Inference on population trees by approximating Wright-Fisher diffusions

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Acknowledgment

Joint work with

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- Pekka Marttinen
  Aalto University
- Bill Hanage
  Harvard University

Population tree – Species tree

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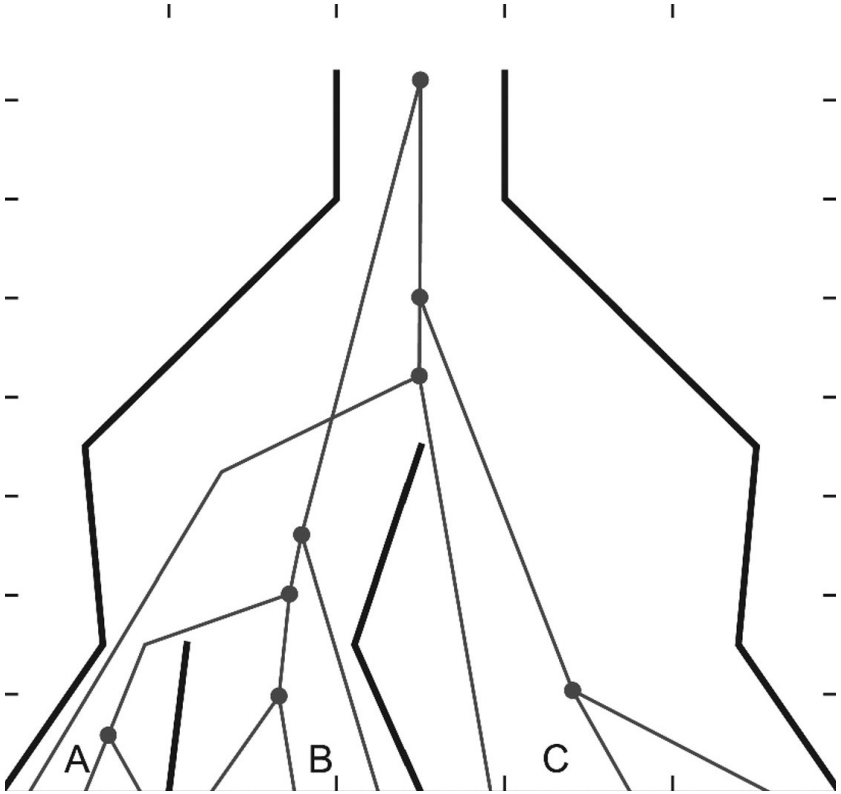
- Difference comes from the main source of genetic variation: mutation vs drift.
- This work concentrates on methods which are applicable to data with large numbers of markers (SNP,AFLP,MLST etc.)

Multi-species coalescent



- Computationally very expensive.

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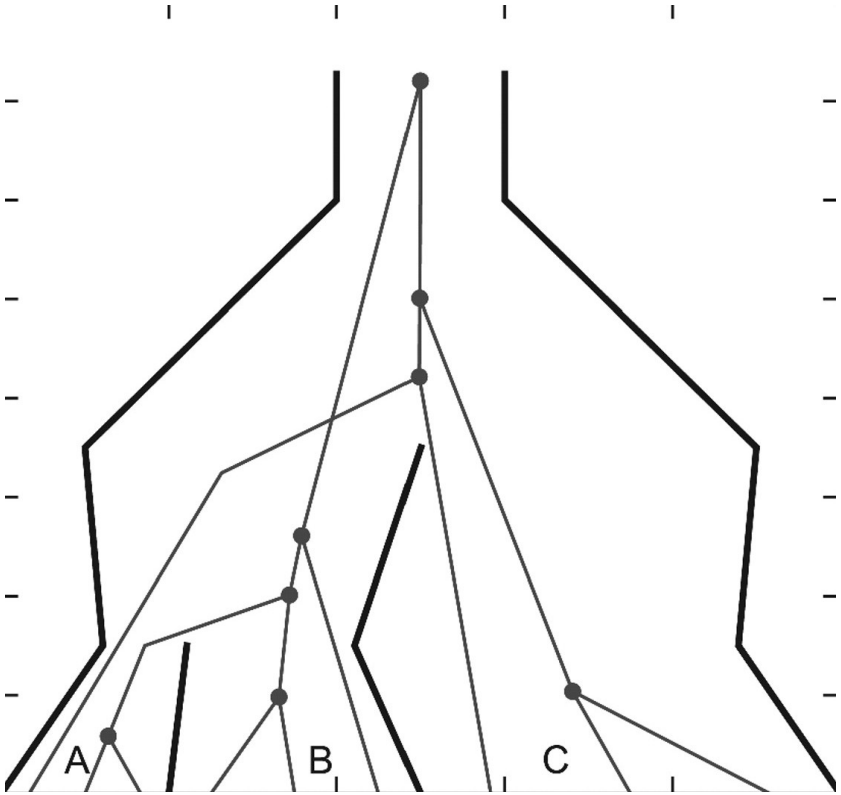

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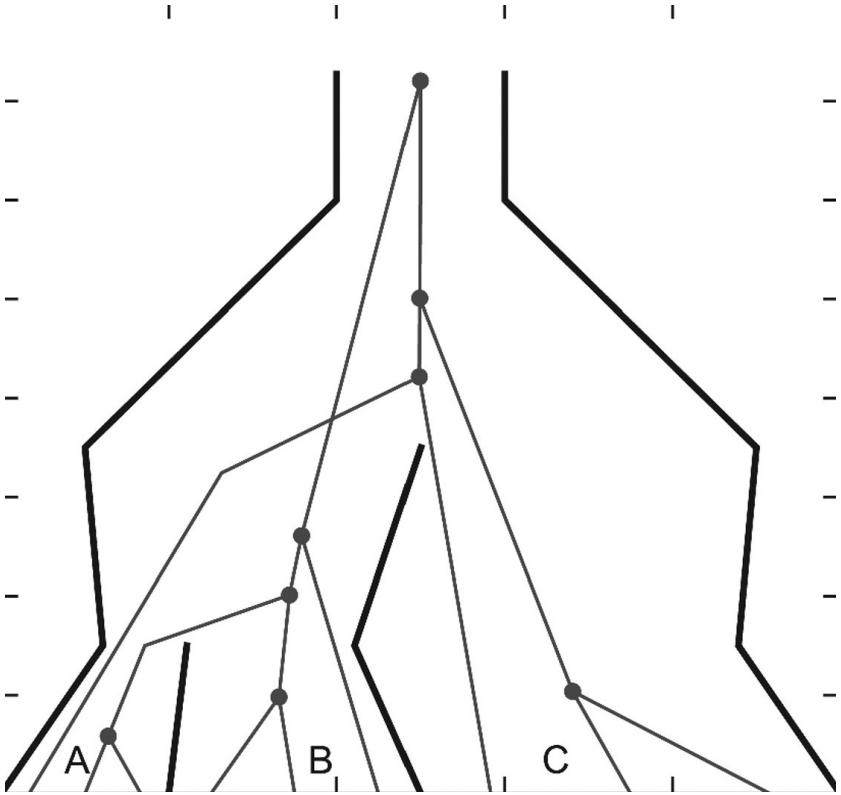

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- Used in phylogenetics by Cavalli-Sforza, Edwards, Felsenstein and others in the 60's and 70's.

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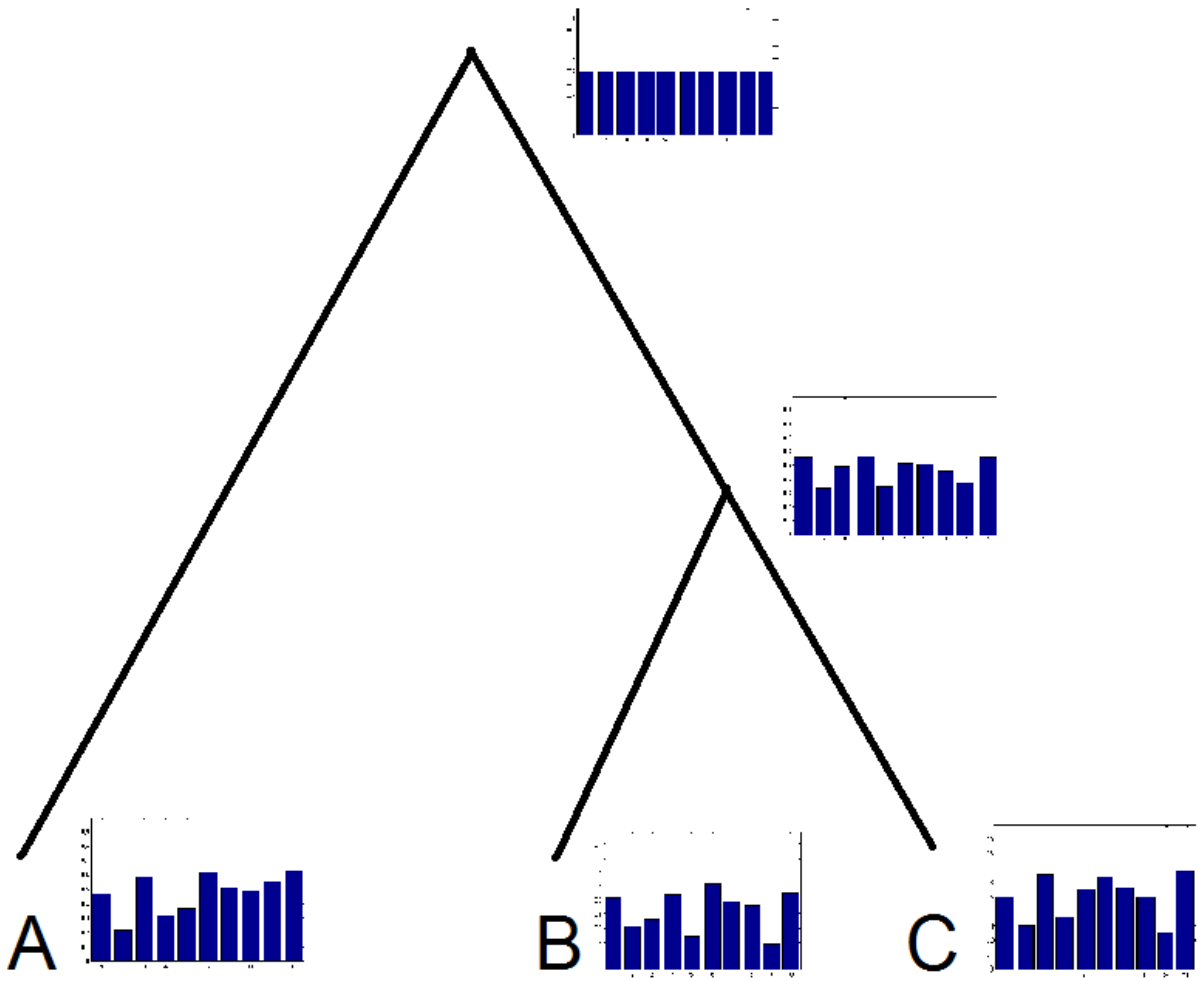
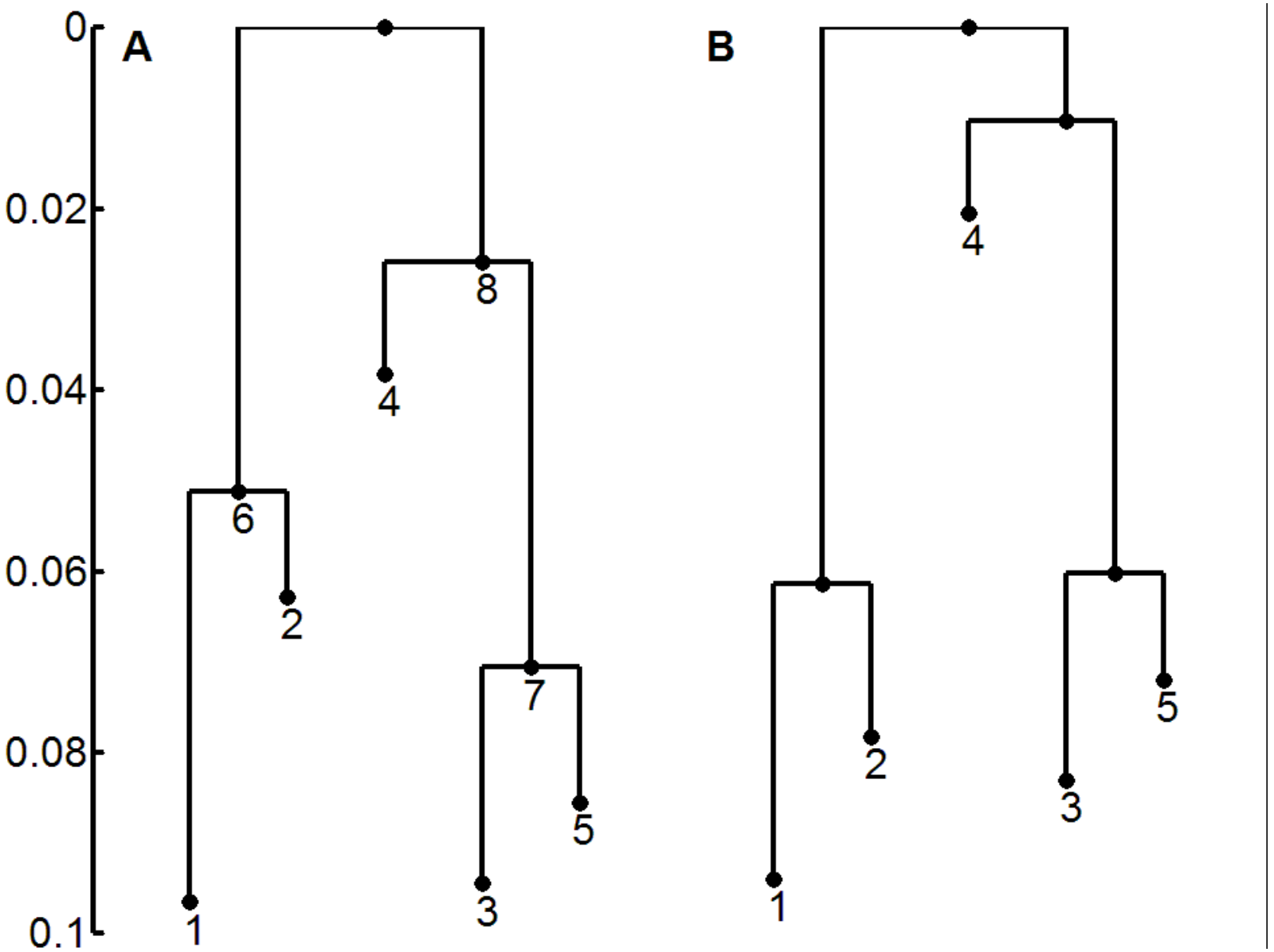
- Also, computational advantages due conjugacy as the sampling from populations often binomial.

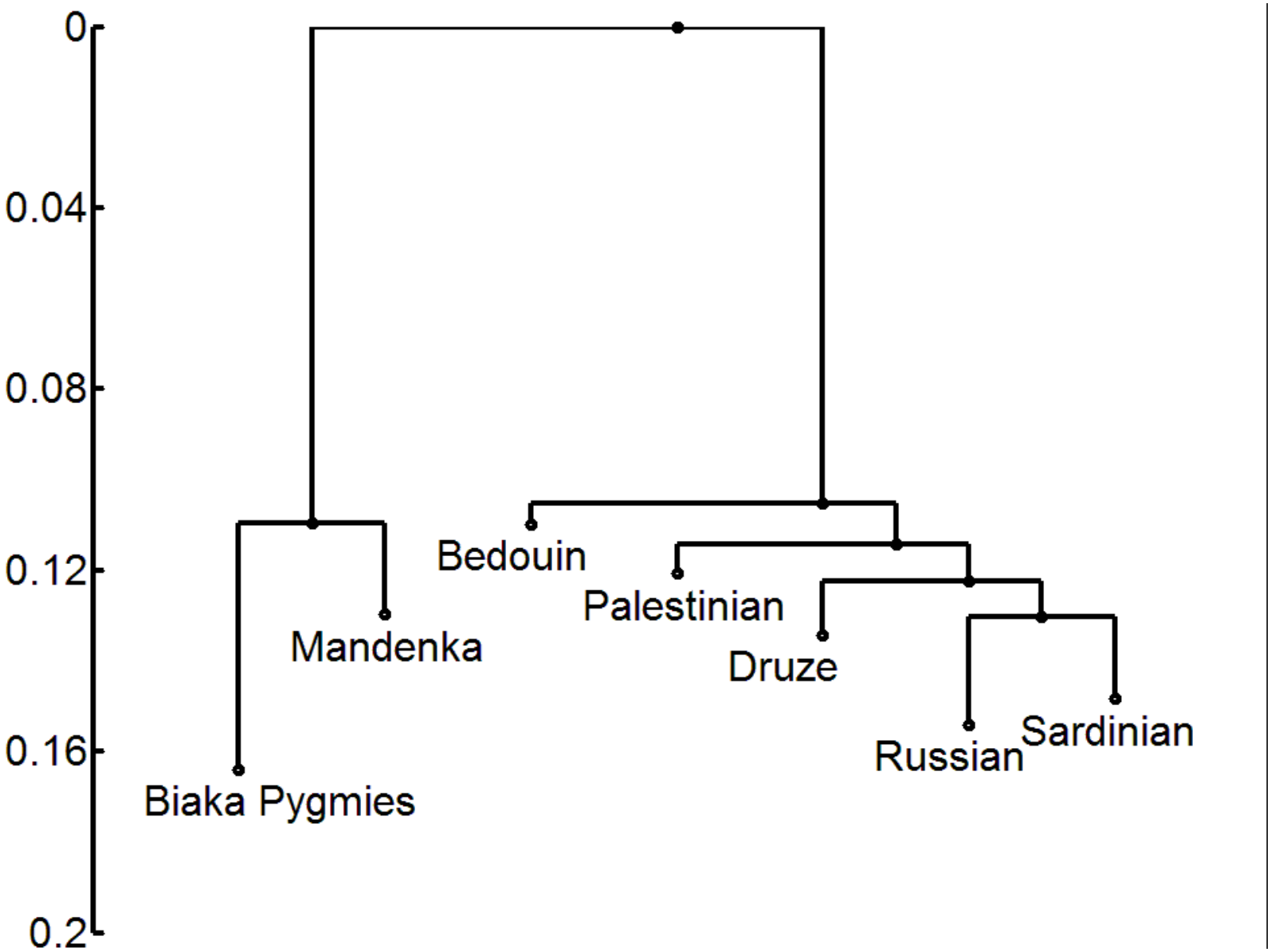
Full model



Tree used in simulation (A) and estimated tree (B)



Tree of human populations from SNPs



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- Poor approximation, as the mean and variance do not scale linearly or nearly linearly with time.

WF-model with mutation

- Solution:
  Compute the actual expectation and variance of the WF process:

$$
\begin{aligned}
E(X_t) &= E(E(X_t \mid X_{t-1})) = \dots \\
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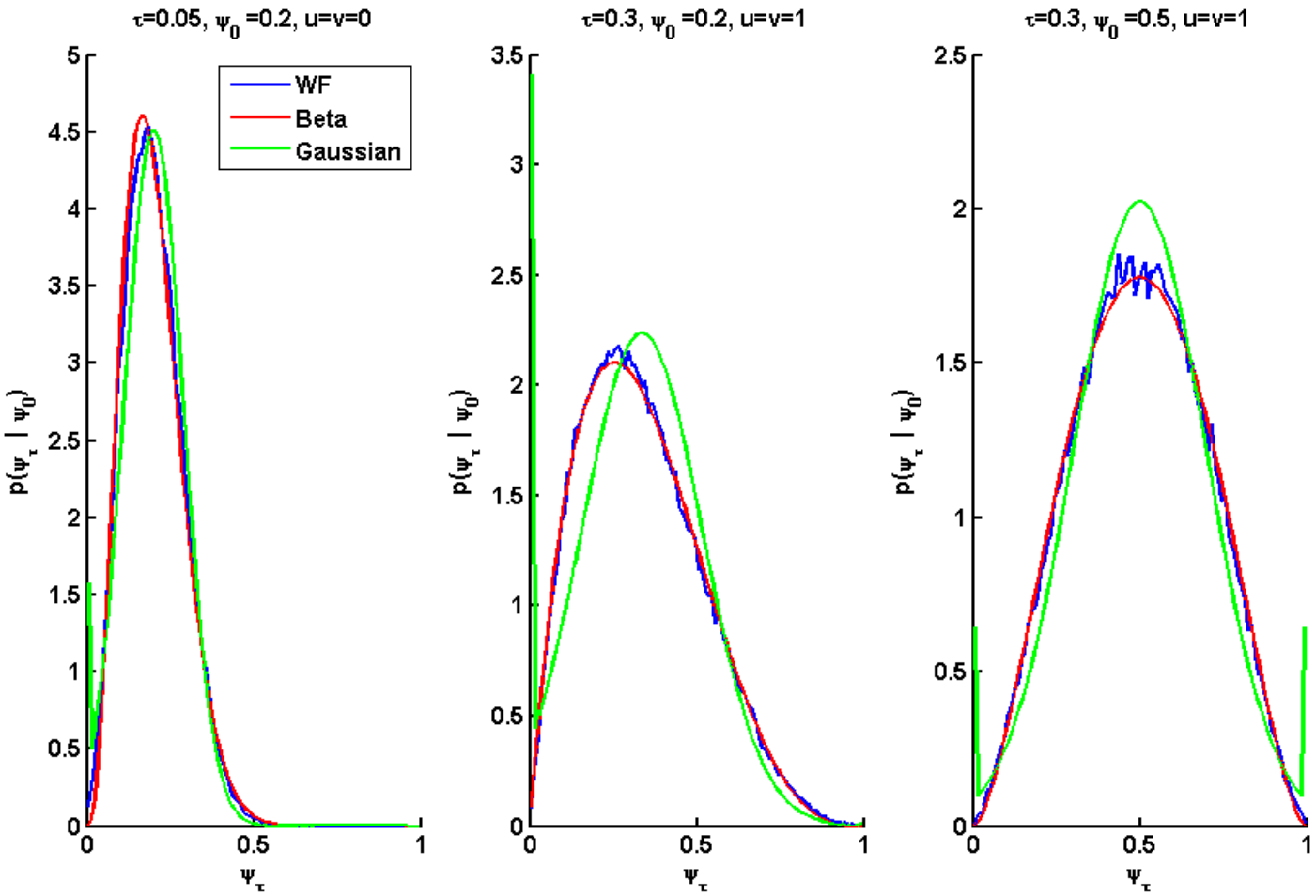
- Then we can approximate the change with

$$\psi_{\tau+\epsilon} \mid \psi_\tau \sim Beta(\alpha_{\tau,\epsilon}, \beta_{\tau,\epsilon}),$$

  where $\alpha_{\tau,\epsilon}$ and $\beta_{\tau,\epsilon}$ are chosen to get the correct mean and variance.

Comparison of approximations



$N = 1e4$

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- Let $X_{i,t}$ denote the number of alleles of type i at time t, with population size N.
- The allele counts have a multinomial distribution conditional on the alleles of the previous generation

$$X_{1t}, \ldots, X_{rt} | X_{1(t-1)}, \ldots, X_{r(t-1)} \sim \mathit{Multinomial}(N, \eta_t),$$

where η_t is a r dimensional vector with entries

$$\eta_{jt} = \begin{cases} 1-(1-u)\left(1-\psi_{r(t-1)}\right) & \text{if } j = r \text{ and} \\ (1-u)\psi_{j(t-1)} & \text{otherwise.} \end{cases}$$

Infinite alleles model

- Similarly, as in the biallelic case, we can explicitly compute the mean and covariance as

$$E(X_{it}) = E(E(X_{it} \mid X_{i(t-1)})) = \dots$$

and

$$\begin{aligned} Cov(X_{it}, X_{jt}) =& E(Cov(X_{it}, X_{jt} \mid X_{i(t-1)}, X_{j(t-1)})) \\ &+ Cov(E(X_{it}, X_{jt} \mid X_{i(t-1)}, X_{j(t-1)})) \\ =& \dots \end{aligned}$$

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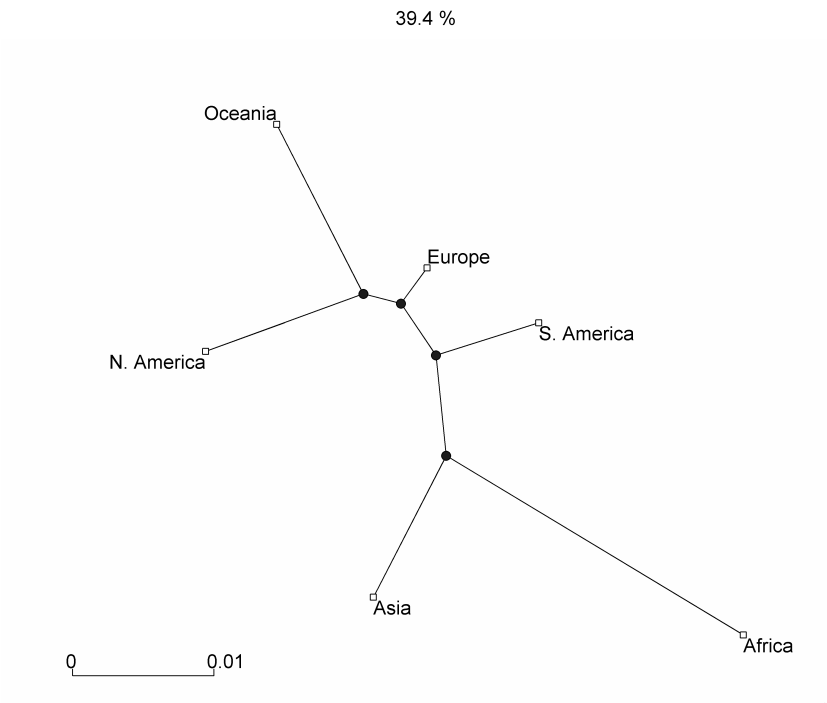
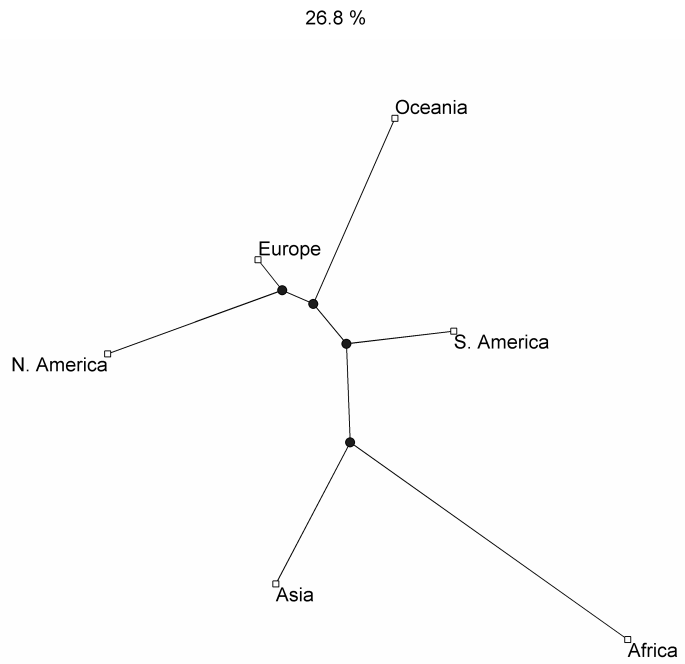
- To get same expectations and covariance structure as with the infinite alleles model, we use

$$\phi = \frac{(m+1)e^{-(m+1)\tau}}{1-e^{-(m+1)\tau}} \text{ and}$$

$$\gamma = \frac{m\left(1-e^{-(m+1)\tau}\right)}{\left(1-e^{-(m+1)\tau}\right) - (m+1)e^{-m\tau}\left(1-e^{-\tau}\right)}.$$

Global population structure of S. pneumoniae





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- For biallelic loci combination of Laplace approximization, AMIS and numerical maximization algorithms.

Future work

- Comparison with the coalescent approach.
- Computational strategies.
- Migration? Graphs instead of trees?
- More complex mutational models? Microsatellites?

References

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Under revision.