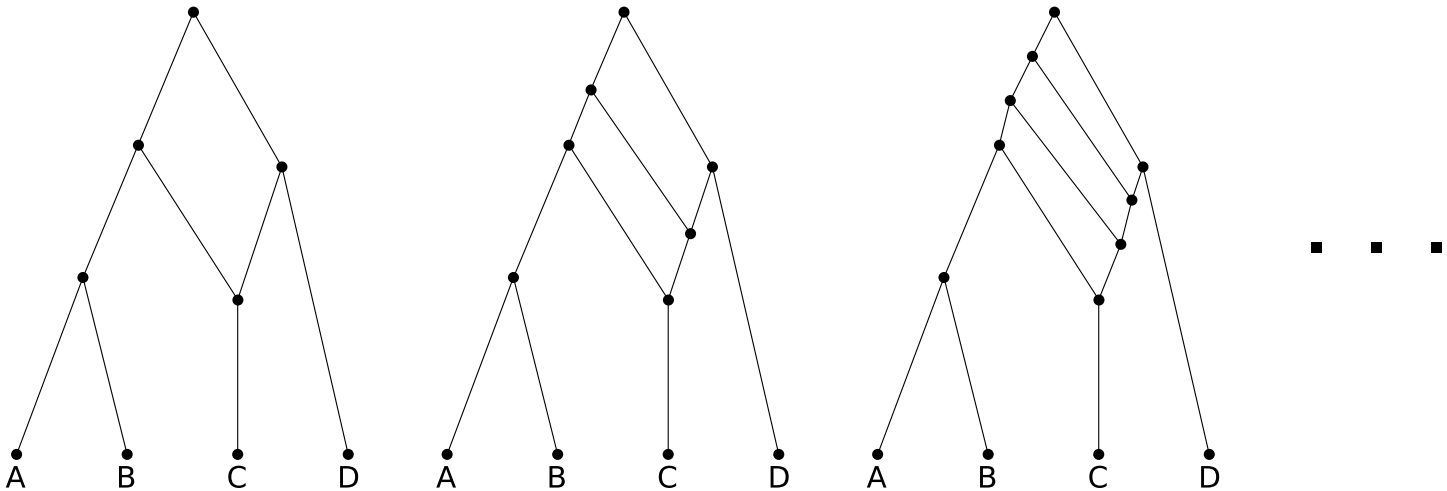

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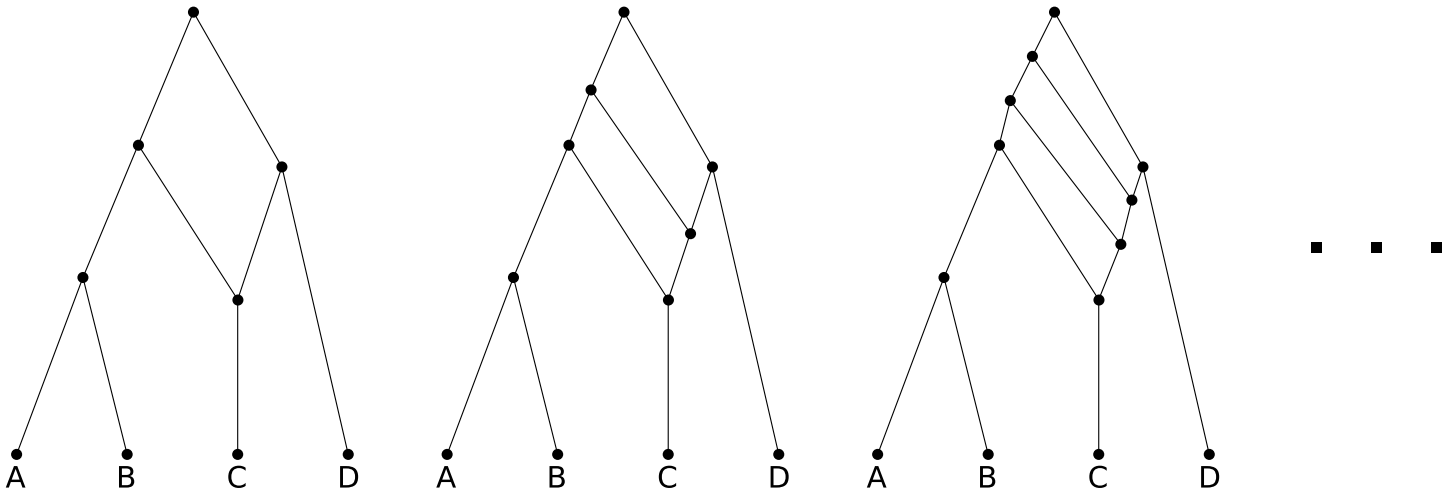

- Recall that there are $(2n-3)!!$ rooted trees with n leaves.

How many networks are there?

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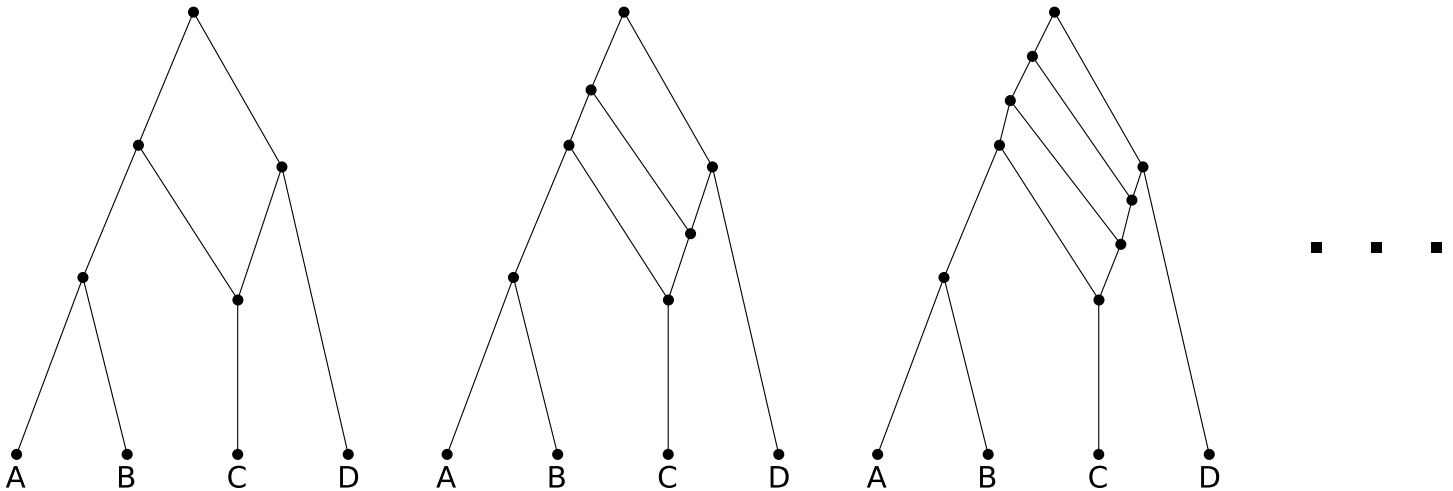

- Recall that there are $(2\mathfrak{n}-3)!!$ rooted trees with $\mathfrak{n}$ leaves.
- There are an **infinite** number of possible ancestral network topologies.

Sexual reproduction and genetic linkage

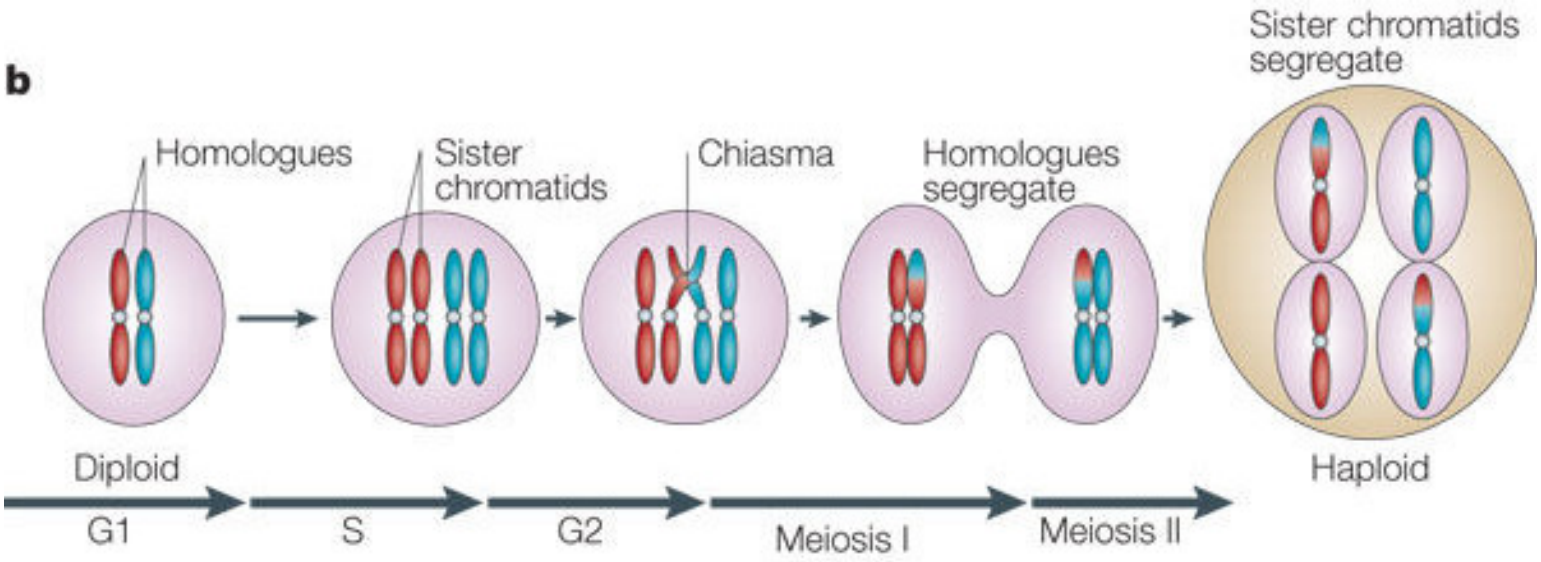

Figure adapted from [Marston and Amon, 2004]

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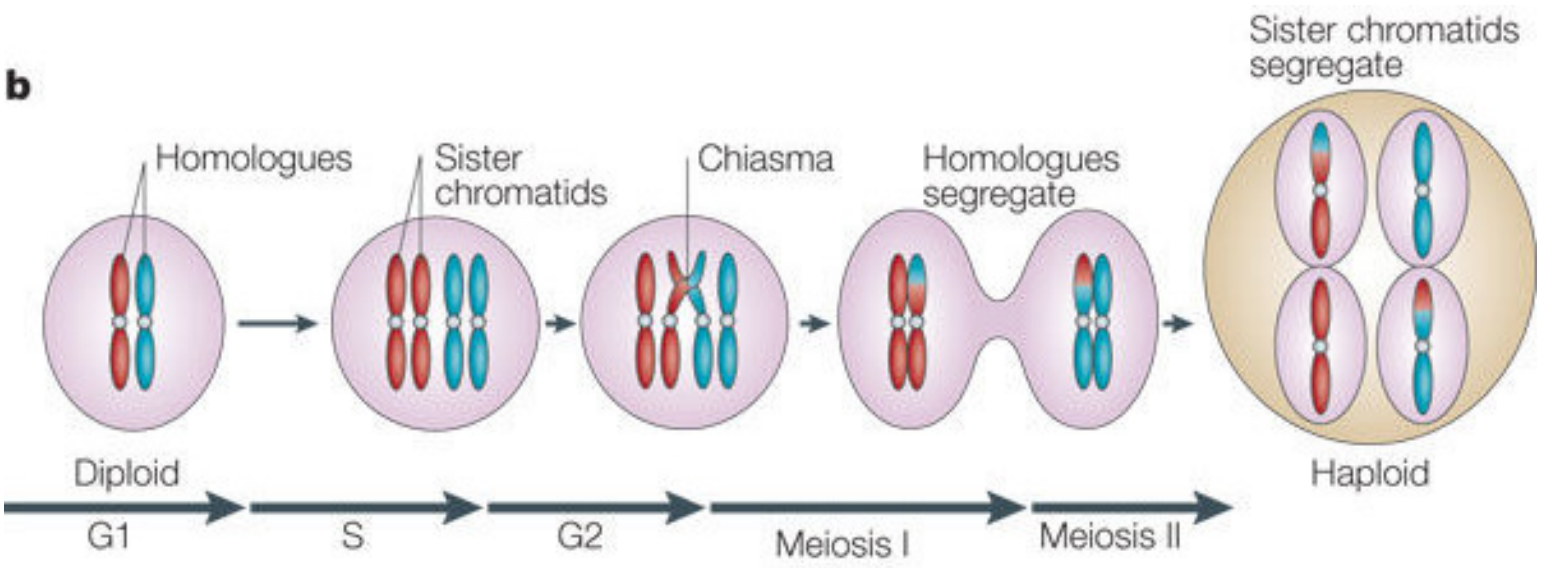
Sexual reproduction and genetic linkage



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- Recall: genetic linkage is the tendency for nearby sites to be inherited together.

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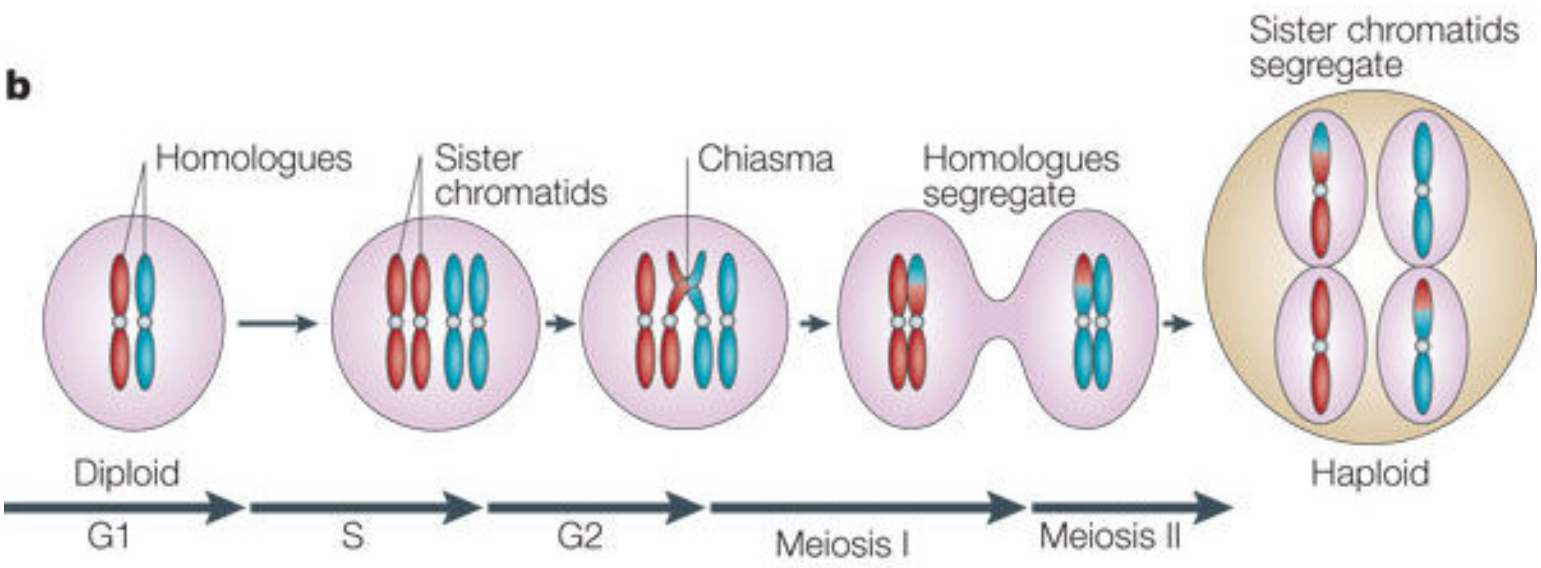

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- Recall: genetic linkage is the tendency for nearby sites to be inherited together.
- For sexually reproducing organisms, sites on different chromosomes are completely unlinked.

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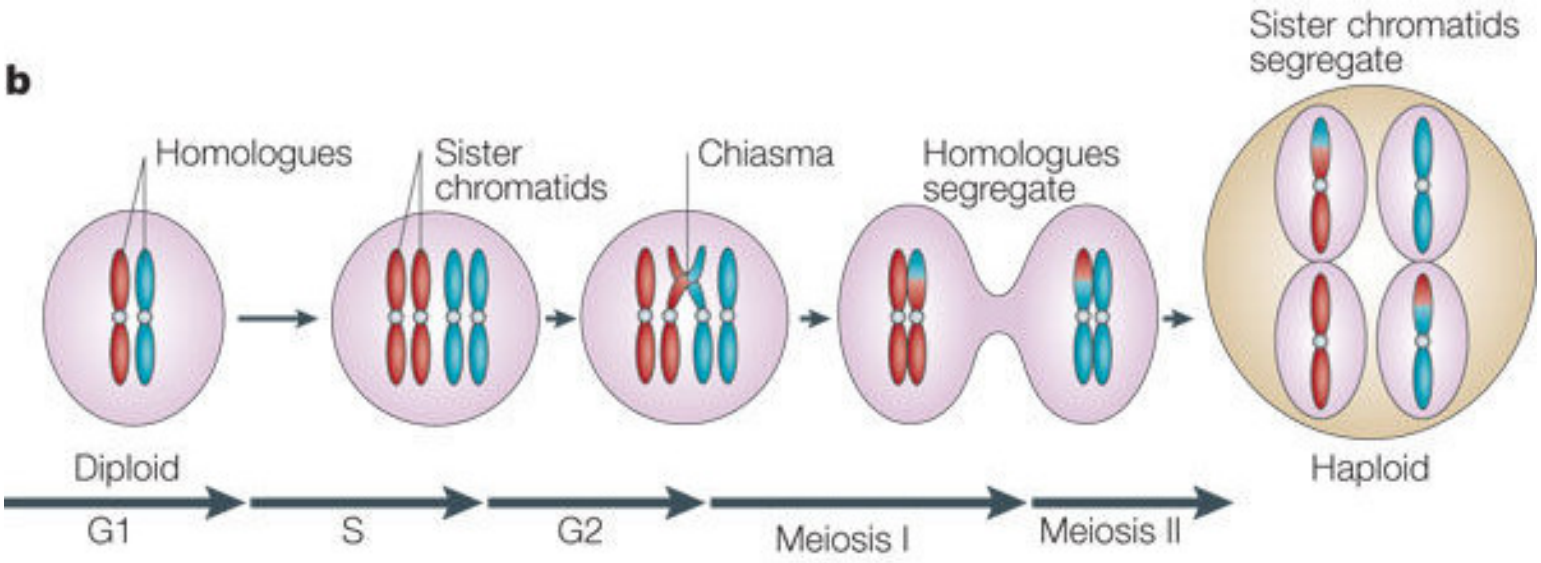

Figure adapted from [Marston and Amon, 2004]

- Recall: genetic linkage is the tendency for nearby sites to be inherited together.
- For sexually reproducing organisms, sites on different chromosomes are completely unlinked.
- Sites on the same chromosome are inherited together unless a homologous recombination event divides them.

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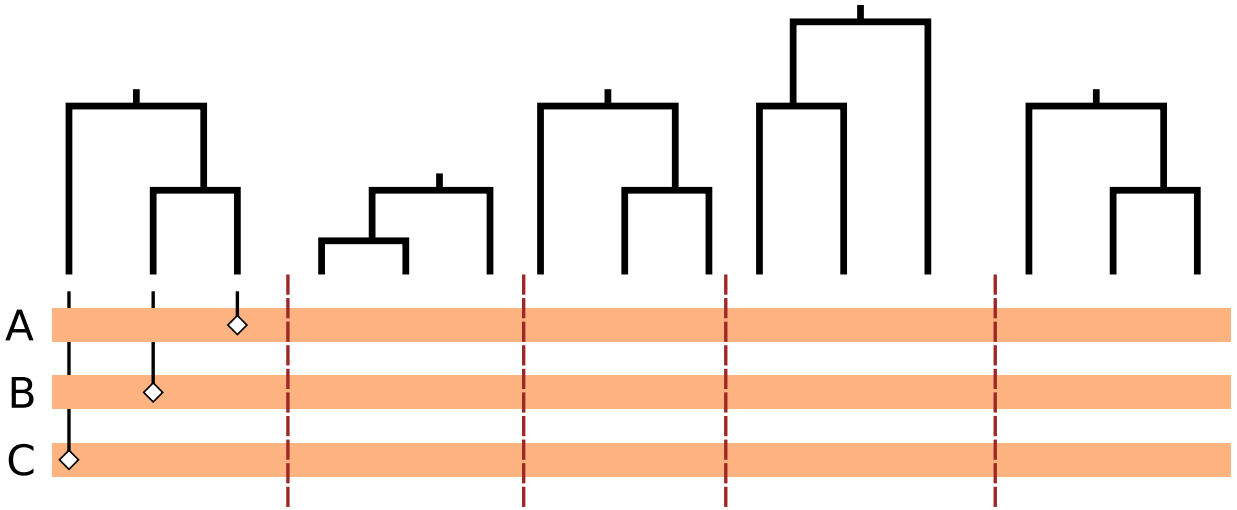
Effect of recombination on phylogeny



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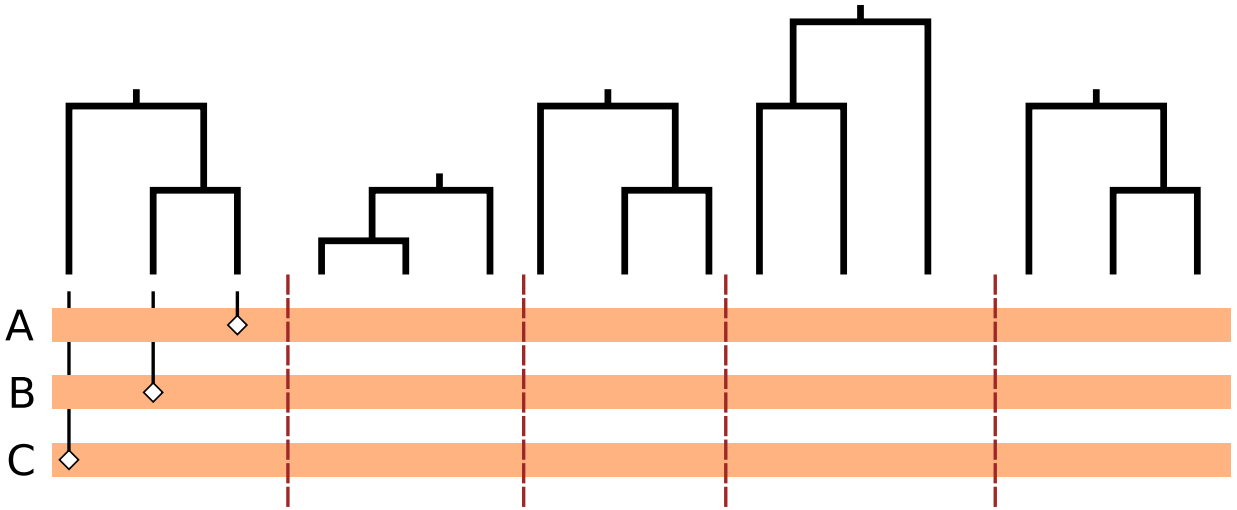

- Different sites correspond to different trees.

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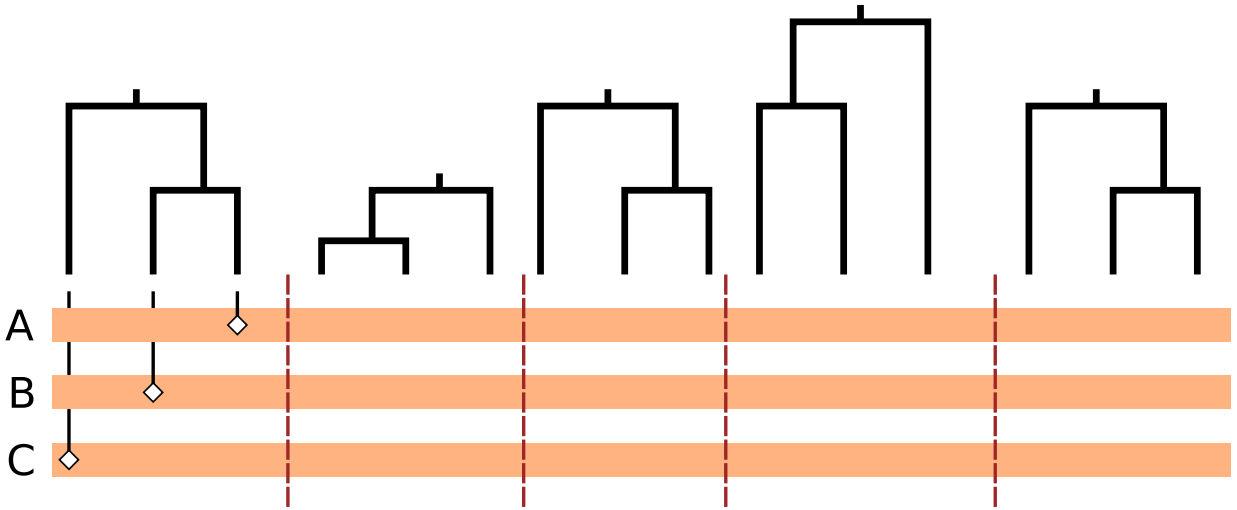

- Different sites correspond to different trees.
- The further away sites are on the alignment, the more likely they are to possess different ancestry.

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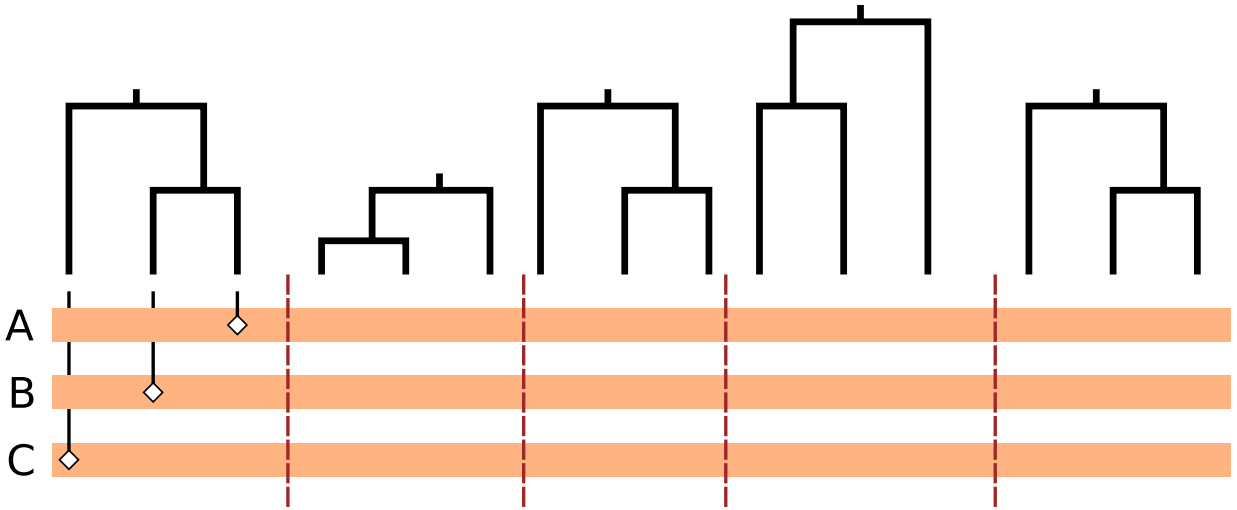

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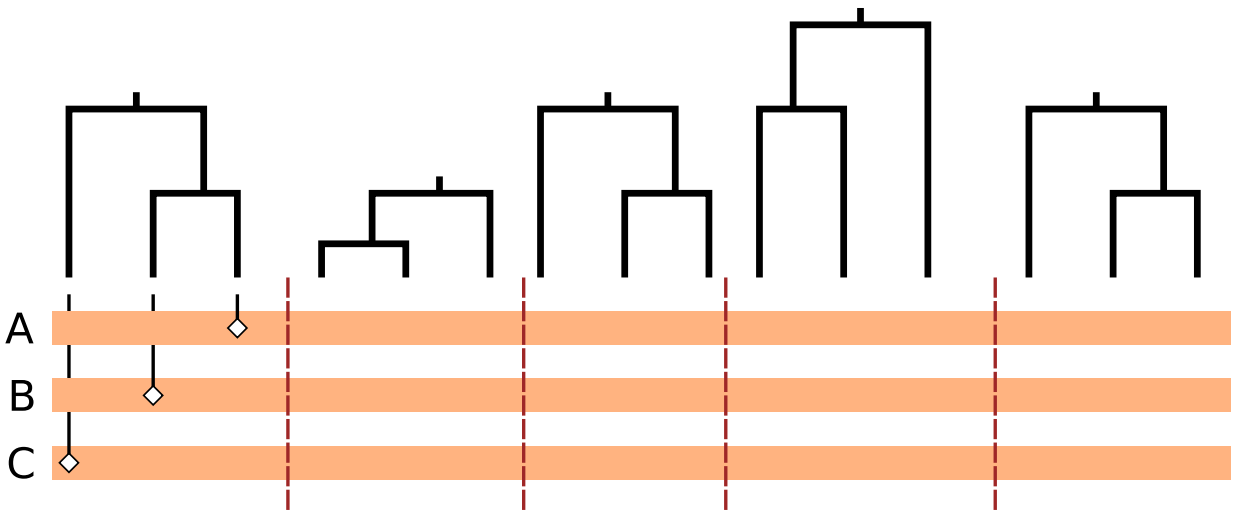

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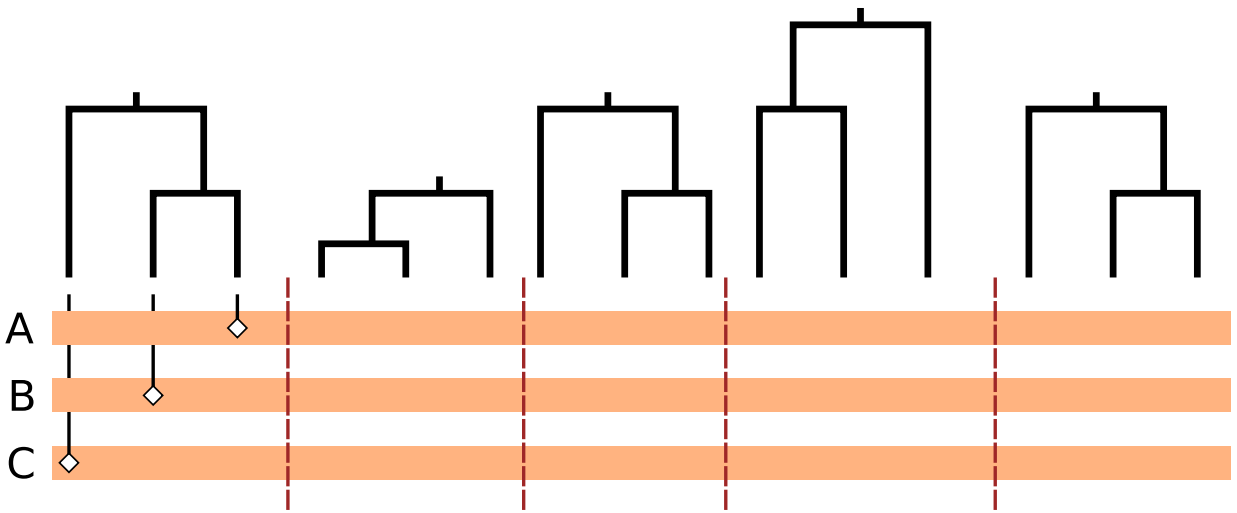

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- The further away sites are on the alignment, the more likely they are to possess different ancestry.
- Single nucleotide polymorphisms (SNPs) are usually widely separated and are thus assumed to be completely unlinked - necessary for the validity of GWAS analyses.
- Short gene sequences often assumed to be completely linked (one tree for all sites).
- Even for asexual entities (viruses, bacteria, etc.) reality is usually somewhere between these extremes.

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Wright-Fisher with Recombination

- Consider a Wright-Fisher population with female and male diploid individuals.

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Wright-Fisher with Recombination

- Consider a Wright-Fisher population with female and male diploid individuals.
- Focus on a small segment of a single autosome.
  - An autosome is a chromosome which is a member of a homologous pair, i.e. not a sex chromosome.

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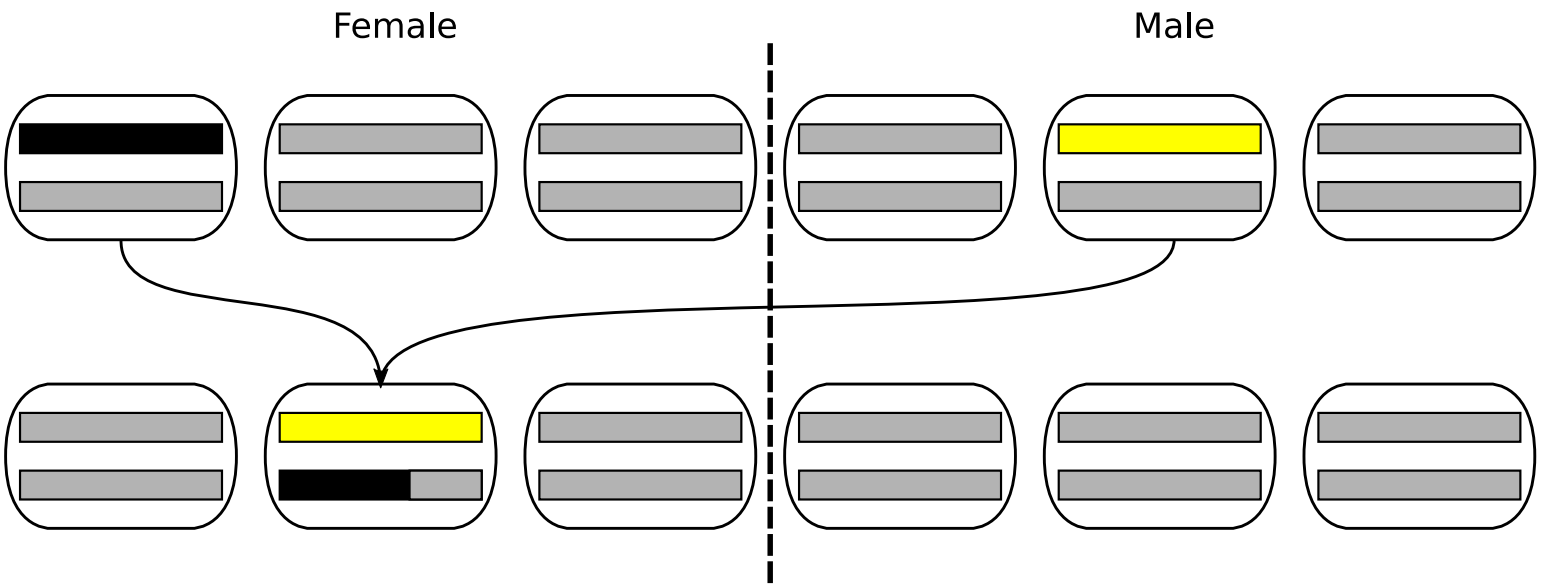

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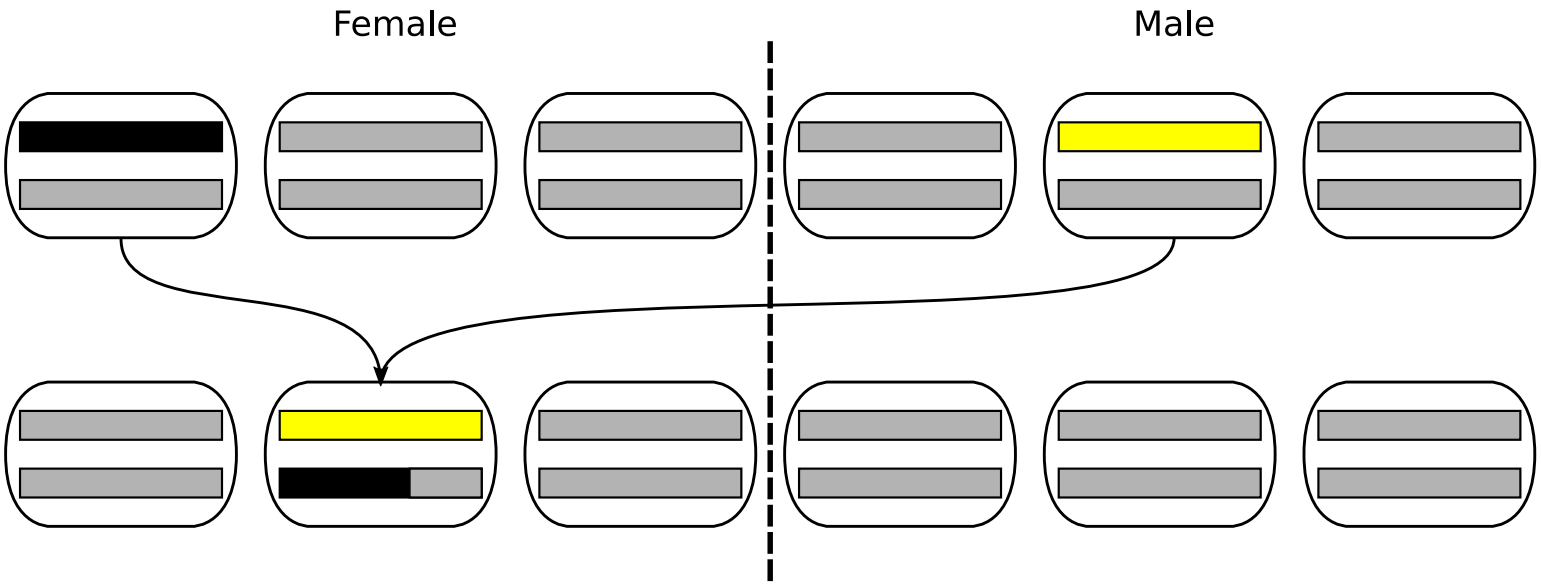

- Each child selects 1 male and 1 female parent randomly from the previous generation.

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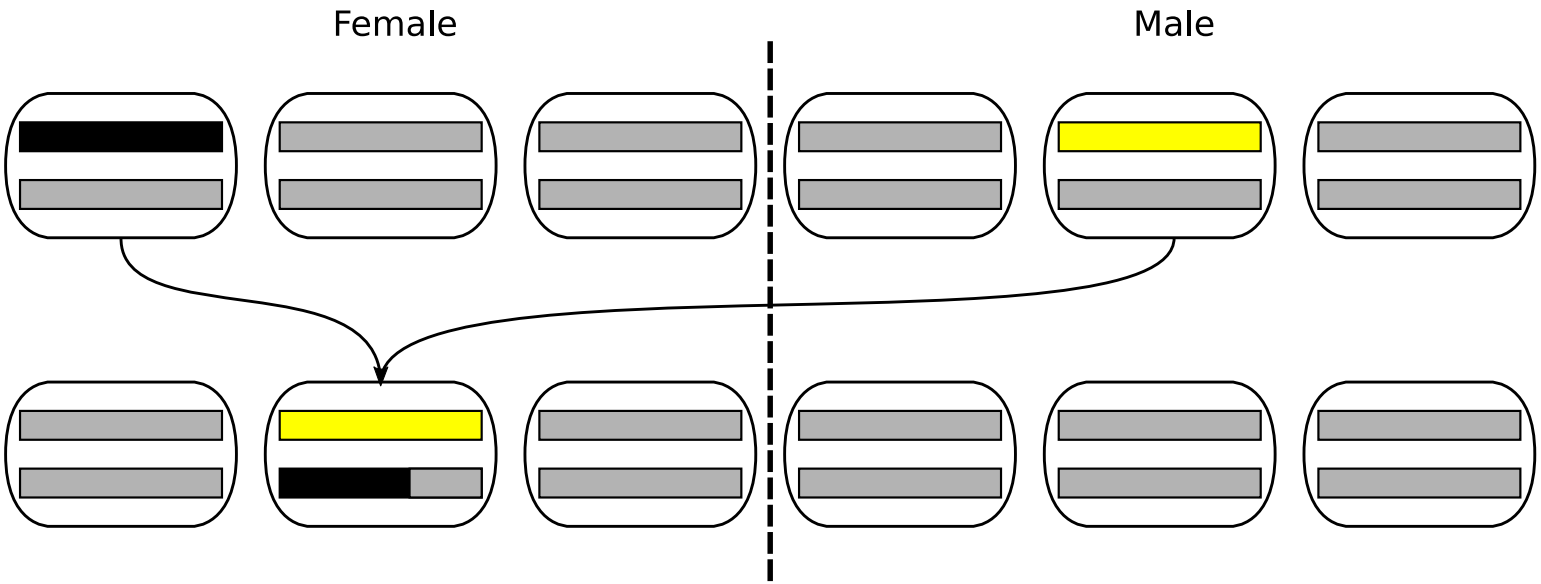

- Each child selects 1 male and 1 female parent randomly from the previous generation.
- With probability r (which depends on the segment length) the homologous pair from one of the parents is recombined.

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- Since the specific pairing of chromosomes only matters over a single generation, in the long term the haploid approximation is very good:

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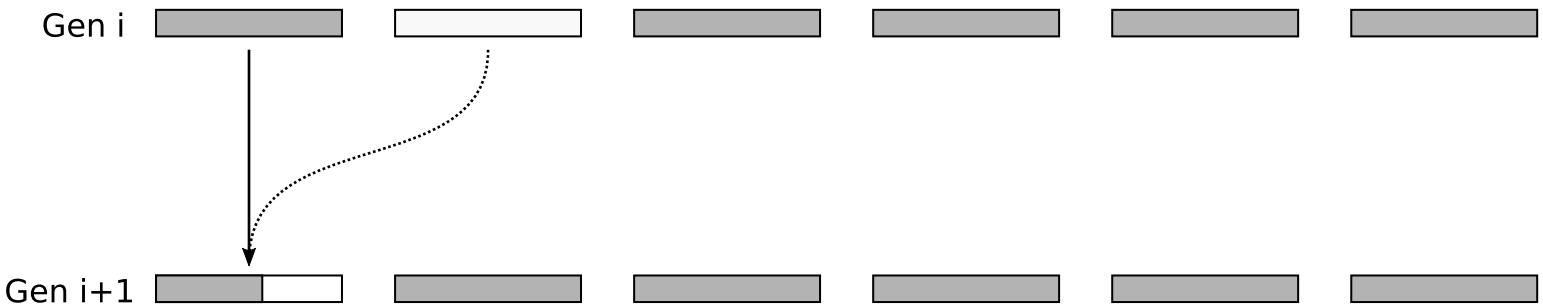

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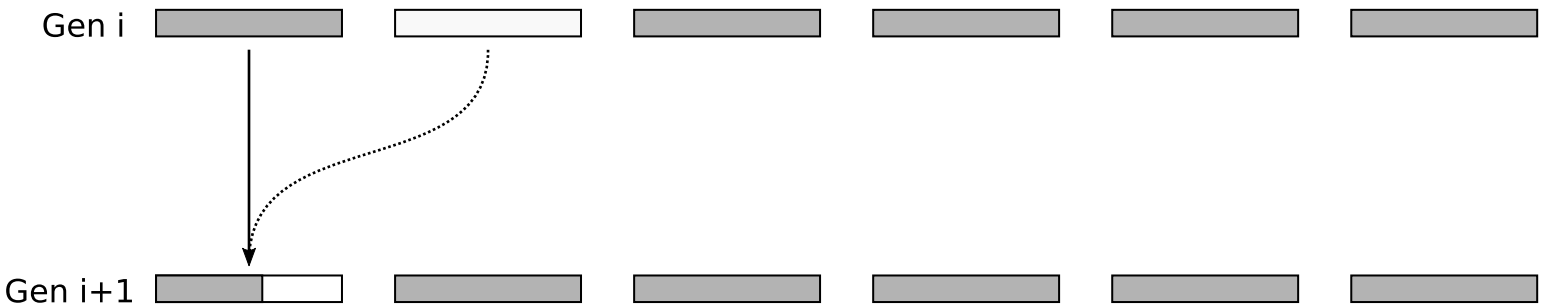

- Each child in $\mathbf{i}+1$ selects a parent at random from gen. $\mathbf{i}$.

Wright-Fisher with Recombination

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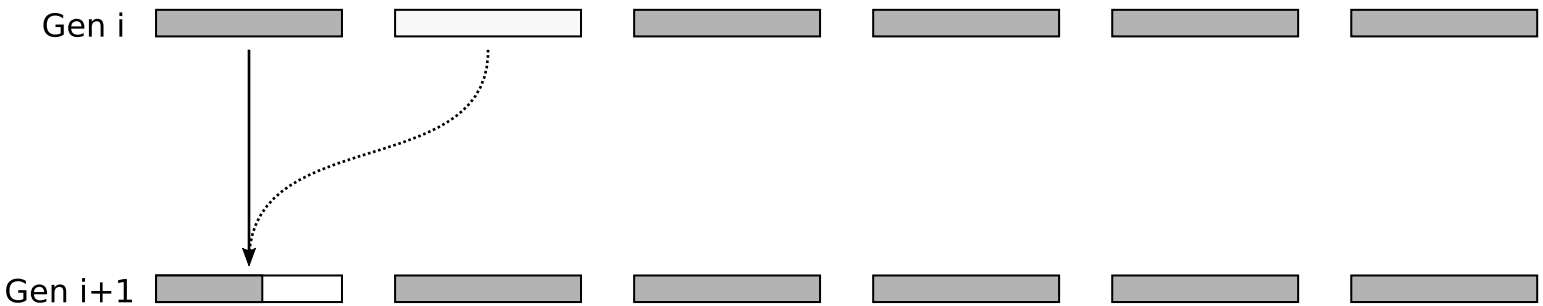

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- With probability $\mathbf{r}$ an additional parent is selected.

Wright-Fisher with Recombination

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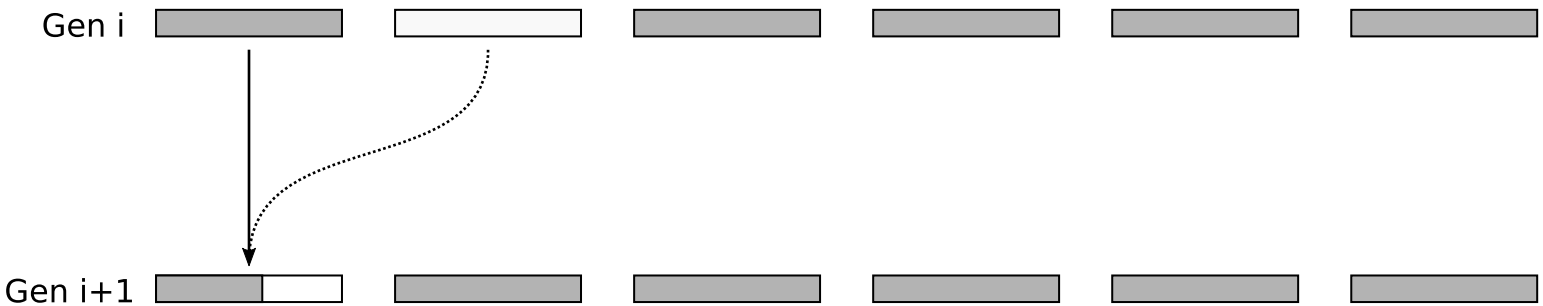
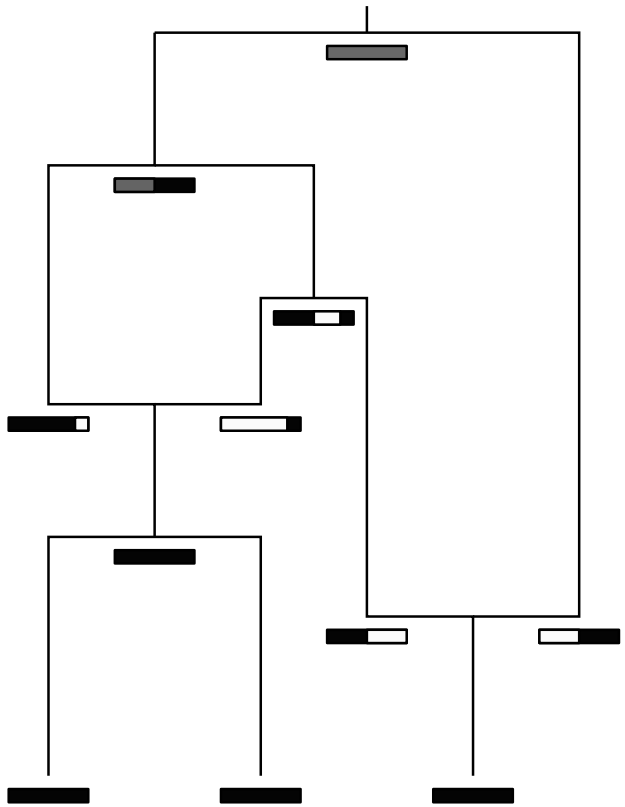


- Each child in $\mathbf{i}+1$ selects a parent at random from gen. $\mathbf{i}$.
- With probability $\mathbf{r}$ an additional parent is selected.
- In this case, a break-point is chosen randomly on the chromosome, and everything to the right is replaced by the homologous section of the second parent's chromosome.

The Coalescent with Recombination

For fixed recombination rate $\rho = r/g$ in the limit $r \ll 1$, $g \ll 1$ and $N \gg 1$, the genealogical process is the coalescent with recombination [Hudson, 1983]:



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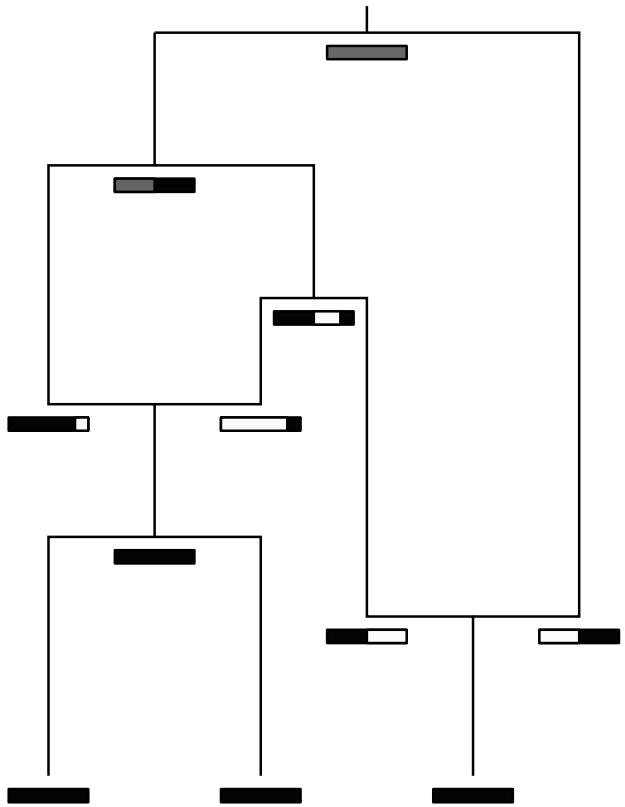

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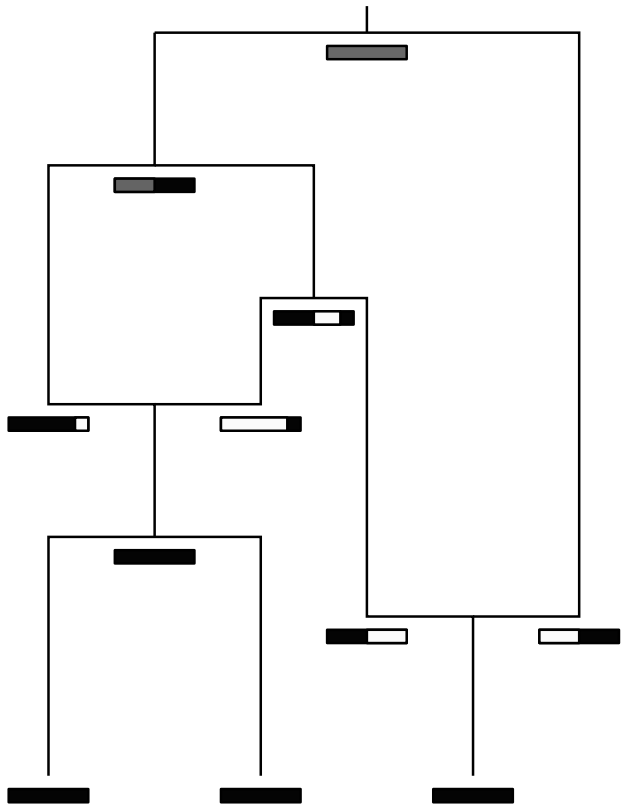

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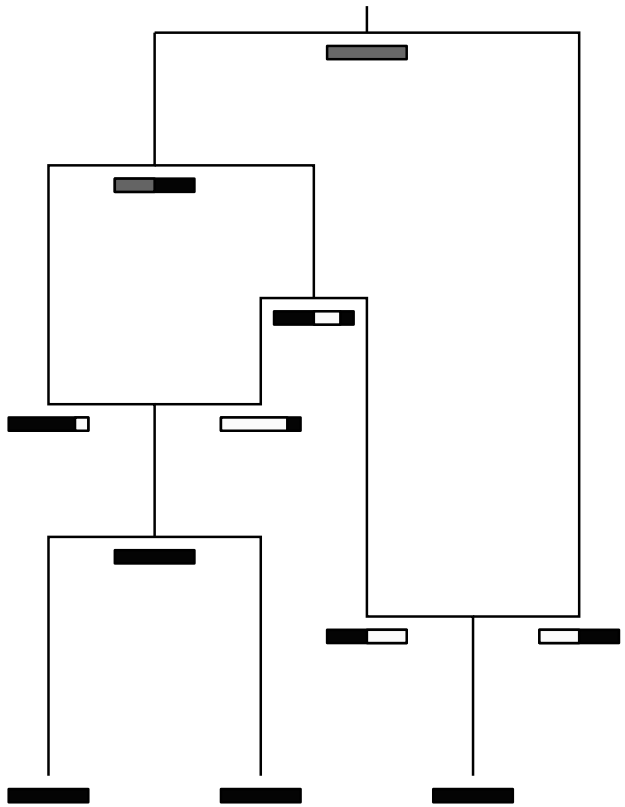

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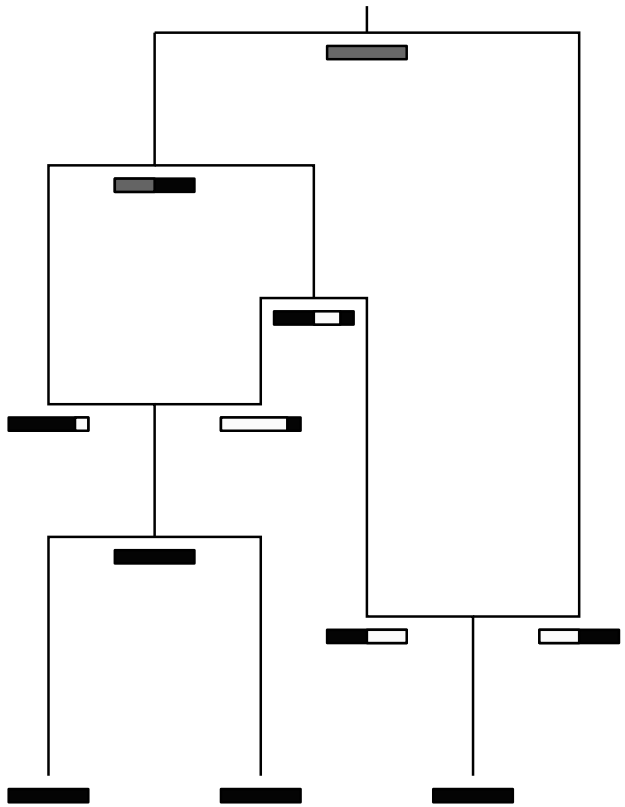

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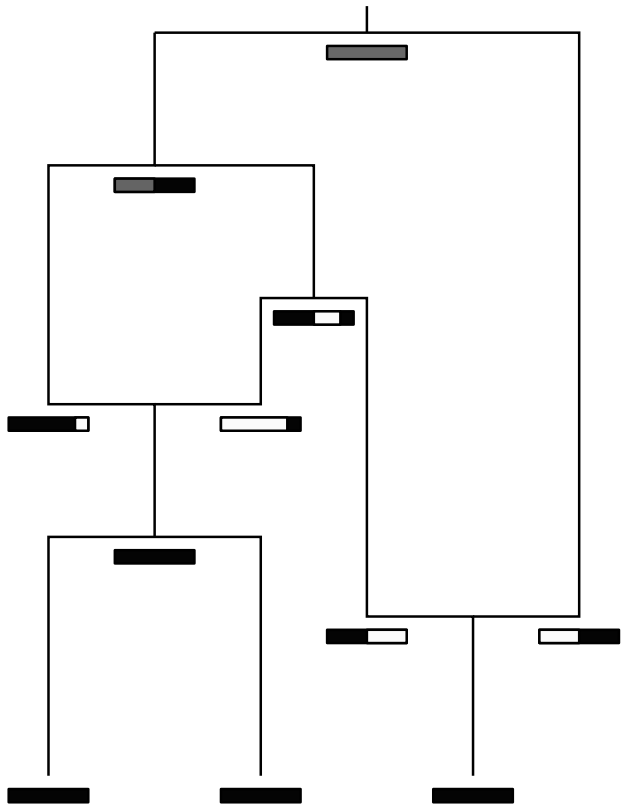

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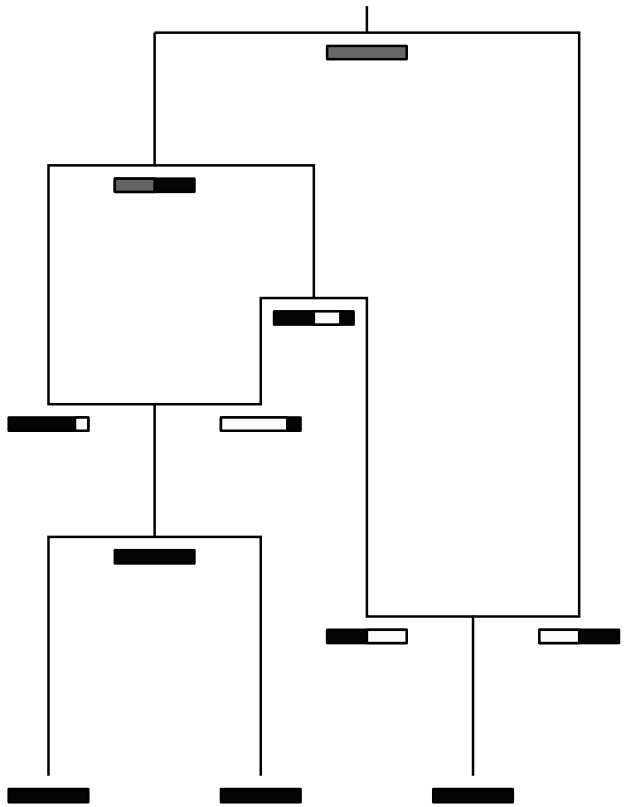

The result is the "ancestral recombination graph" or ARG.

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Bayesian phylogenetic network inference

Can easily write down an expression for the posterior distribution for a phylogenetic network given a sequence alignment:

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$$\mathrm{P}(\mathrm{G}, \rho, \mathrm{N}, \mathrm{Q}|A) = \frac{1}{\mathrm{P}(A)}\mathrm{P}(A|\mathrm{G}, \mathrm{Q})\mathrm{P}(\mathrm{G}|\rho, \mathrm{N})\mathrm{P}(\rho, \mathrm{N}, \mathrm{Q})$$

- G is the recombination graph/network.
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- N is the effective population size.

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Despite this, many approximate algorithms exist.

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Algorithms for Bayesian ARG inference

SMARTIE : [Bloomquist and Suchard, 2010] (BEAST) MCMC sampler under a "non-informative" network prior rather than the CwR.

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Bacter : [Vaughan et al., 2017] (BEAST 2)
Re-implementation of the ClonalOrigin model with fewer restrictions.

Bayesian ARG inference example

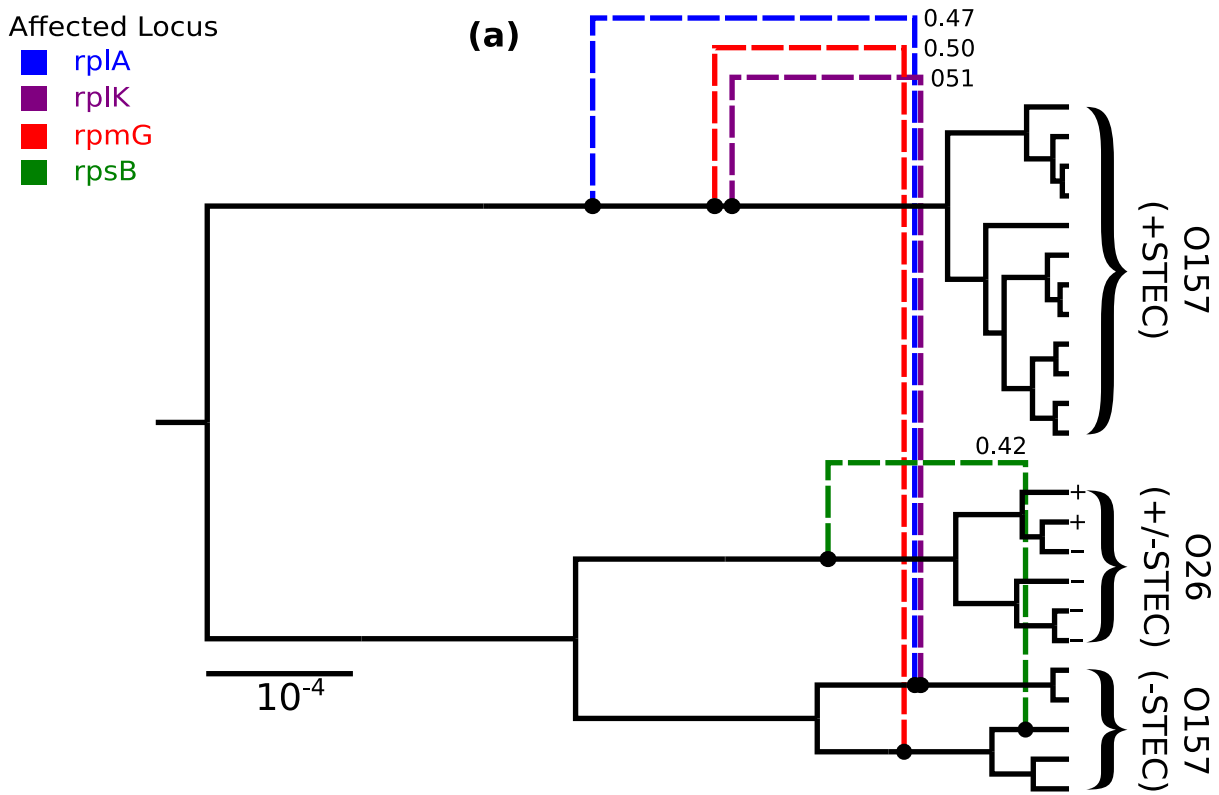

Figure adapted from [Vaughan et al., 2017]

Phylogenetic network describing ancestry of E. coli sequences produced using Bayesian inference.

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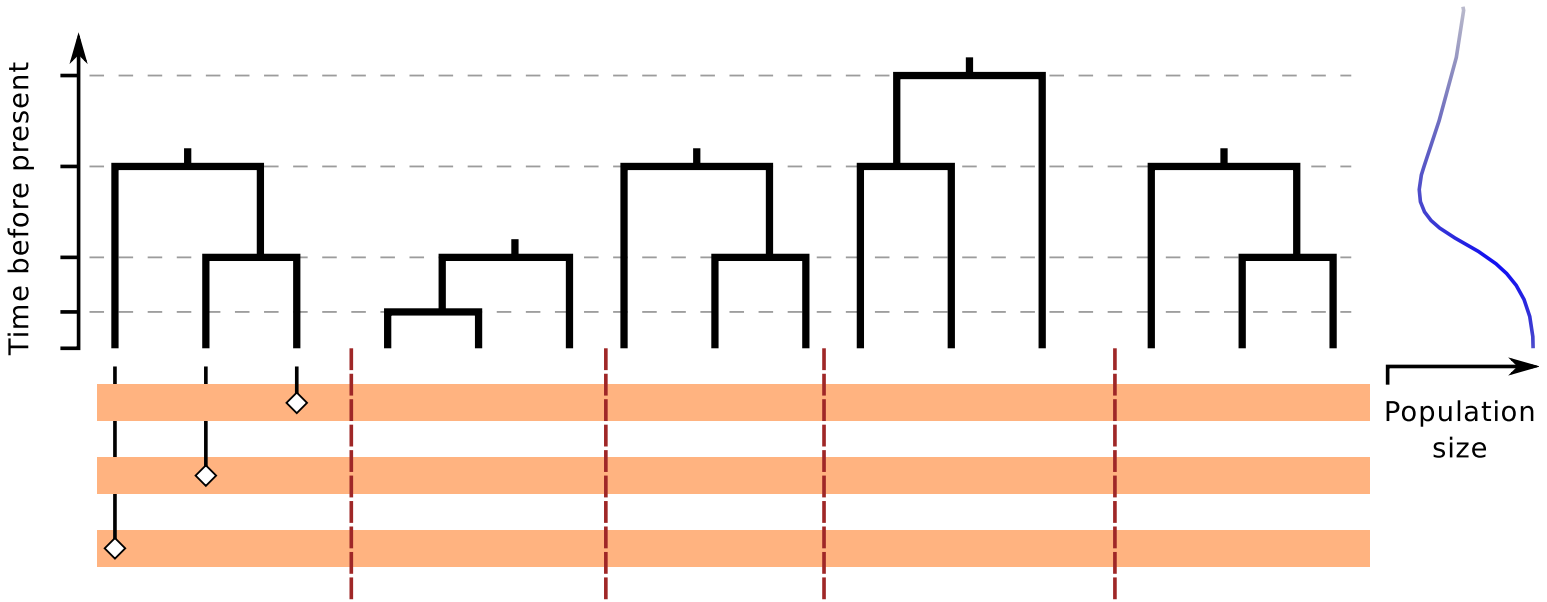
Inference of population dynamics



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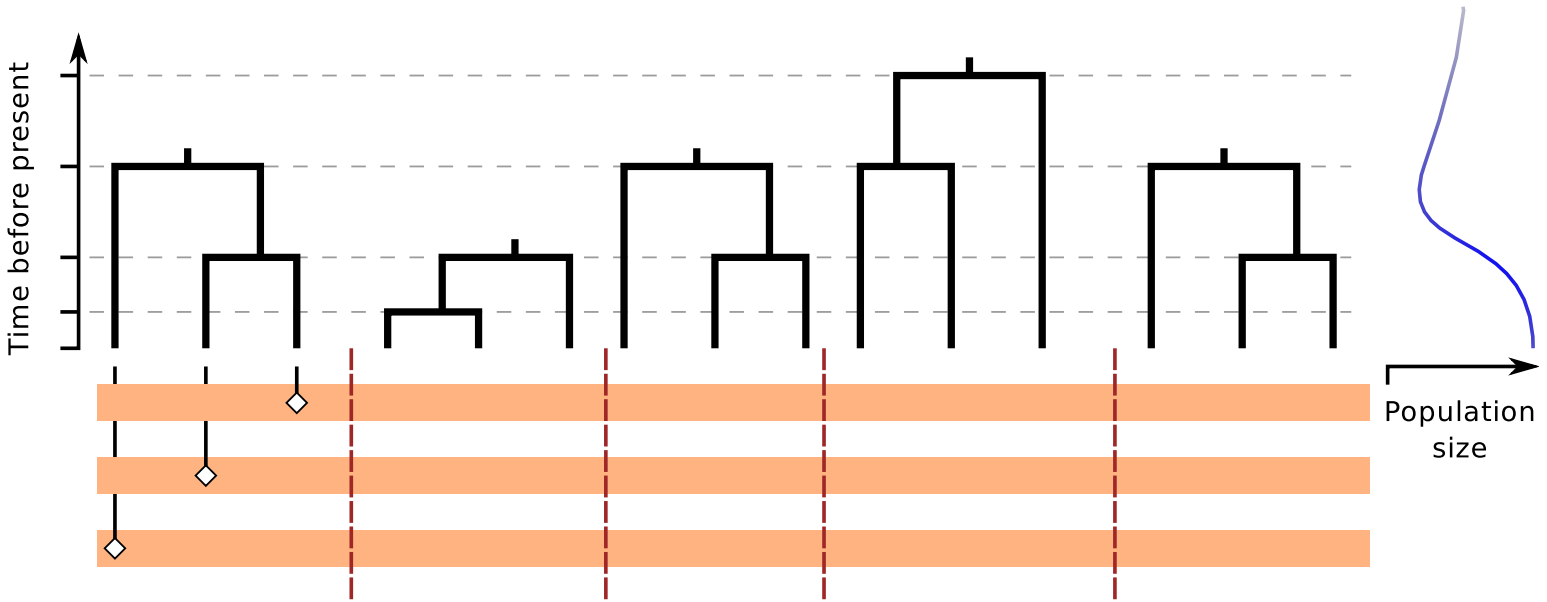

- Each local tree contributes additional information to the inference of population size.

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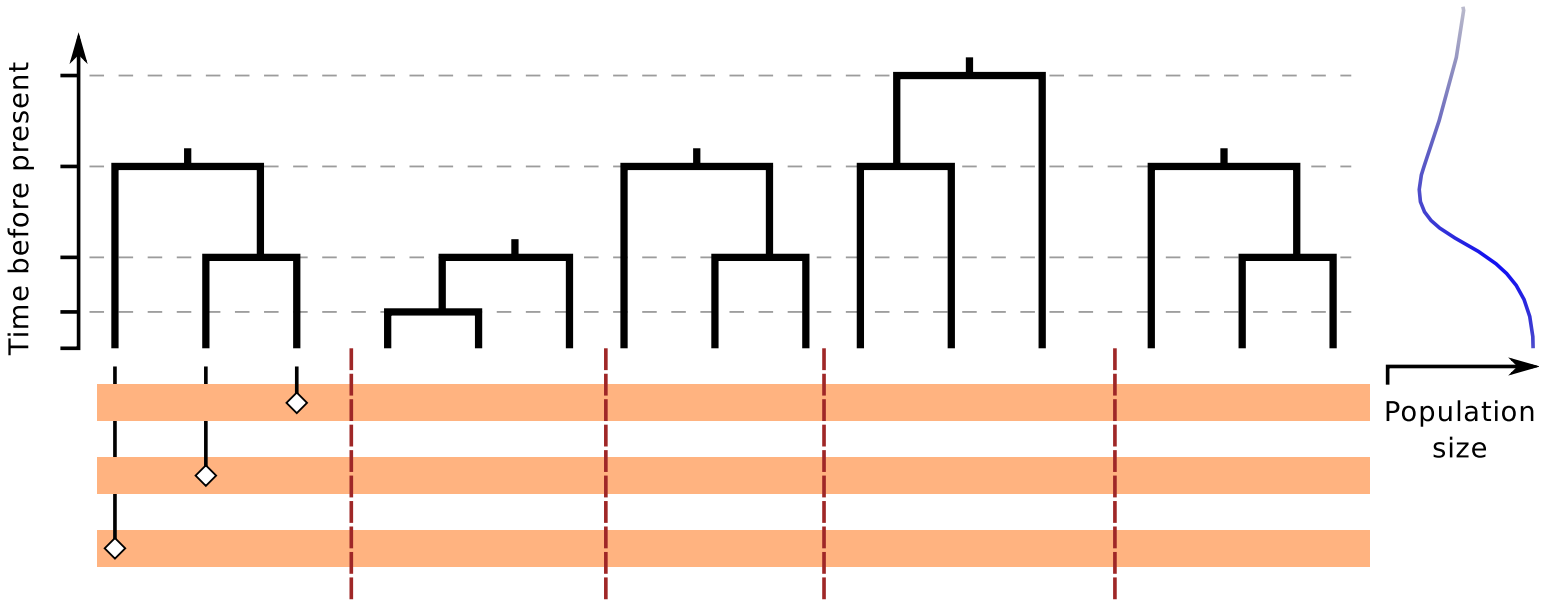

- Each local tree contributes additional information to the inference of population size.
- The longer the sequence, assuming the local trees can be accurately inferred, the more powerful the population dynamics inference.

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The Sequentially Markovian Coalescent

- [Wiuf and Hein, 1999] reformulated the CwR as a "spatial" process along sequences.

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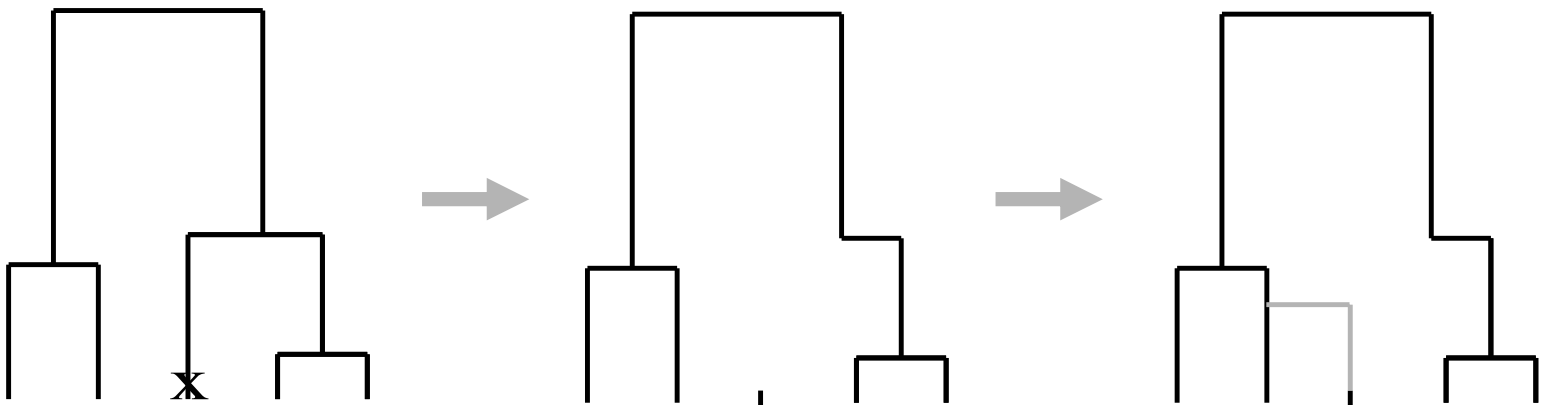

Figure adapted from [McVean and Cardin, 2005]

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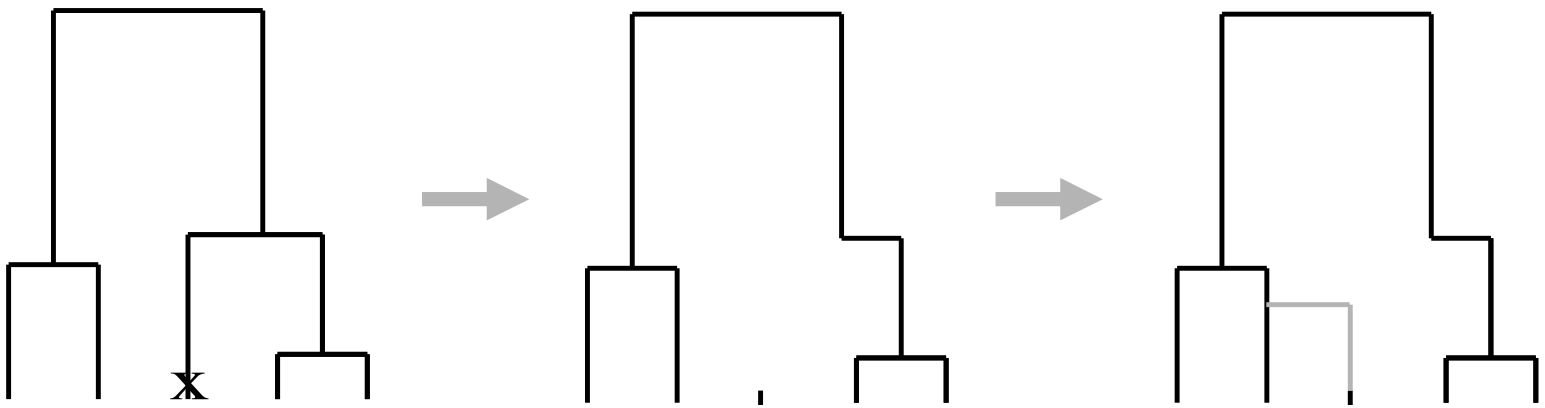

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- Sites between breakpoints exponentially distributed with rate ρL where L is the total edge length of the current local tree.

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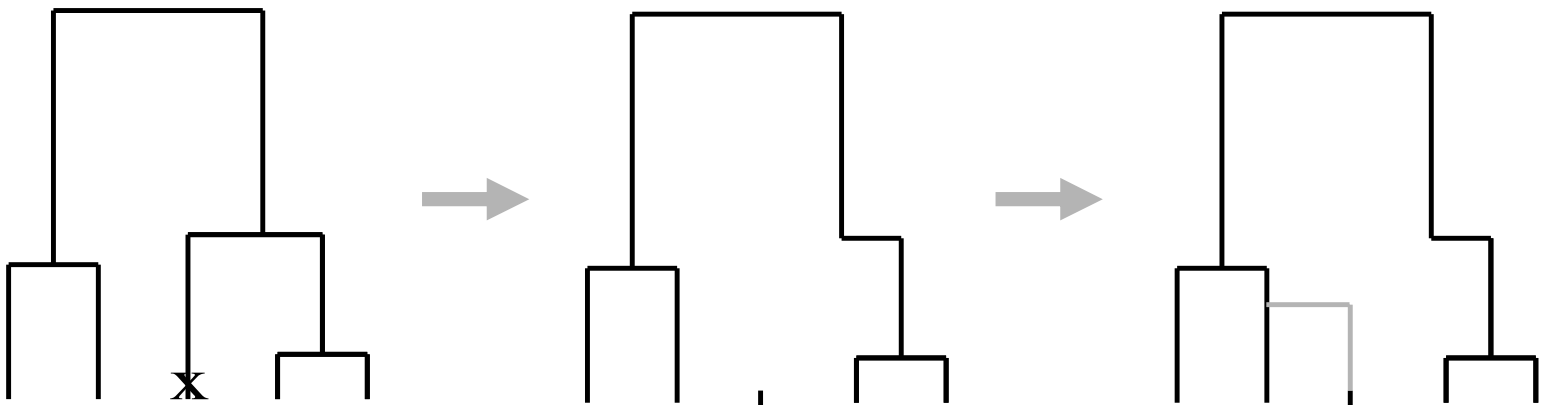

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- Sites between breakpoints exponentially distributed with rate ρL where L is the total edge length of the current local tree.
- It neglects some possible recombinations, e.g. those that do not affect the data.

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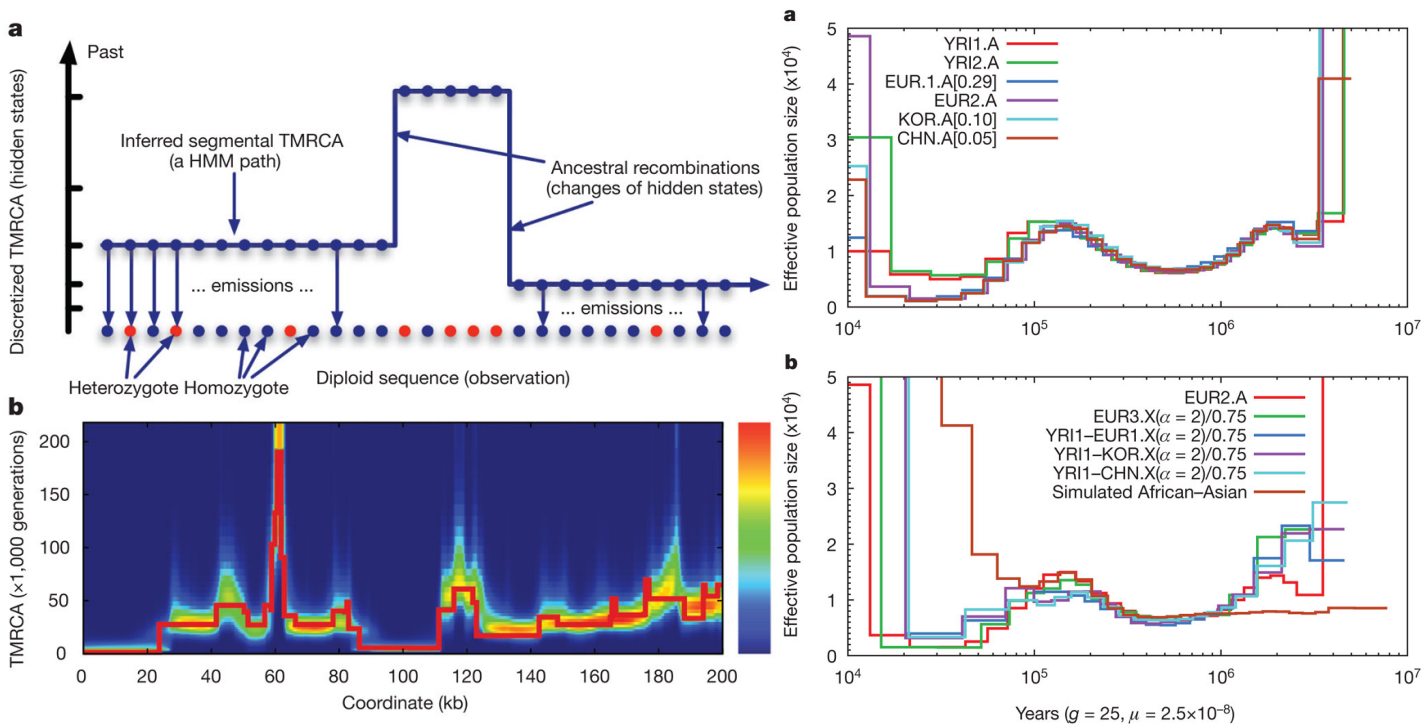

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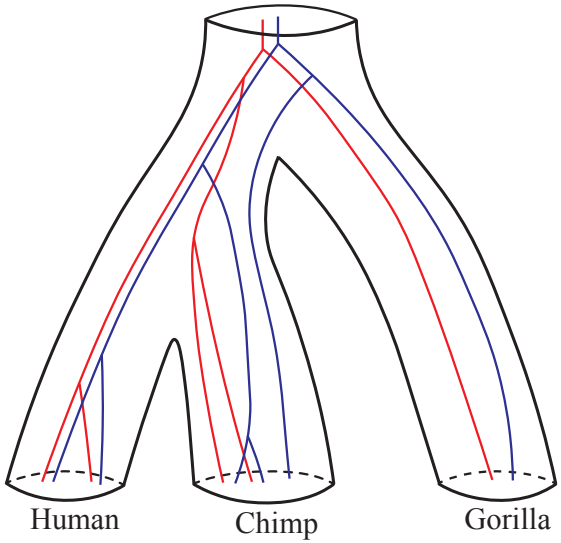
Species tree models: Multi-species coalescent



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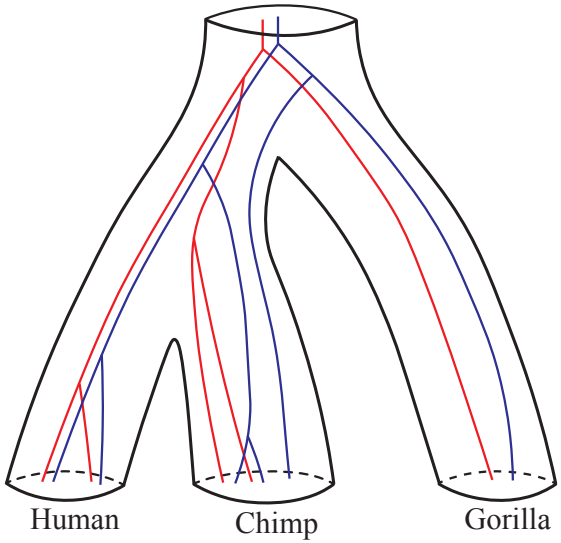

Figure adapted from [Zhang et al., 2017]

- Each gene has its own gene tree which is embedded within a species tree (or transmission tree).

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Species tree models: Multi-species coalescent

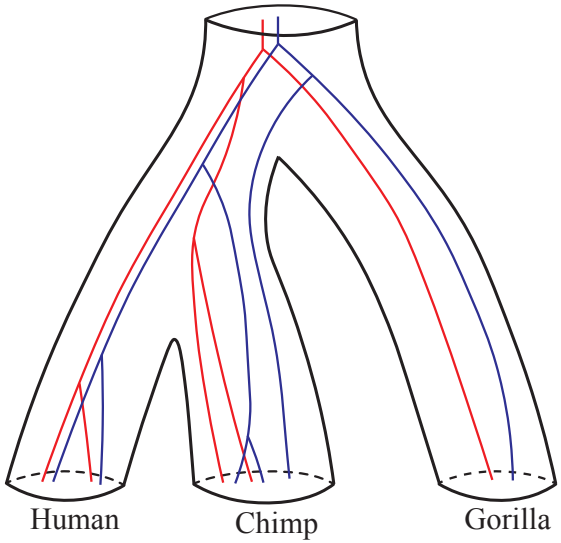

Figure adapted from [Zhang et al., 2017]

- Each gene has its own gene tree which is embedded within a species tree (or transmission tree).
- Gene trees may be different to the species tree as the genes may coalesce any time prior to being in the same population.

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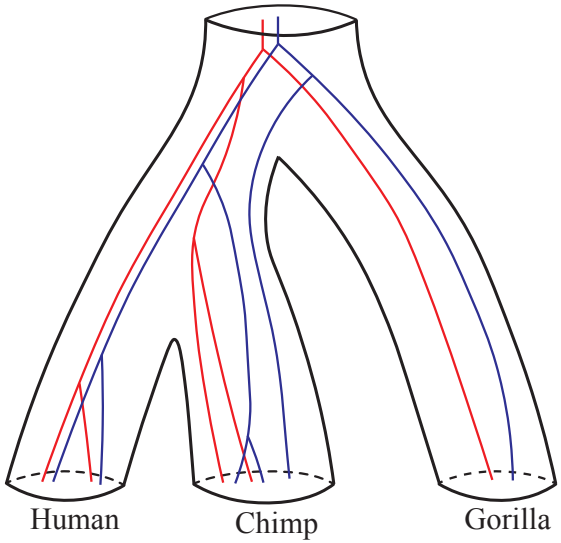

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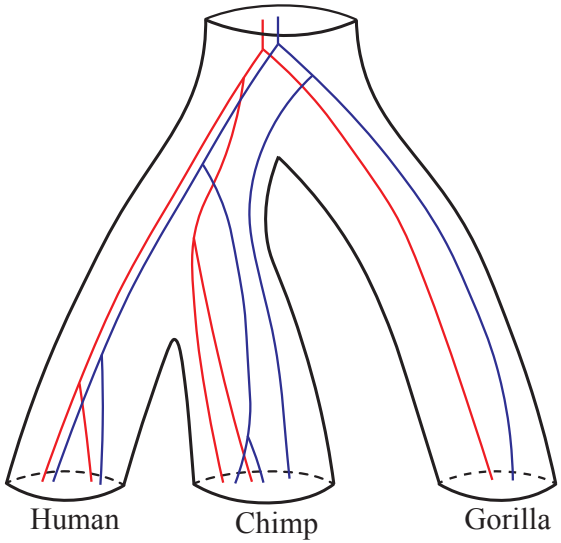

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- Software: *BEAST, *BEAST2 [Heled and Drummond, 2010, Ogilvie et al., 2016].

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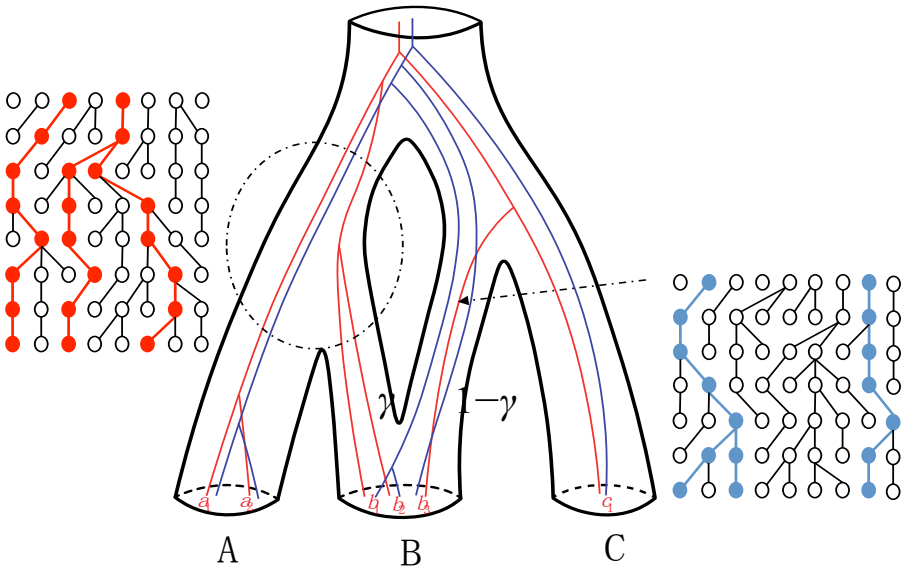
Species network inference



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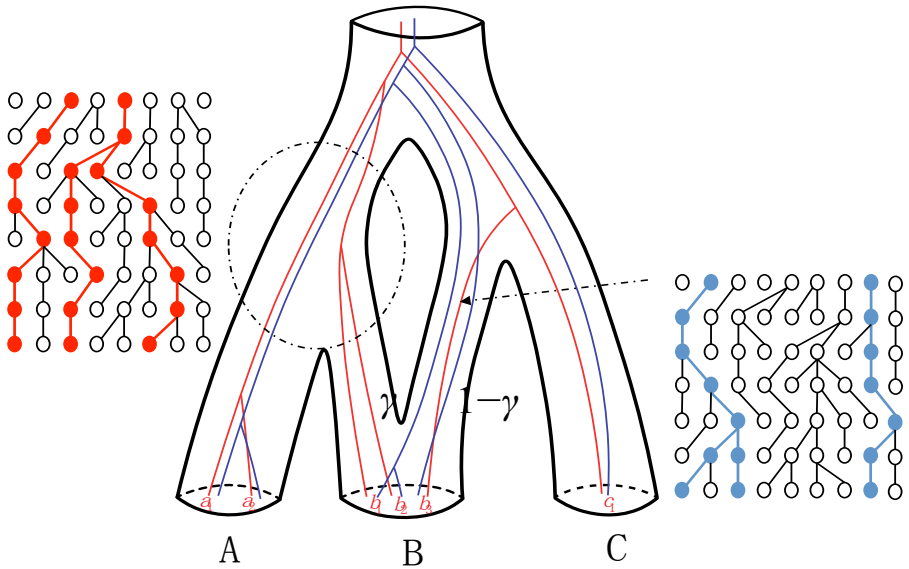

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- Each gene has its own gene tree which is embedded within a hybridization network or a lateral gene transfer network.

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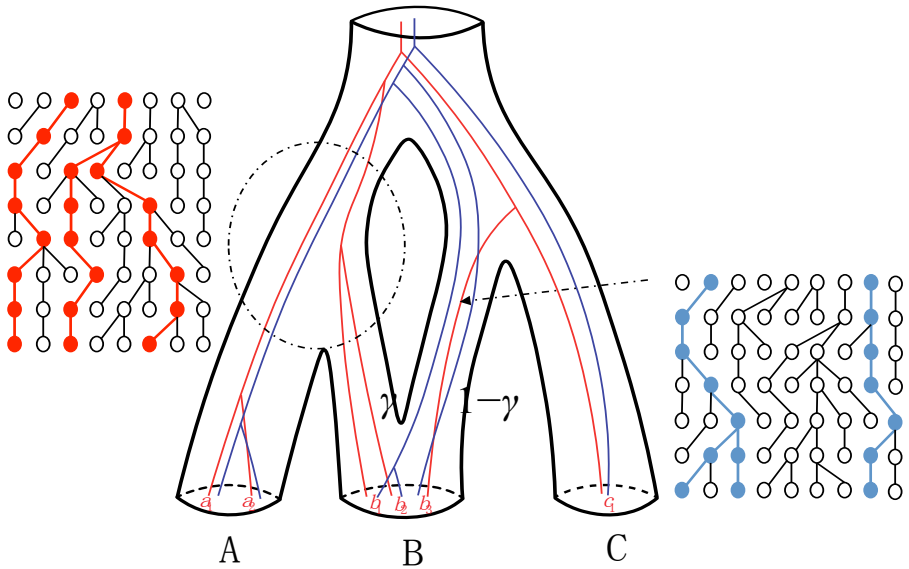

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- Each gene has its own gene tree which is embedded within a hybridization network or a lateral gene transfer network.
- A hybrid node has two ancestor lineages and one descendant lineage.

Species network inference

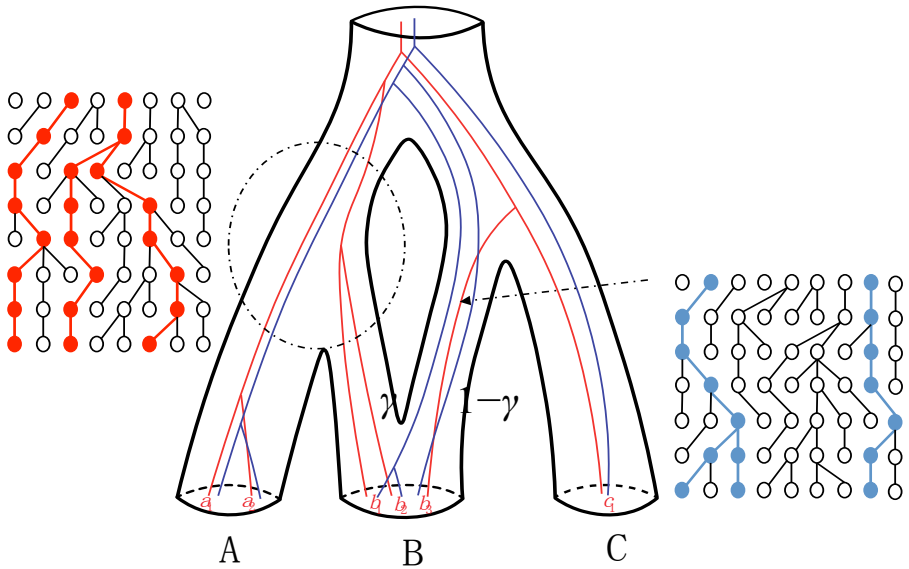

Figure adapted from [Zhang et al., 2017]

- Each gene has its own gene tree which is embedded within a hybridization network or a lateral gene transfer network.
- A hybrid node has two ancestor lineages and one descendant lineage.
- *BEAST2 has been extended [Zhang et al., 2017] to allow for hybridization, lateral gene transfer.

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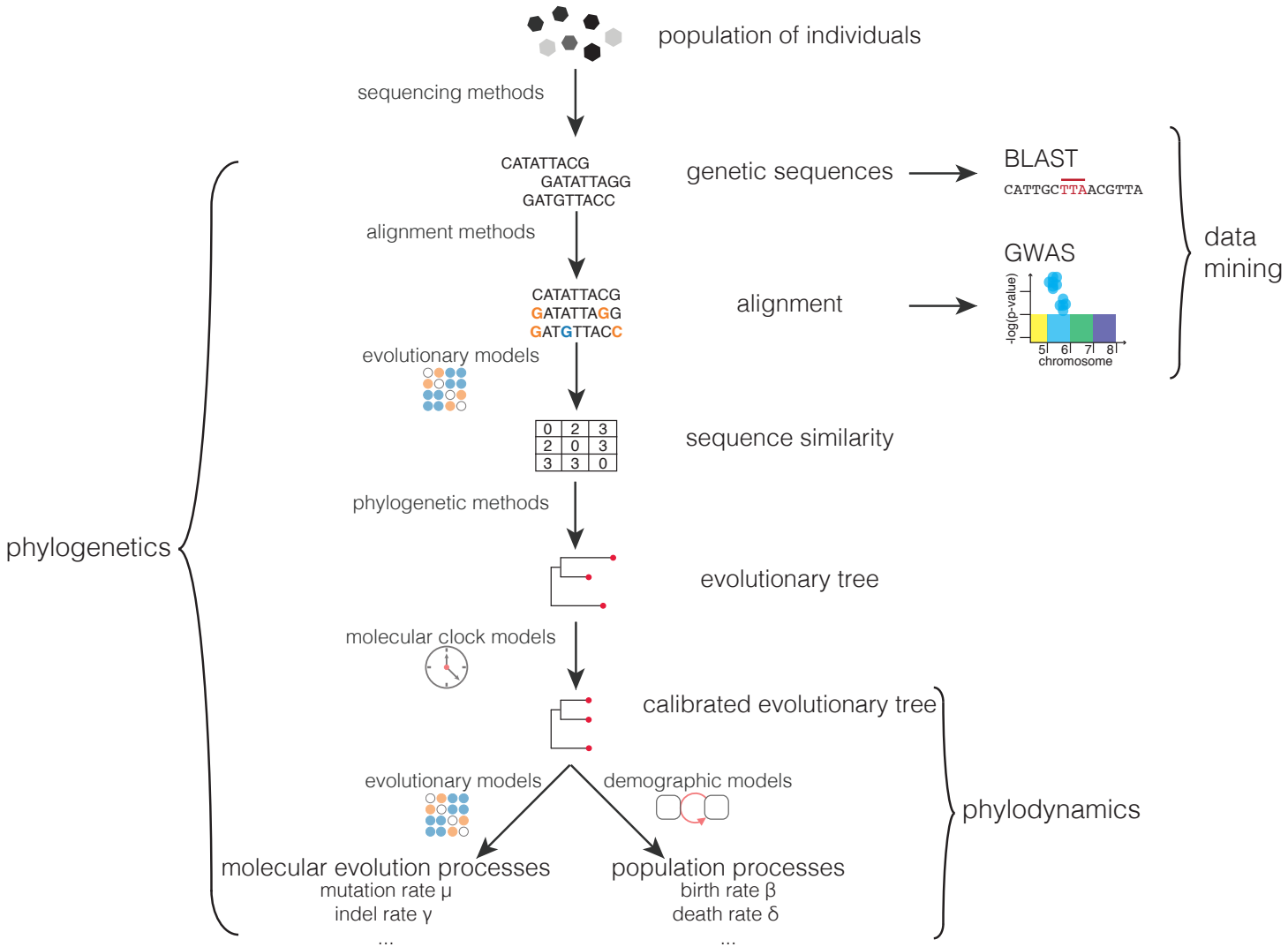
From sequences to population dynamics



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- What is the maximum number of local trees that can correspond to a sequence alignment?

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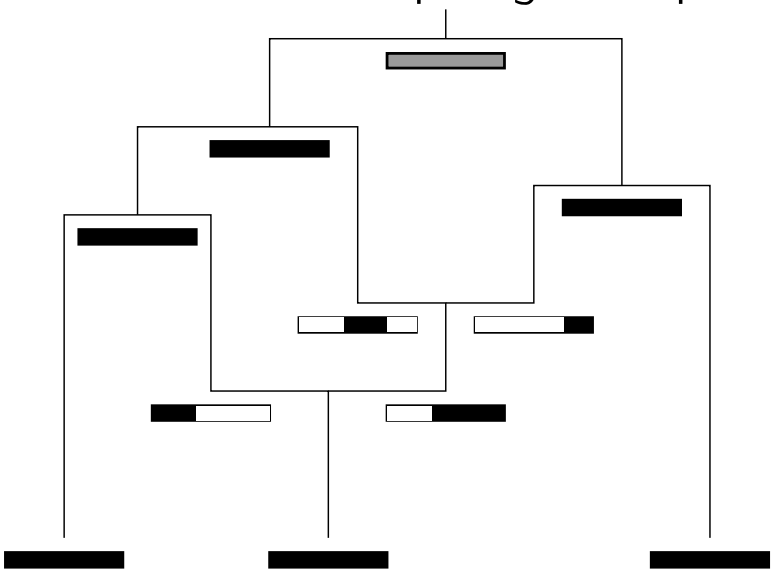
Questions

- What is the maximum number of local trees that can correspond to a sequence alignment?
- Draw the local topologies implied by the following ARG:



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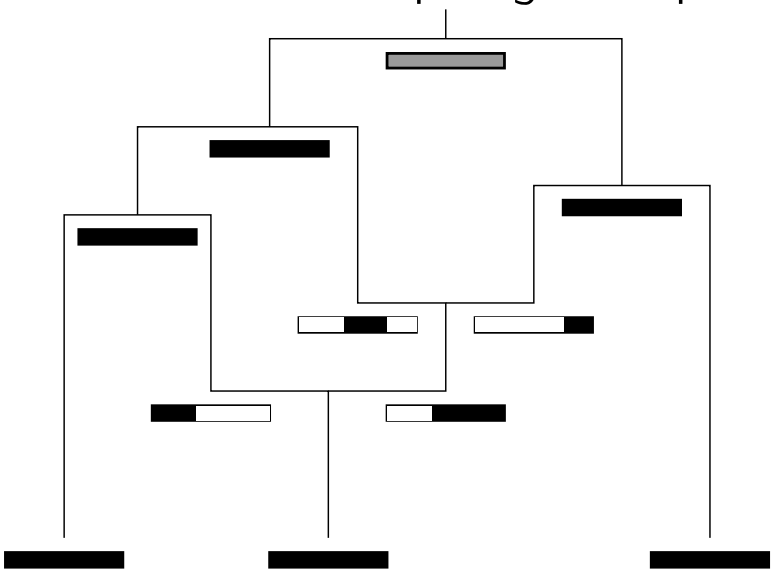

- We saw how recombination can improve our ability to infer ancestral population dynamics. Would you expect higher recombination rates to always improve this? Why/Why not?

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- Bloomquist, E. W. and Suchard, M. A. (2010). Unifying vertical and nonvertical evolution: a stochastic arg-based framework. *Syst Biol*, 59(1):27–41.
- Didelot, X., Lawson, D., Daarling, A., and Falush, D. (2010). Inference of homologous recombination in bacteria using whole-genome sequences. *Genetics*, 186:1435.
- Heled, J. and Drummond, A. J. (2010). Bayesian inference of species trees from multilocus data. *Mol Biol Evol*, 27(3):570–80.
- Hudson, R. R. (1983). Properties of a neutral allele model with intragenic recombination. *Theor Popul Biol*, 23(2):183–201.
- Li, H. and Durbin, R. (2011). Inference of human population history from individual whole-genome sequences. *Nature*, 475(7357):493–496.
- Marston, A. L. and Amon, A. (2004). Meiosis: cell-cycle controls shuffle and deal. *Nature Reviews Molecular Cell Biology*, 5(12):983–997.
- McVean, G. A. T. and Cardin, N. J. (2005). Approximating the coalescent with recombination. *Philos Trans R Soc Lond B Biol Sci*, 360(1459):1387–1393.
- Ogilvie, H. A., Heled, J., Xie, D., and Drummond, A. J. (2016). Computational performance and statistical accuracy of *beast and comparisons with other methods. *Systematic biology*, page syv118.
- Rasmussen, M. D., Hubisz, M. J., Gronau, I., and Siepel, A. (2014). Genome-wide inference of ancestral recombination graphs. *PLoS genetics*, 10(5):e1004342.
- Vaughan, T. G., Welch, D., Drummond, A. J., Biggs, P. J., George, T., and French, N. P. (2017). Inferring ancestral recombination graphs from bacterial genomic data. *Genetics*, 205:857–870.
- Wiuf, C. and Hein, J. (1999). Recombination as a point process along sequences. *Theor Popul Biol*, 55(3):248–259.
- Zhang, C., Ogilvie, H. A., Drummond, A. J., and Stadler, T. (2017). Bayesian inference of species networks from multilocus sequence data. *Molecular Biology and Evolution*, page msx307.

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