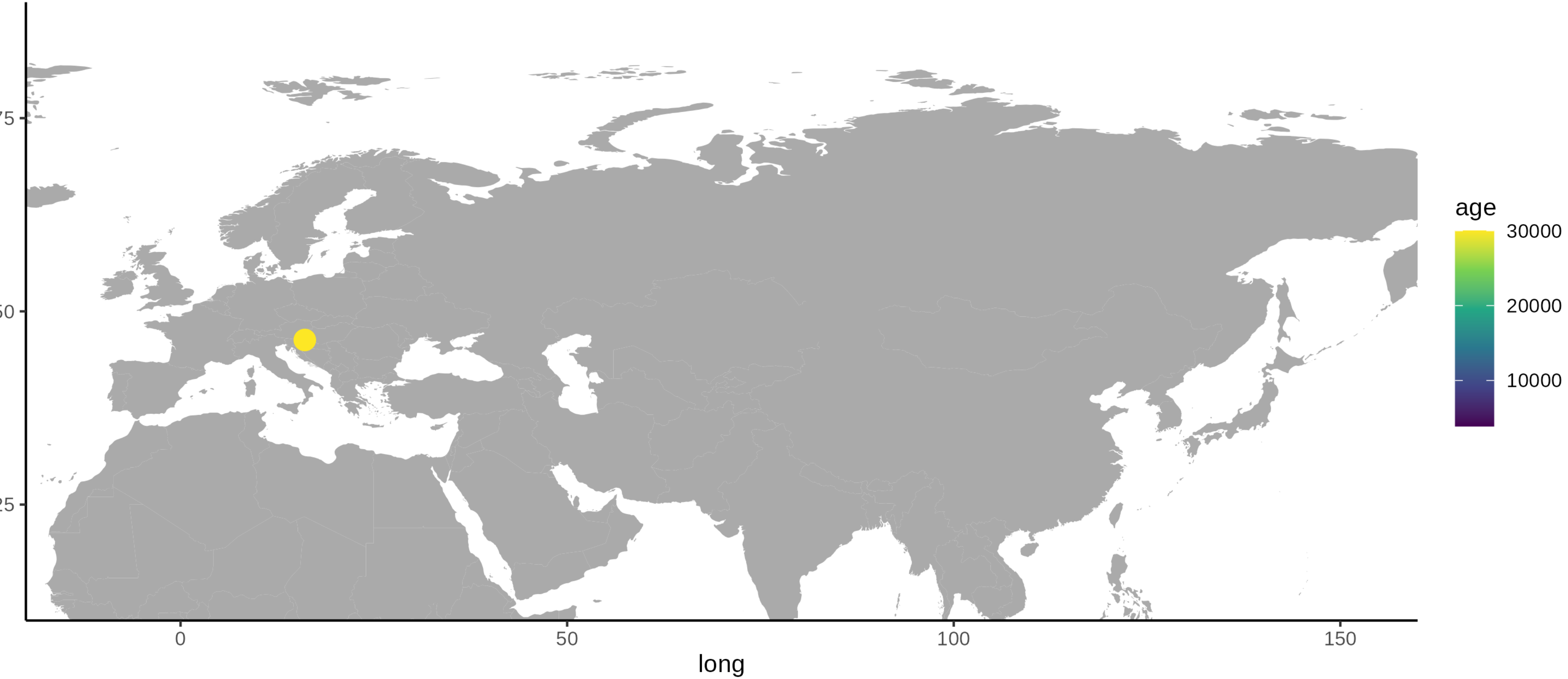
F-statistics and Population Structure

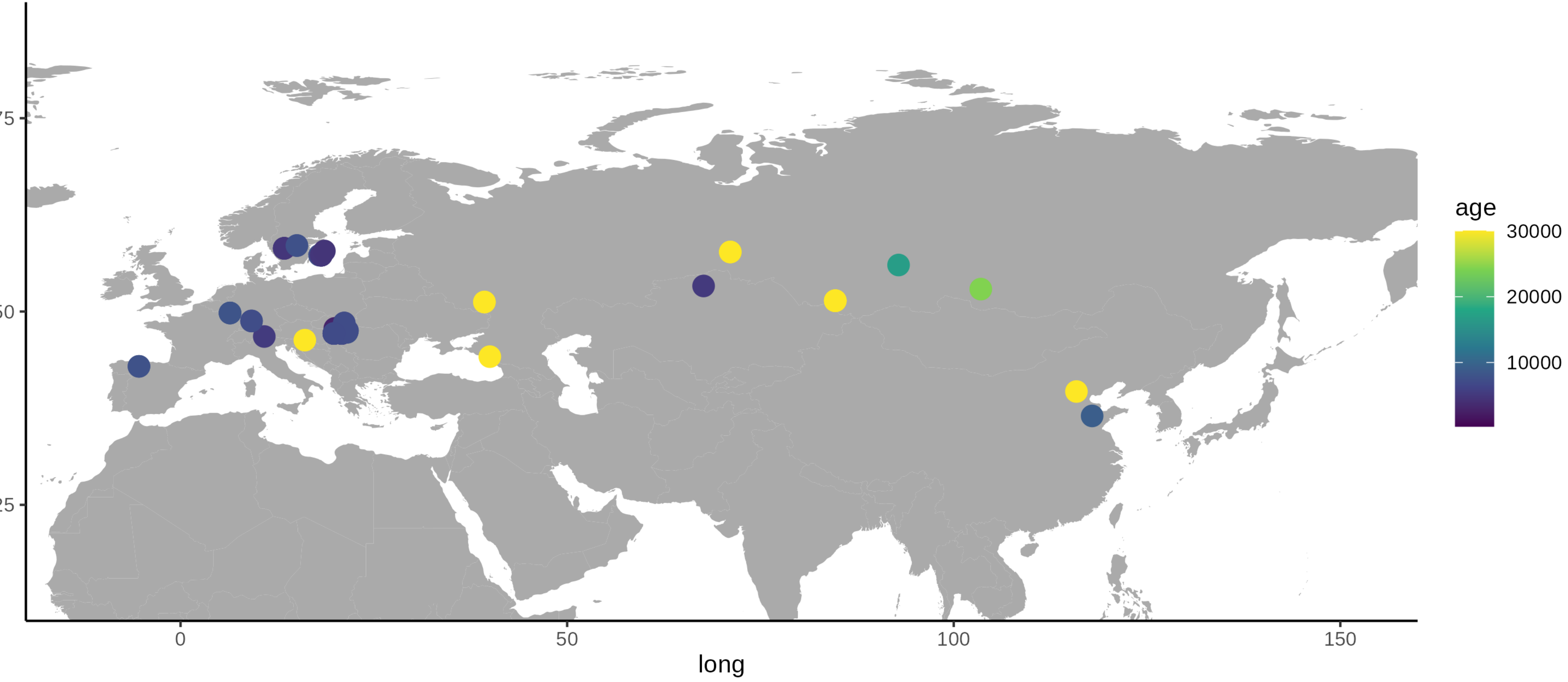
Benjamin Peter, MPI for Evolutionary Anthropology

Hominin Ancient DNA (2010)



Data compiled by D. Reich et al.

Hominin Ancient DNA (2014)



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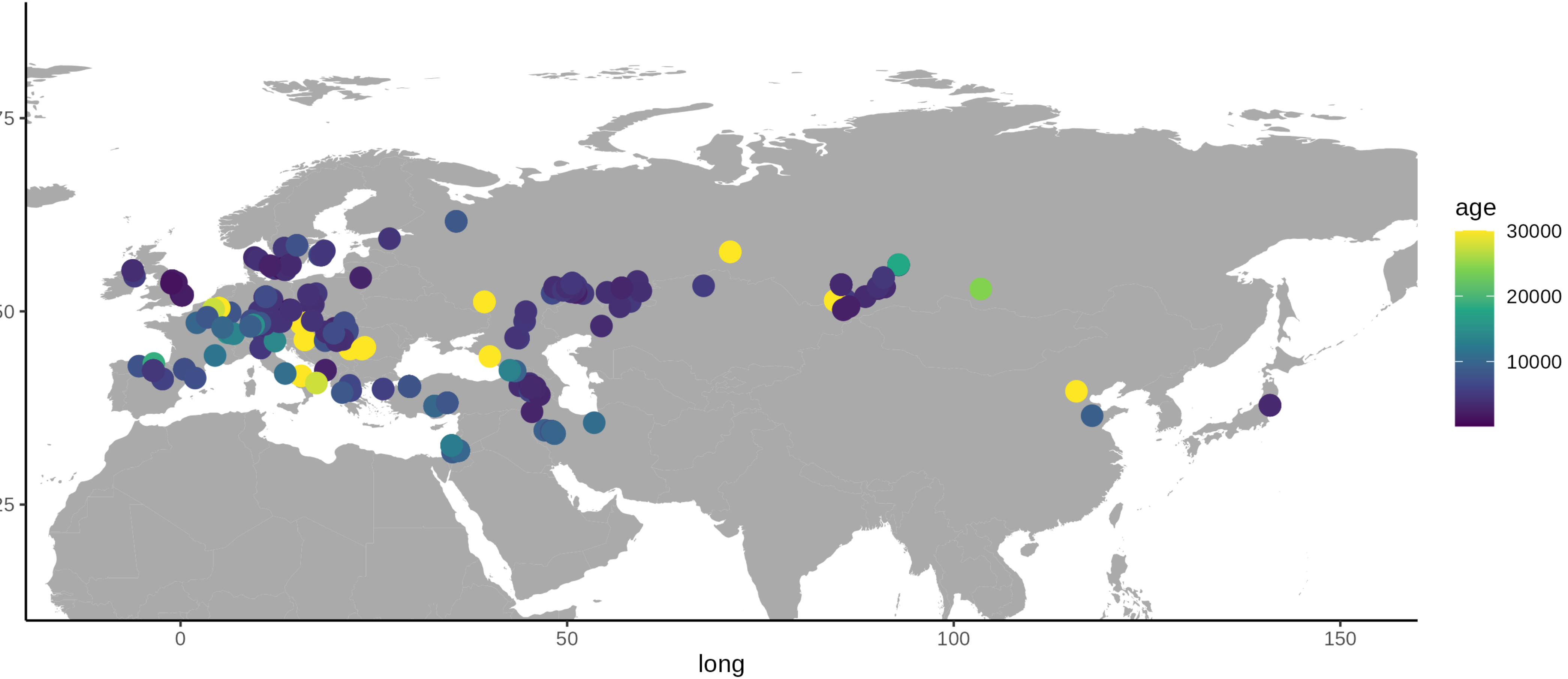
Hominin Ancient DNA (2016)



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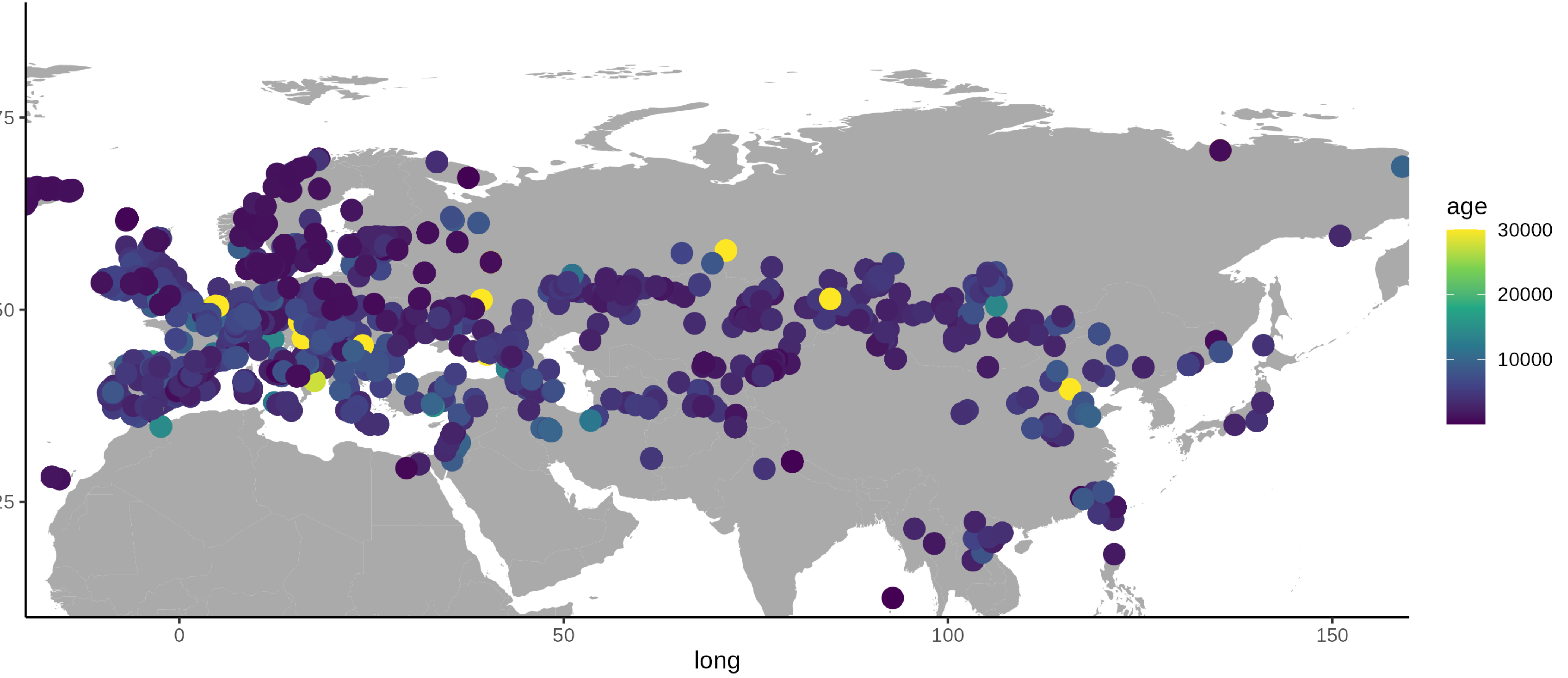
Hominin Ancient DNA (2020)



Data compiled by D. Reich et al.

Main Reference

GENETICS | INVESTIGATION

Admixture, Population Structure, and *F*-Statistics

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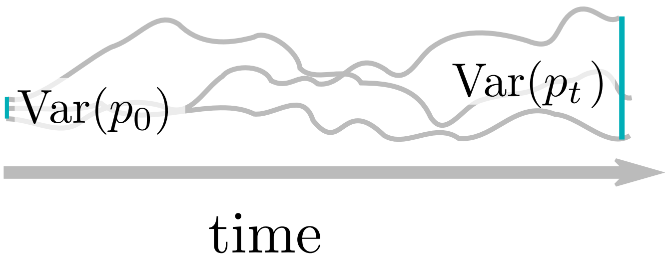
Setup

- Today: Theory of F-statistics and Computations
- Tomorrow: Using F-statistics to build more complex models

Measuring Genetic Drift

Measuring Genetic Drift

Change in Allele Frequency



Measuring Genetic Drift

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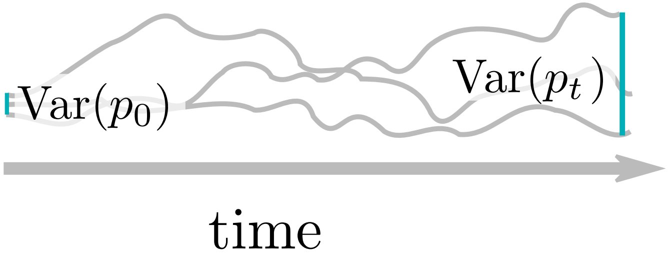
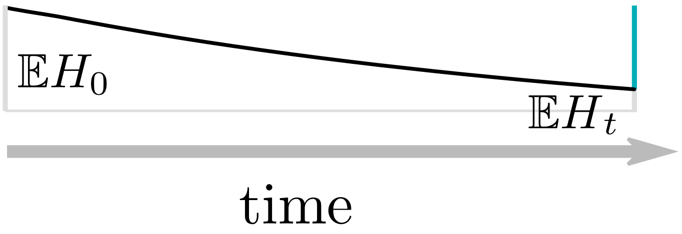
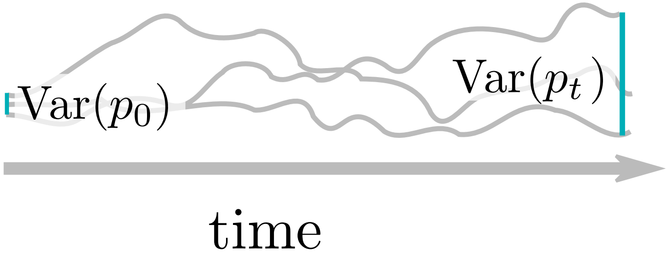


Decay of Heterozygosity



Measuring Genetic Drift

Change in Allele Frequency



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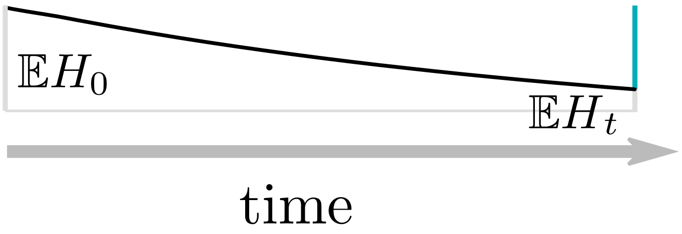
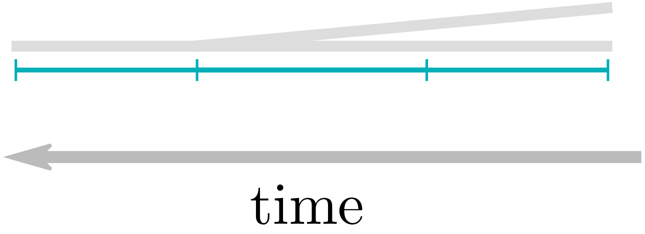


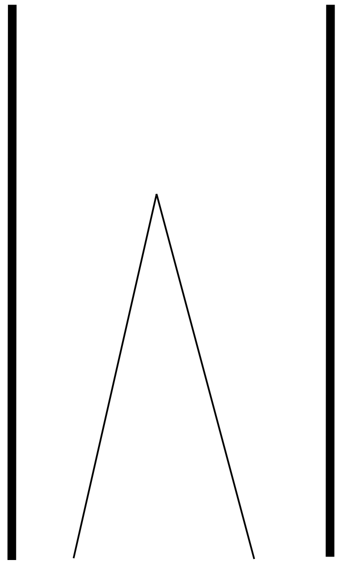
Coalescence rates

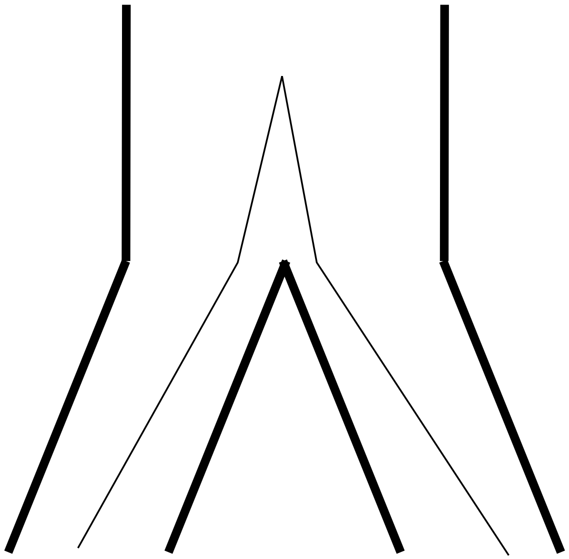


Pairwise differences

$$\mathbb{E}[\pi] = 4N\mu = \theta$$

$$\mathbb{E}[\pi_{12}] = t_{12} + 4N_{anc}\mu = t_{12} + \theta$$



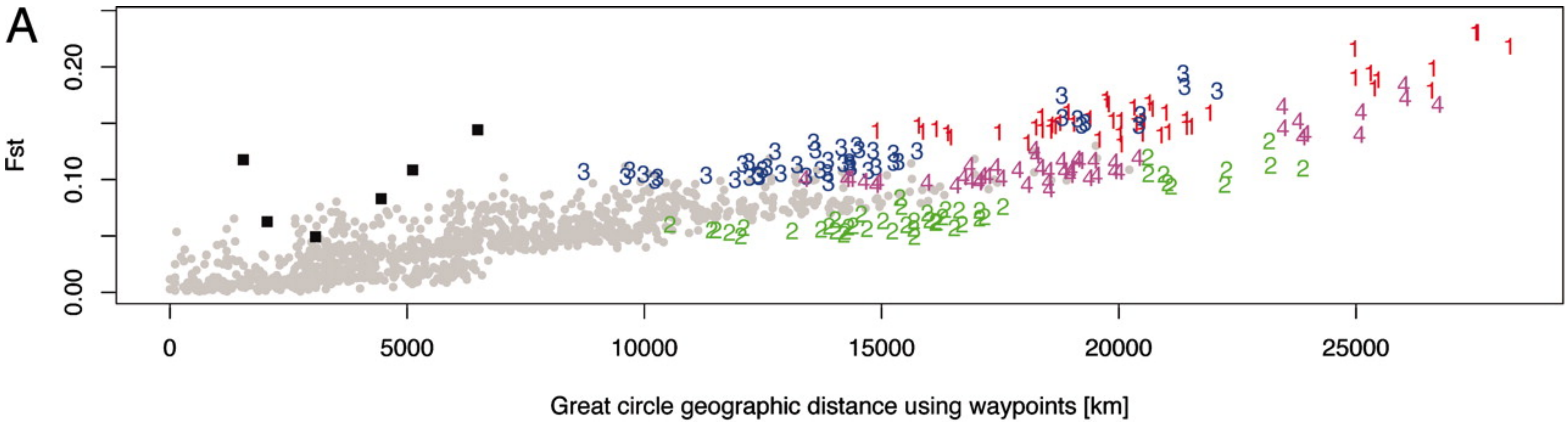


Fixation Index F_{ST}

$$F_{ST}(P_1, P_2) = \frac{\pi_{12} - \frac{\pi_1 + \pi_2}{2}}{\pi_{12}}$$

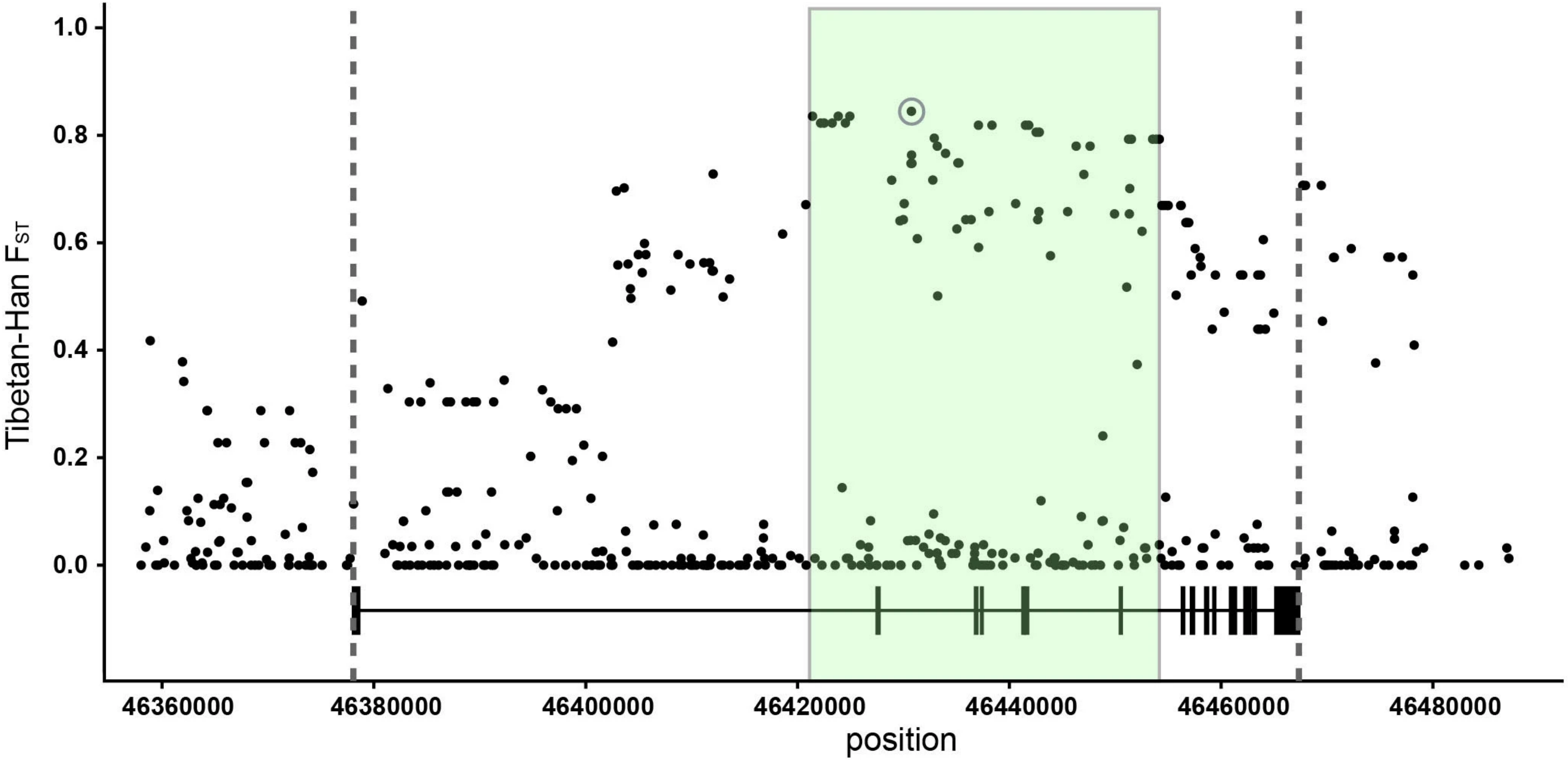
- F_{ST} is a correlation coefficient
- Between 0 and 1
- Hierarchical partitioning (AMOVA)
- Many estimators exist
  - Hudson (1991)
  - Weir & Cockerham (1984)

Fixation Index F_{ST}



Ramachandran et al. 2005

F_{ST} Outliers



Huerta-Sanchez et al. 2014

F_2-statistic

$$F_{ST}(P_1, P_2) = \frac{\pi_{12} - \frac{\pi_1 + \pi_2}{2}}{\pi_{12}}$$

- F_{ST} is a correlation coefficient
- Between 0 and 1
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- Many estimators exist
  - Hudson (1991)
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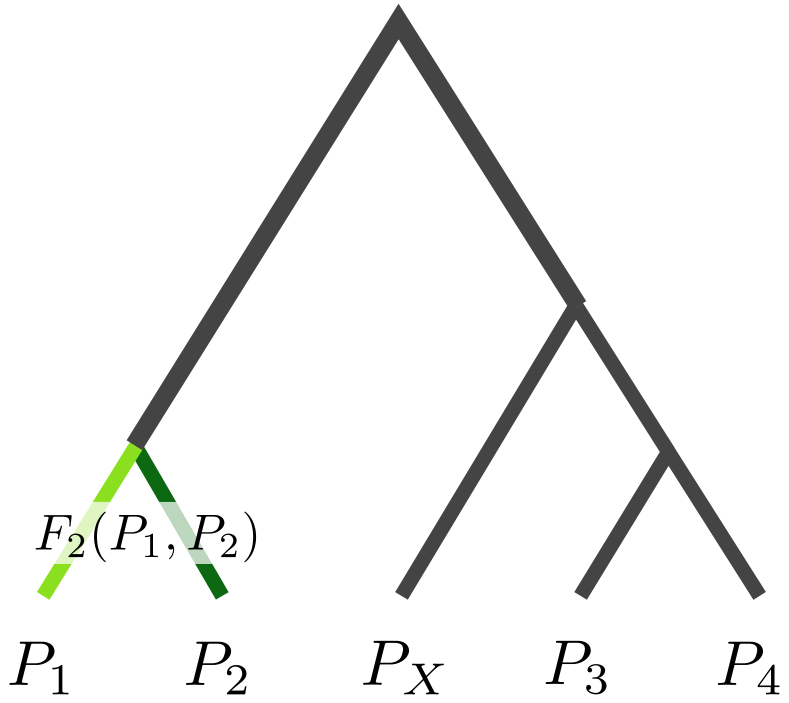
$$\begin{aligned} F_2(P_1, P_2) &= 2\pi_{12} - \pi_1 - \pi_2 \\ &= \sum_l (p_{1l} - p_{2l})^2 \end{aligned}$$

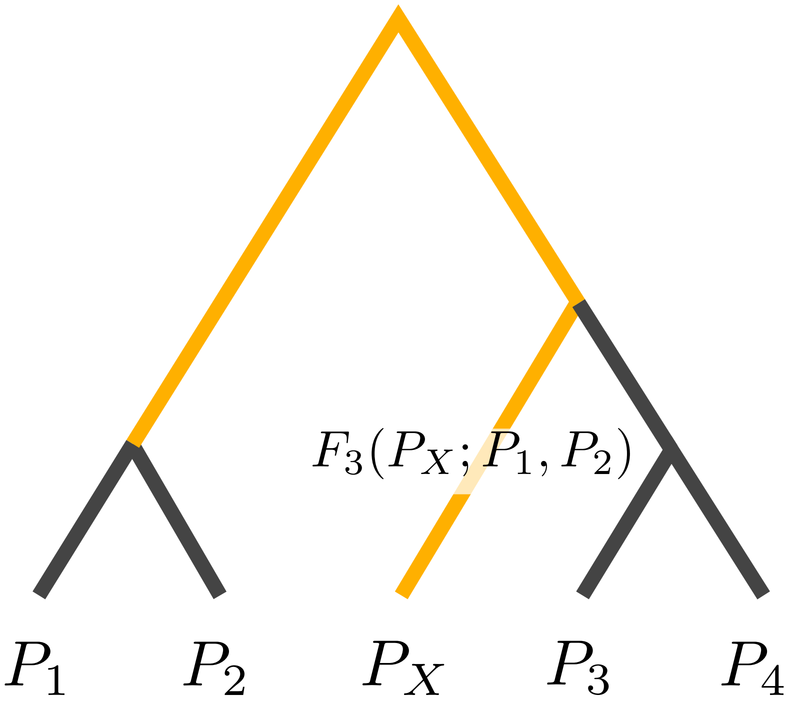
- F_2 is a covariance
- Bigger than 0
- Tree-additive
- Testing for treeness

Tree-additive



F_3-statistic

Given all F2-values, how can we calculate the yellow branch length?



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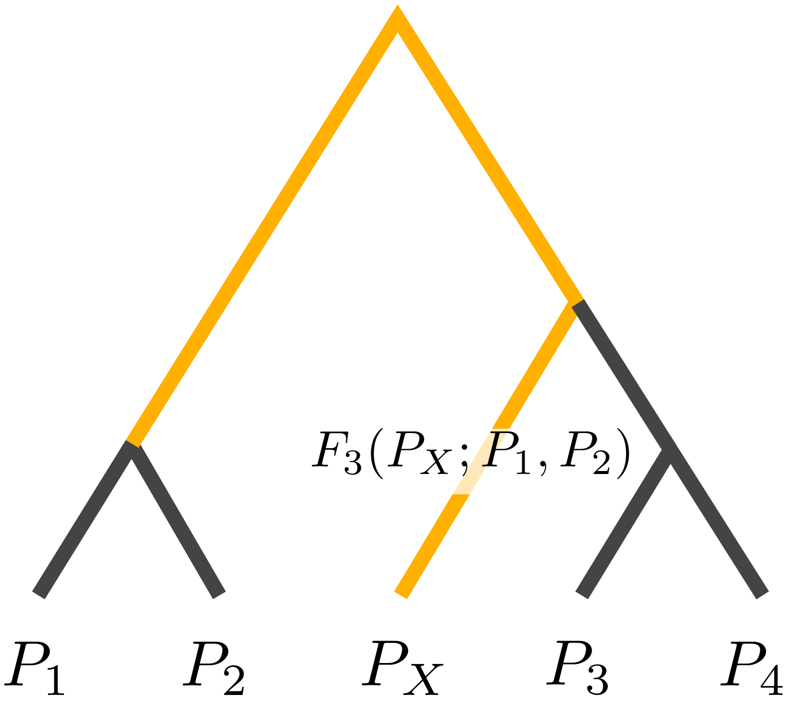
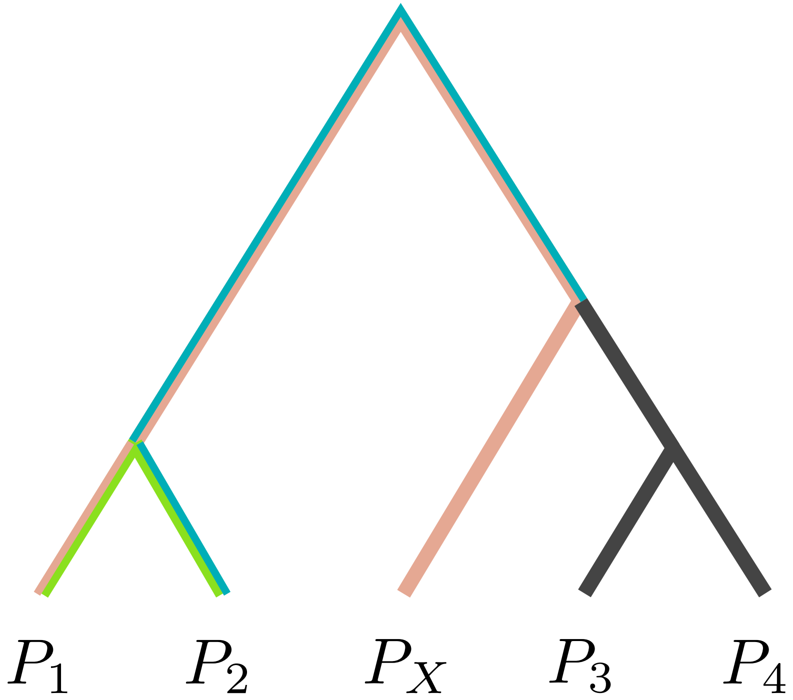
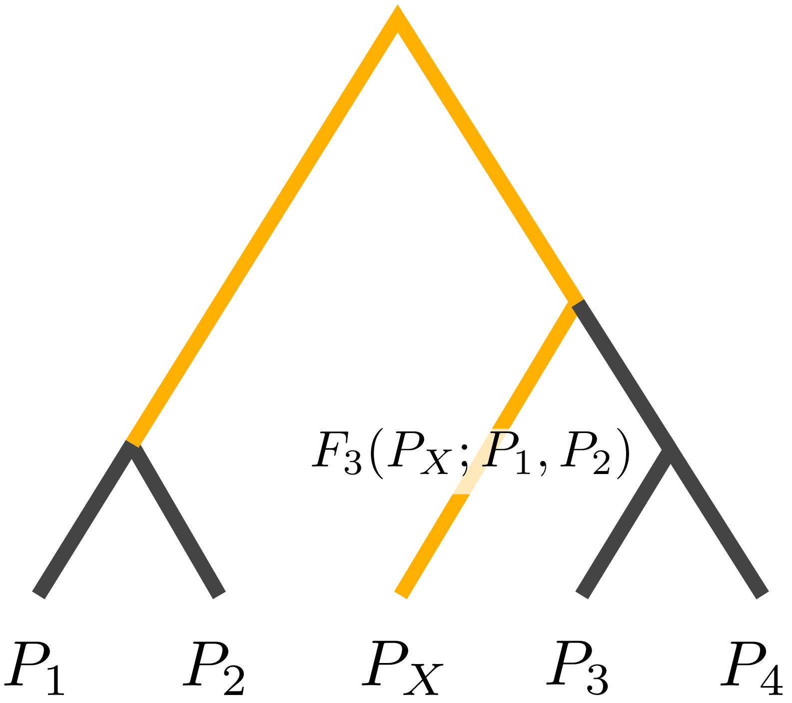
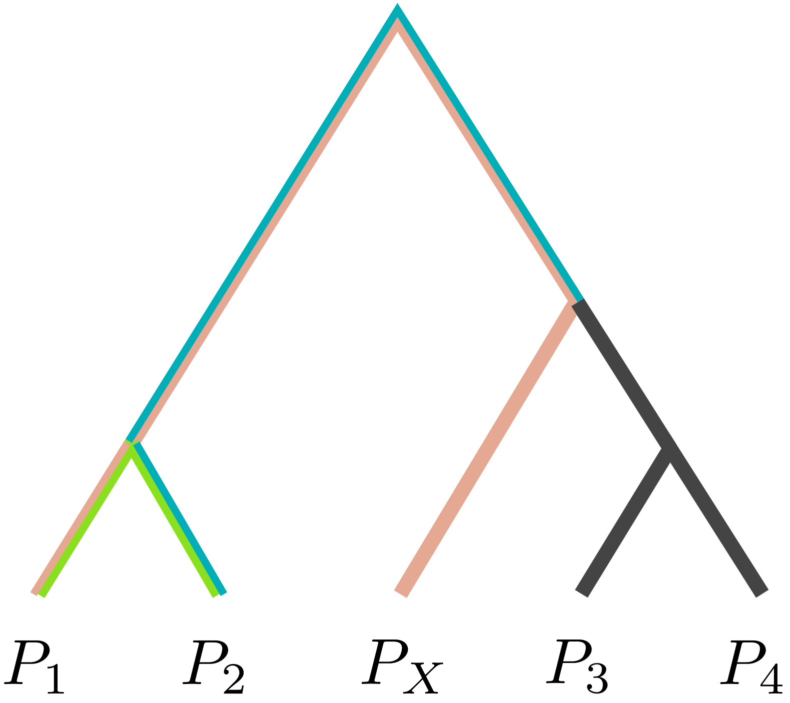




F_3-statistic

$$F_3(P_X; P_1, P_2) = \frac{1}{2}\left(F_2(P_X, P_1) + F_2(P_X, P_2) - F_2(P_1, P_2) \right)$$





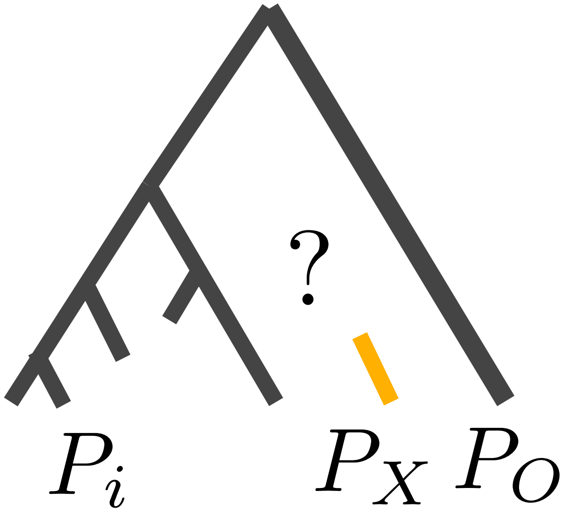
F_3-statistic equations

$$F_3(P_X; P_1, P_2) = \frac{1}{2}\left(F_2(P_X, P_1) + F_2(P_X, P_2) - F_2(P_1, P_2)\right)$$

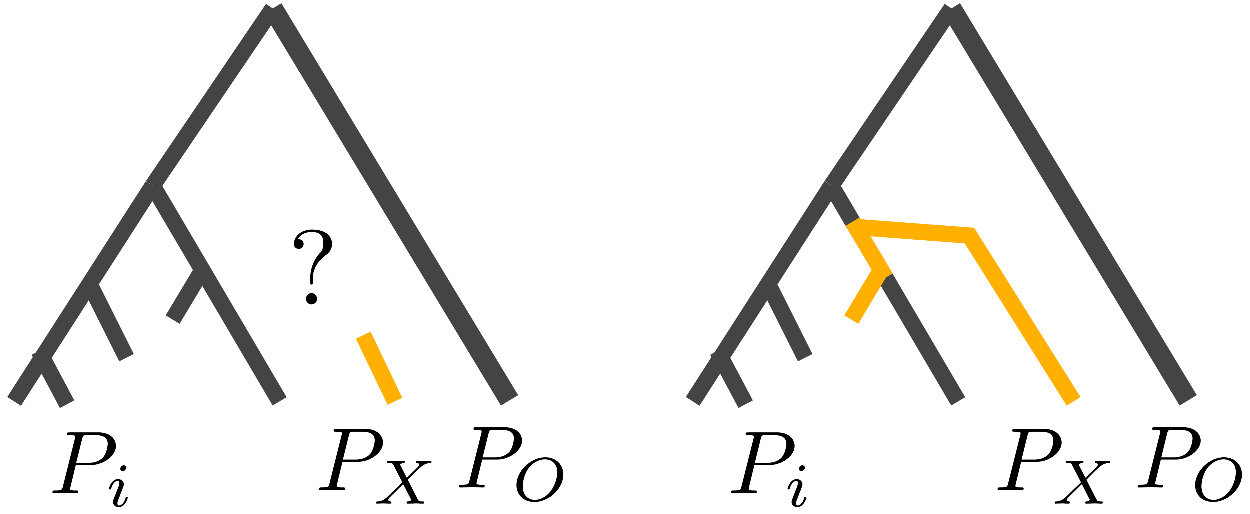
$$F_3(P_X; P_1, P_2) = \sum_l (p_{xl} - p_{x1})(p_{xl} - p_{x2})$$

$$F_3(P_X; P_1, P_2) = \pi_{1x} + \pi_{2x} - \pi_{12} - \pi_x$$

Outgroup-F_3-statistic



Outgroup-F_3-statistic



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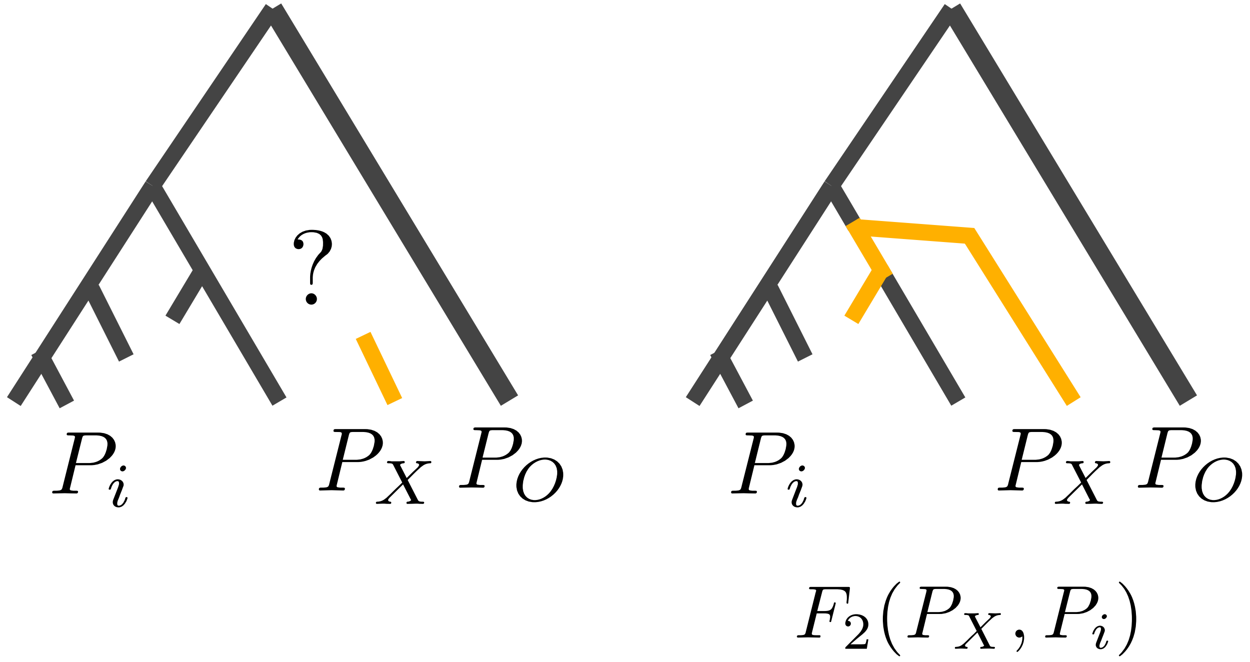
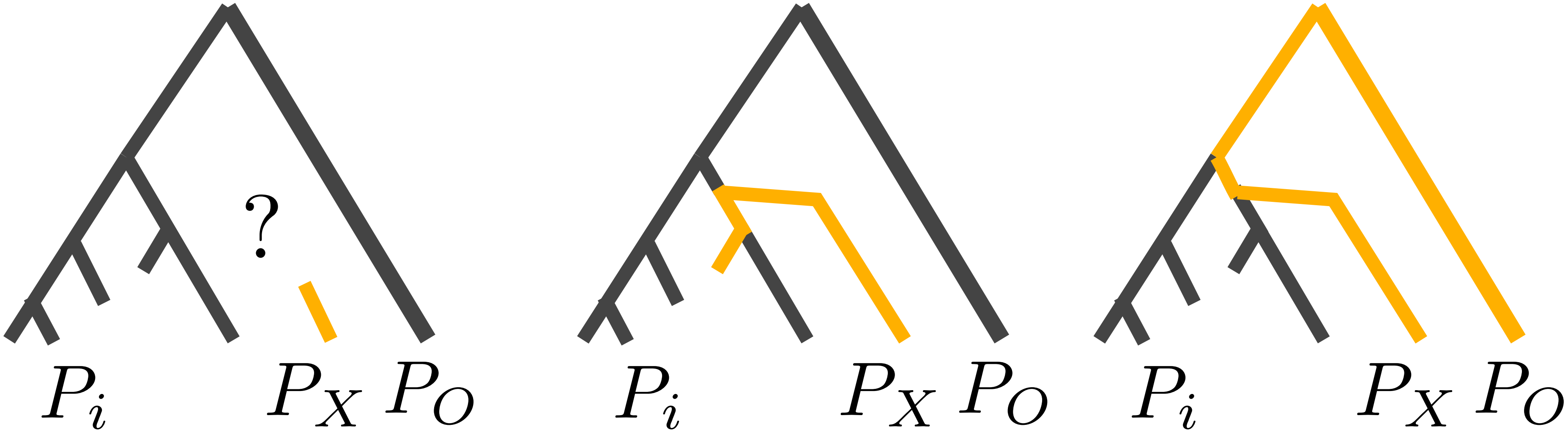


Outgroup-F_3-statistic

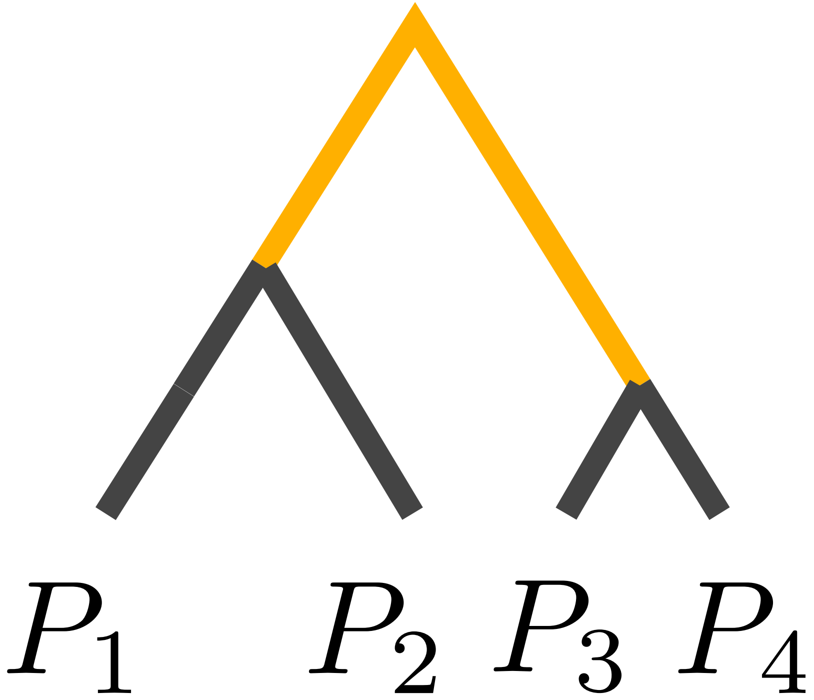


$F_2(P_X, P_i)$

$F_3(P_O; P_X, P_i)$

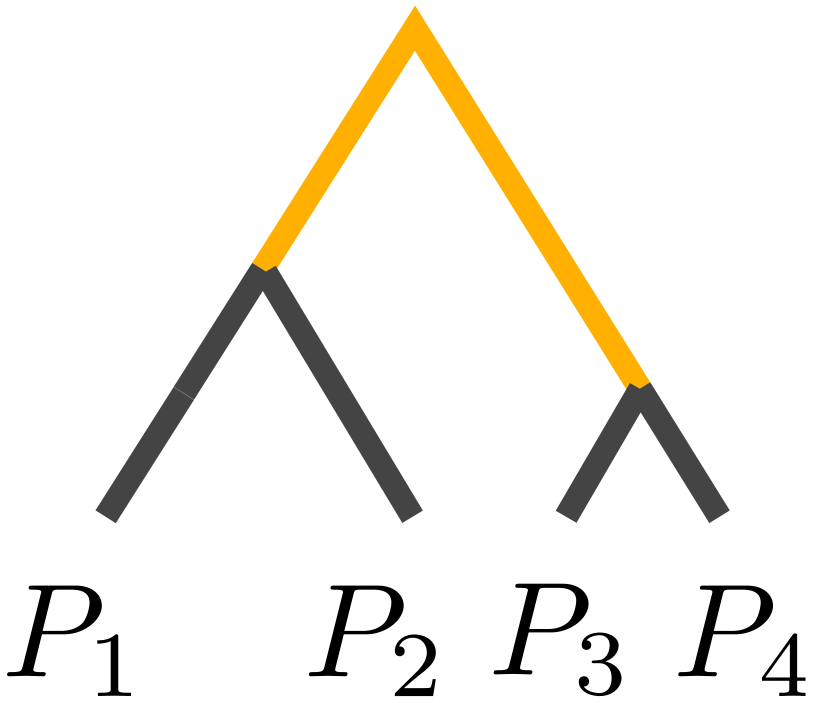
(Branch)-F_4-statistic

$$F_4^{(B)}(P_1, P_2; P_3, P_4) = \frac{1}{2}\Big(F_2(P_1, P_3) + F_2(P_2, P_4) - F_2(P_1, P_2) - F_2(P_3, P_4)\Big)$$



(Branch)-F_4-statistic

$$F_4^{(B)}(P_1, P_2; P_3, P_4) = \frac{1}{2}\Big(F_2(P_1, P_3) + F_2(P_2, P_4) - F_2(P_1, P_2) - F_2(P_3, P_4)\Big)$$

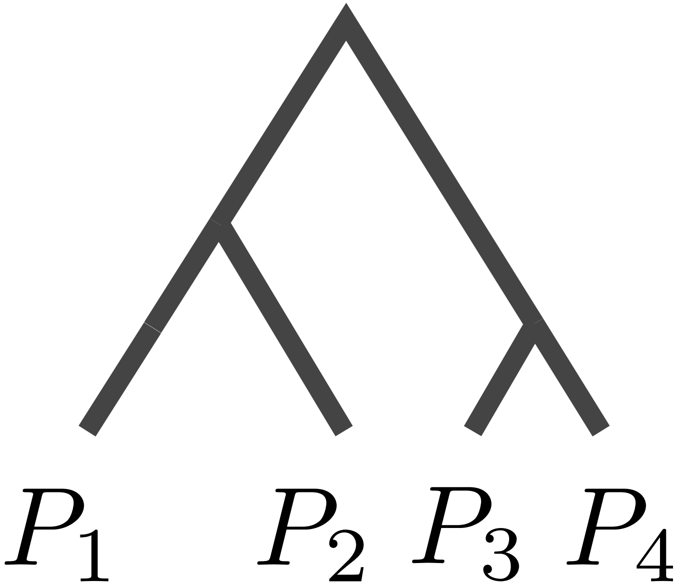


What if we reorder the arguments?

$$F_4^{(T)}(P_1, P_2; P_3, P_4) = F_4^{(B)}(P_1, P_4; P_3, P_2)$$

(Treeness)-F_4-statistic

$$F_4^{(T)}(P_1, P_2; P_3, P_4) = \frac{1}{2}\Big(F_2(P_1, P_3) + F_2(P_2, P_4) - F_2(P_1, P_4) - F_2(P_2, P_3)\Big)$$



F_4 -statistic-equations

$$F_4^{(T)}(P_1, P_2; P_3, P_4) = \frac{1}{2}\Big(F_2(P_1, P_3) + F_2(P_2, P_4) - F_2(P_1, P_4) - F_2(P_2, P_3)\Big)$$

$$F_4^{(T)}(P_1, P_2; P_3, P_4) = \sum_l (p_{l1} - p_{l2})(p_{l3} - p_{l4})$$

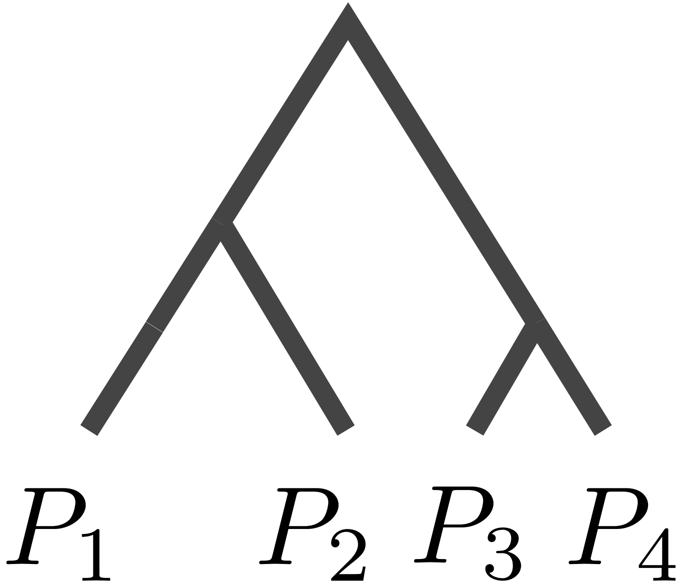
$$F_4^{(T)}(P_1, P_2; P_3, P_4) = \pi_{13} + \pi_{24} - \pi_{14} - \pi_{23}$$

Testing Treeness

If data is generated from a tree:

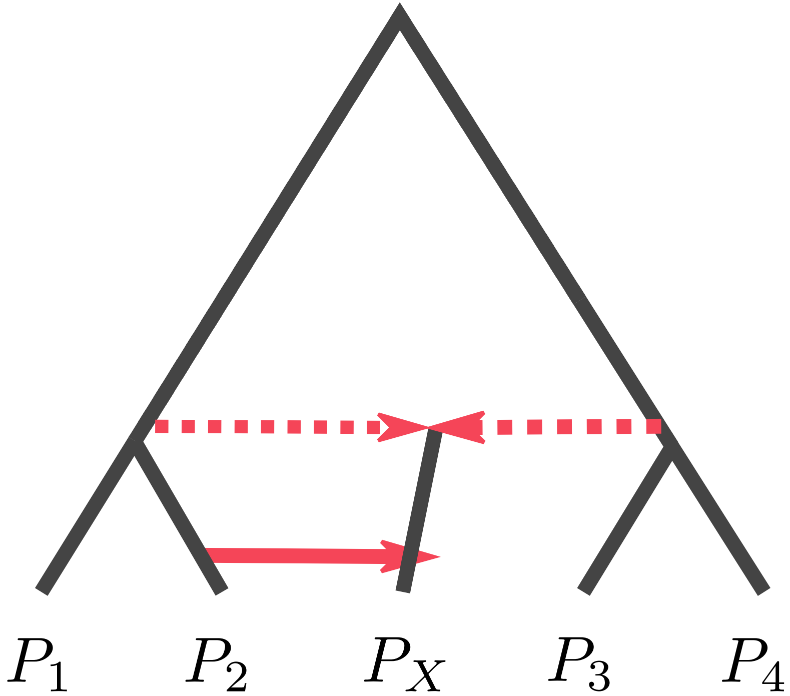
$$F_3(P_3; P_1; P_2) \geq 0$$

$$F_4^{(T)}(P_1, P_2; P_3, P_4) = 0$$



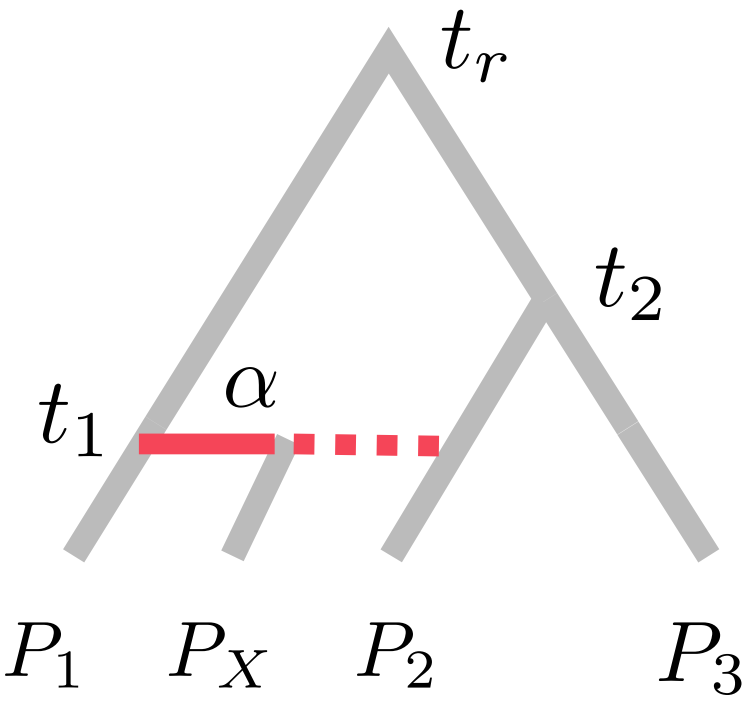
Buneman 1974

Admixture Graphs



F3 in an admixture graph

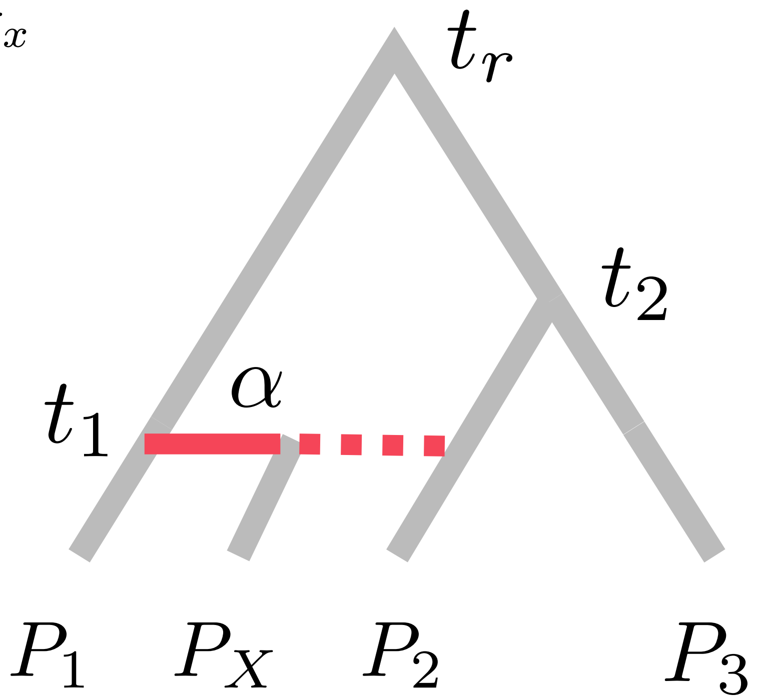
$$F_3(P_X; P_1, P_2) \approx \theta\left[t_1 - 2\alpha(1-\alpha)t_r\right]$$



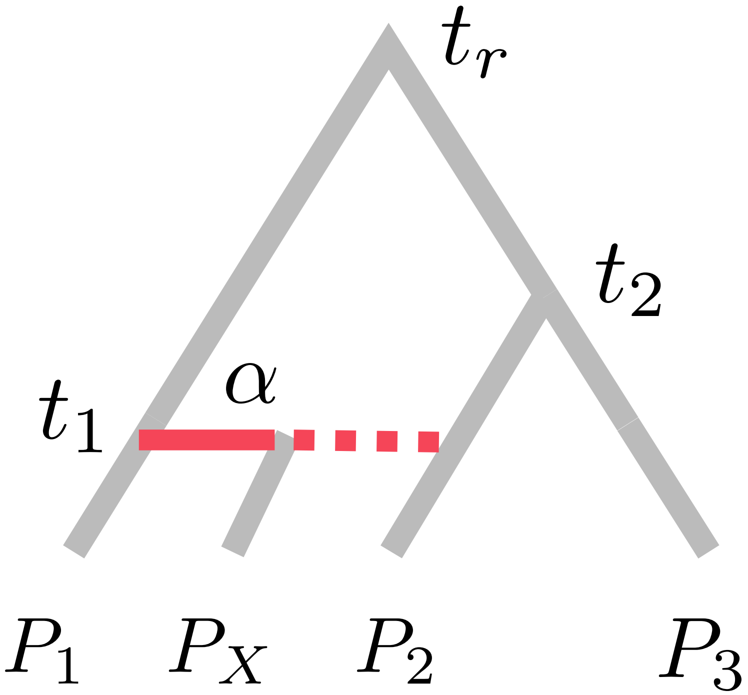
F3 in an admixture graph

$$F_3(P_X; P_1, P_2) = \pi_{1x} + \pi_{2x} - \pi_{12} - \pi_x$$

$$F_3(P_X; P_1, P_2) \approx \theta\left[t_1 - 2\alpha(1-\alpha)t_r\right]$$

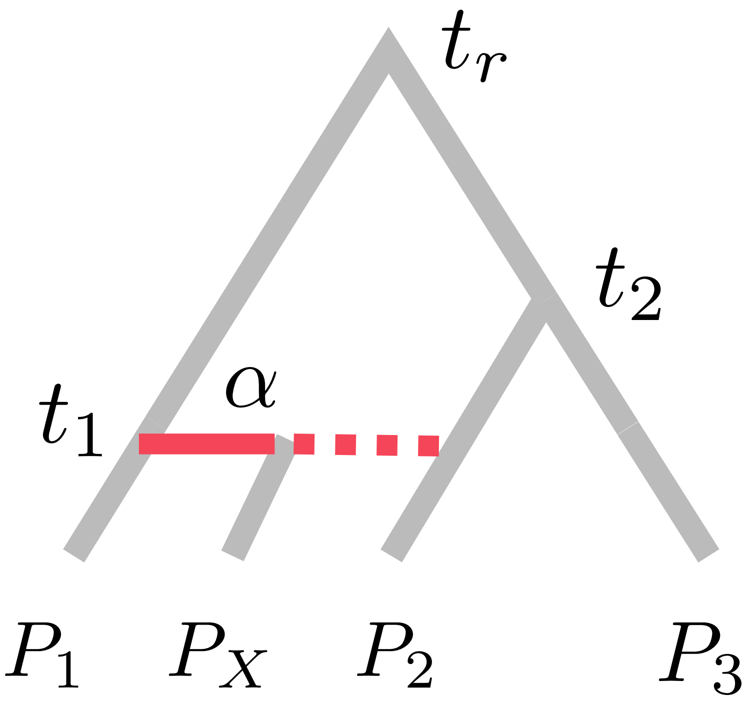


F4 in an admixture graph



F4 in an admixture graph

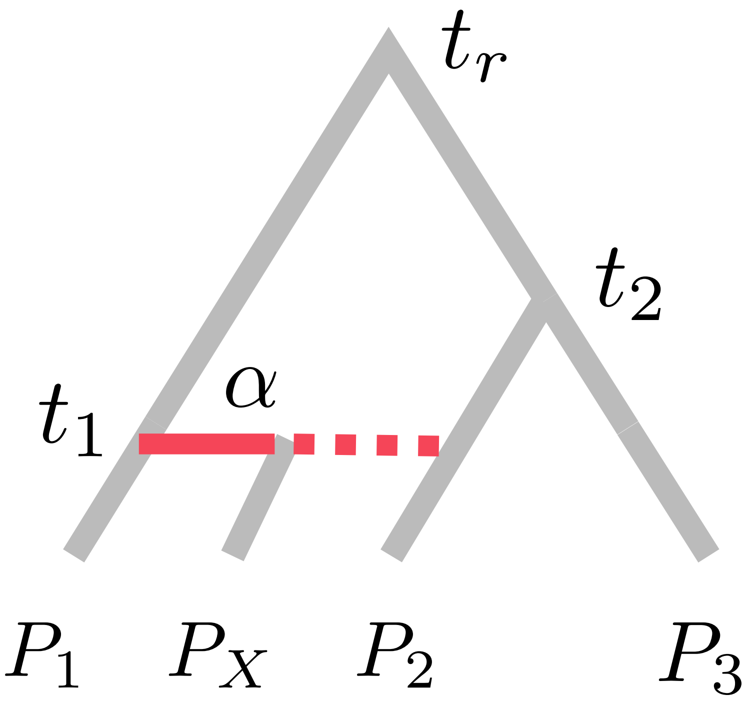
$$F_4^{(T)}(P_1, P_X; P_2, P_3) = \pi_{12} + \pi_{3x} - \pi_{13} - \pi_{2x}$$



F4 in an admixture graph

$$F_4^{(T)}(P_1, P_X; P_2, P_3) = \pi_{12} + \pi_{3x} - \pi_{13} - \pi_{2x}$$

$$F_4^{(T)}(P_1, P_X; P_2, P_3) = (1-\alpha)(t_2 - t_1) \neq 0$$

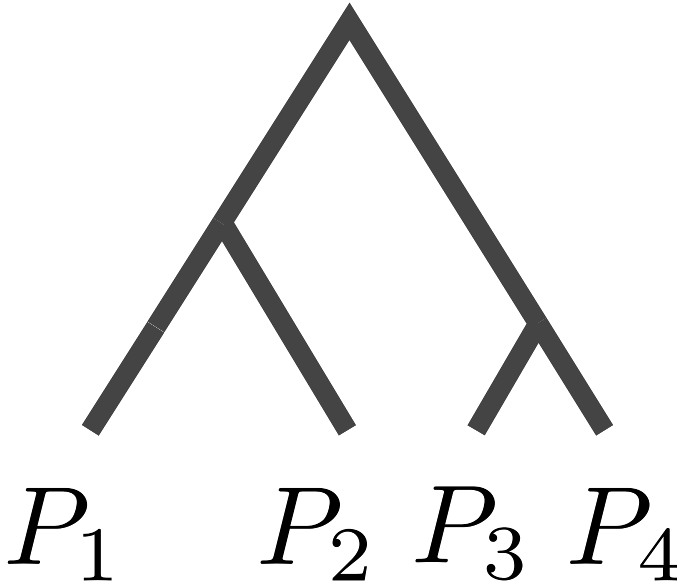


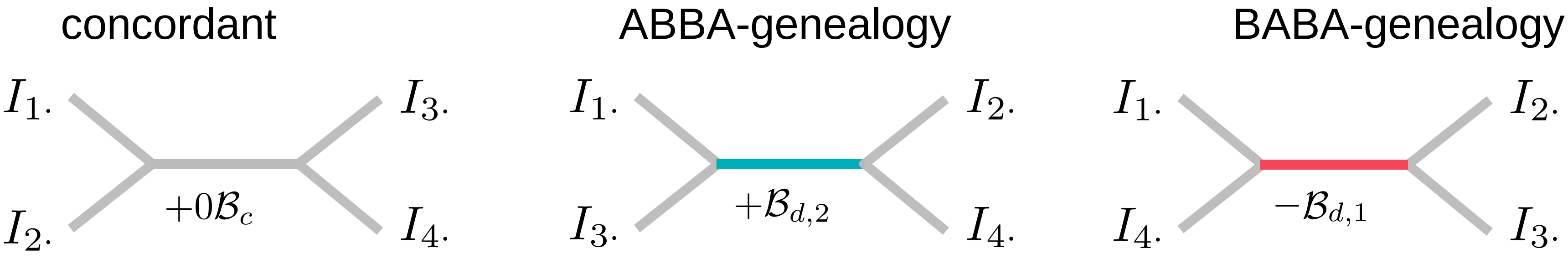
D-statistic

$$D = \frac{\mathrm{ABBA} - \mathrm{BABA}}{\mathrm{BABA} + \mathrm{ABBA}}$$

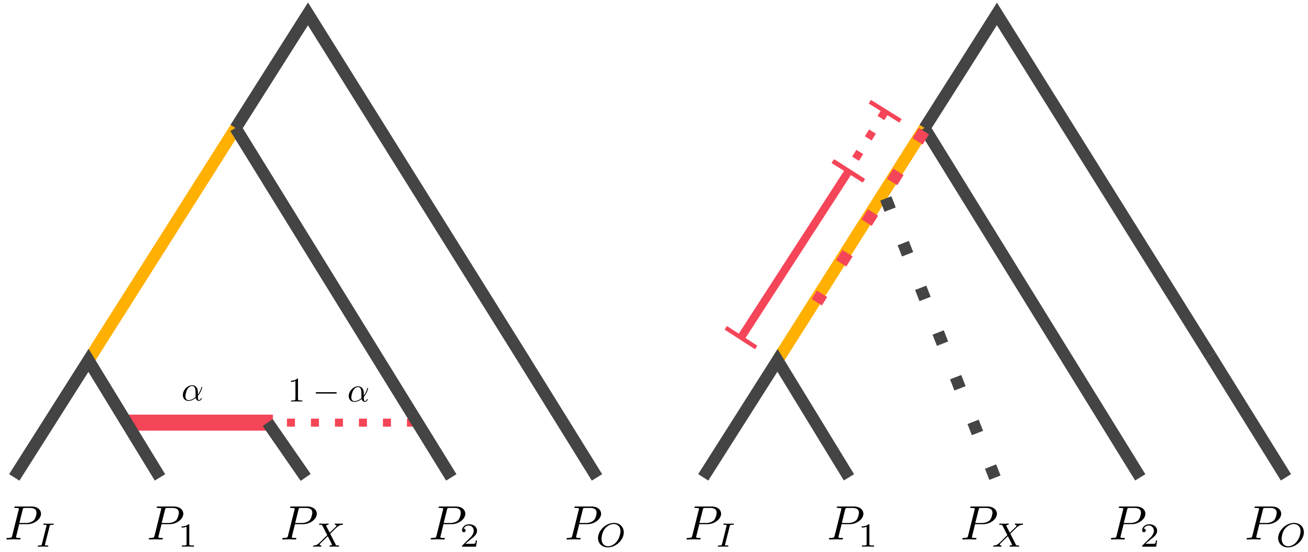
- D-statistic and F4 are closely related

$$F_4^{(T)}(P_1, P_2; P_3, P_4) = \pi_{13} + \pi_{24} - \pi_{14} - \pi_{23}$$



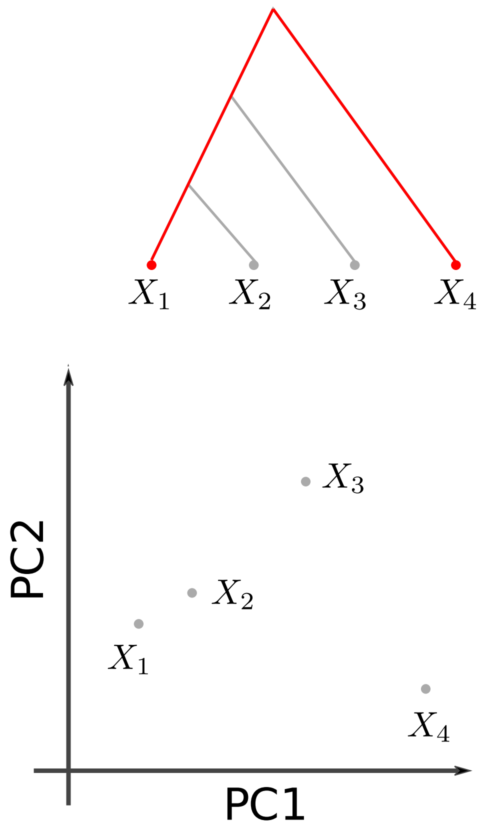


F4-ratio



$$\alpha = 1 - \frac{F_4^{(B)}(P_I, P_1; P_X, P_O)}{F_4^{(B)}(P_I, P_1; P_2, P_O)}$$

A $F_2(X_1; X_4)$



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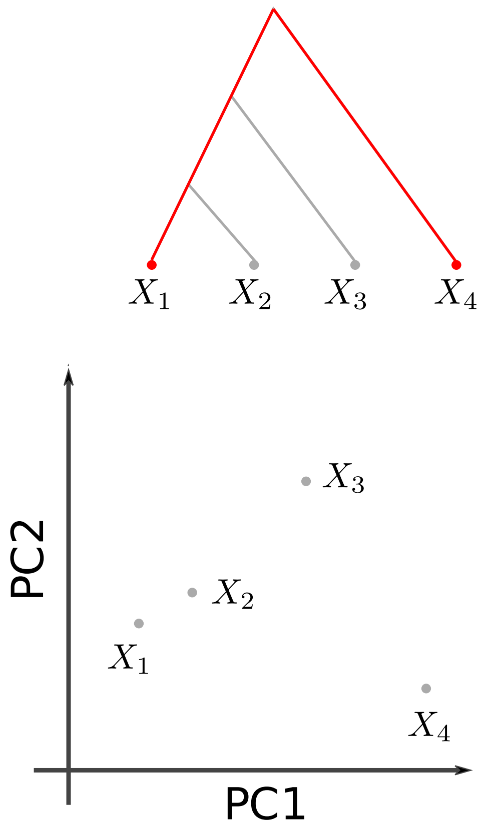

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One contribution of 15 to a theme issue 'Celebrating 50 years since Lewontin's

A geometric relationship of F_2, F_3 and F_4-statistics with principal component analysis

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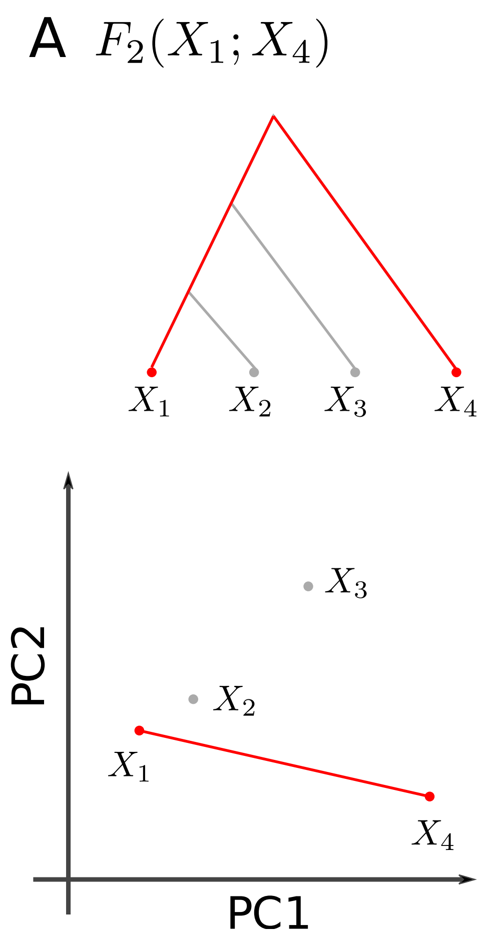
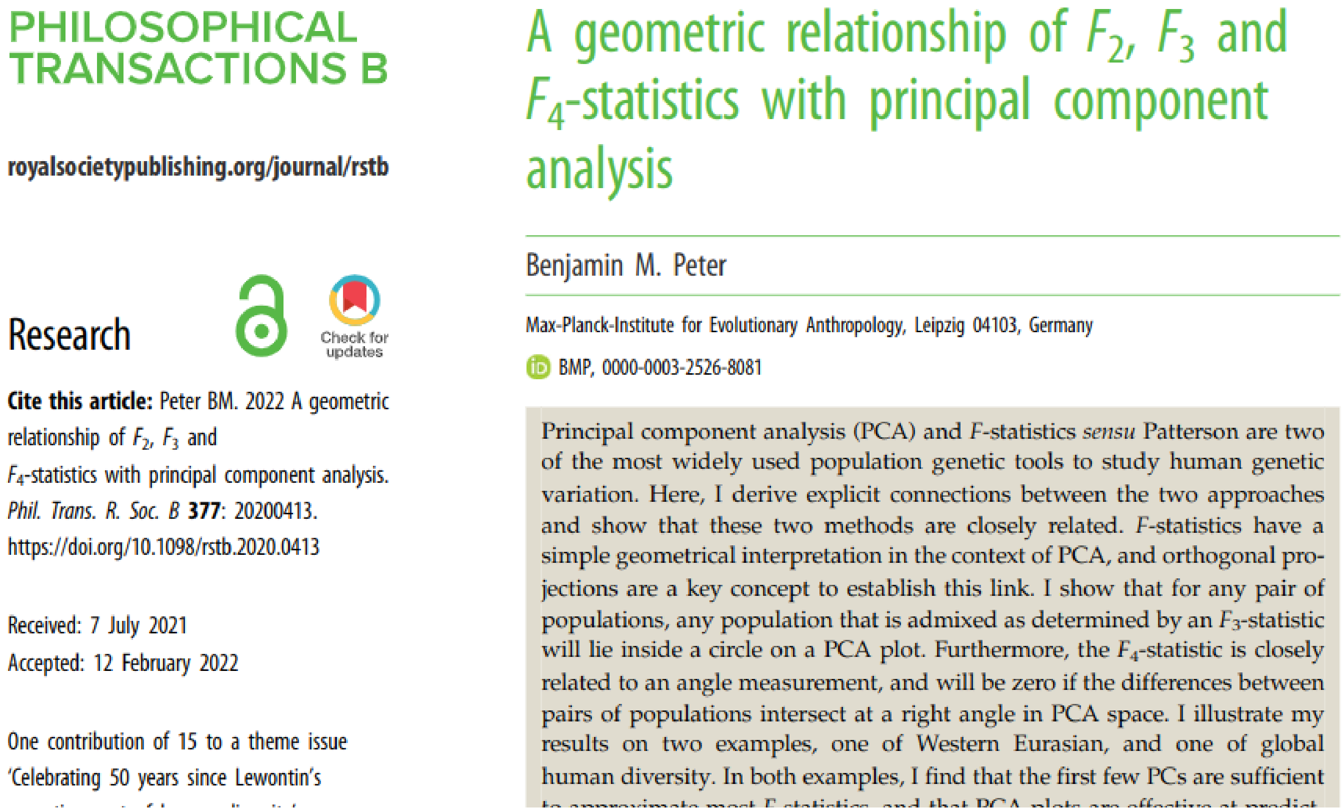
Principal component analysis (PCA) and *F*-statistics *sensu* Patterson are two of the most widely used population genetic tools to study human genetic variation. Here, I derive explicit connections between the two approaches and show that these two methods are closely related. *F*-statistics have a simple geometrical interpretation in the context of PCA, and orthogonal projections are a key concept to establish this link. I show that for any pair of populations, any population that is admixed as determined by an F_3-statistic will lie inside a circle on a PCA plot. Furthermore, the F_4-statistic is closely related to an angle measurement, and will be zero if the differences between pairs of populations intersect at a right angle in PCA space. I illustrate my results on two examples, one of Western Eurasian, and one of global human diversity. In both examples, I find that the first few PCs are sufficient

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* true if all PCs are used, optimal approximation otherwise

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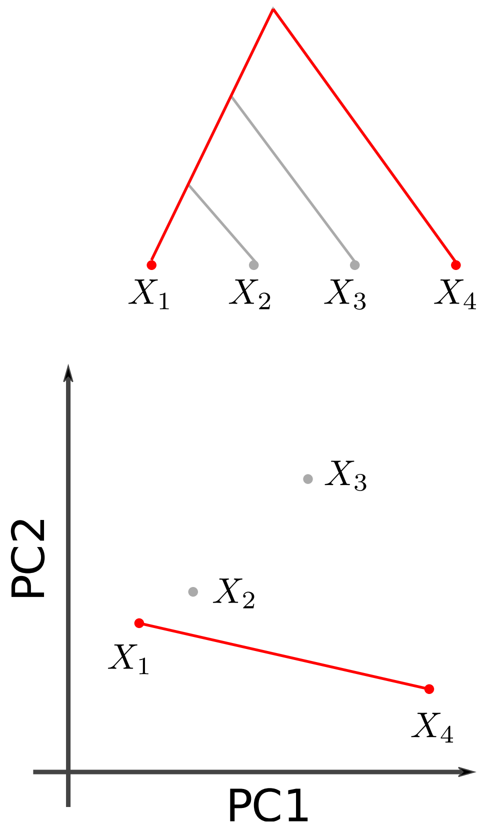

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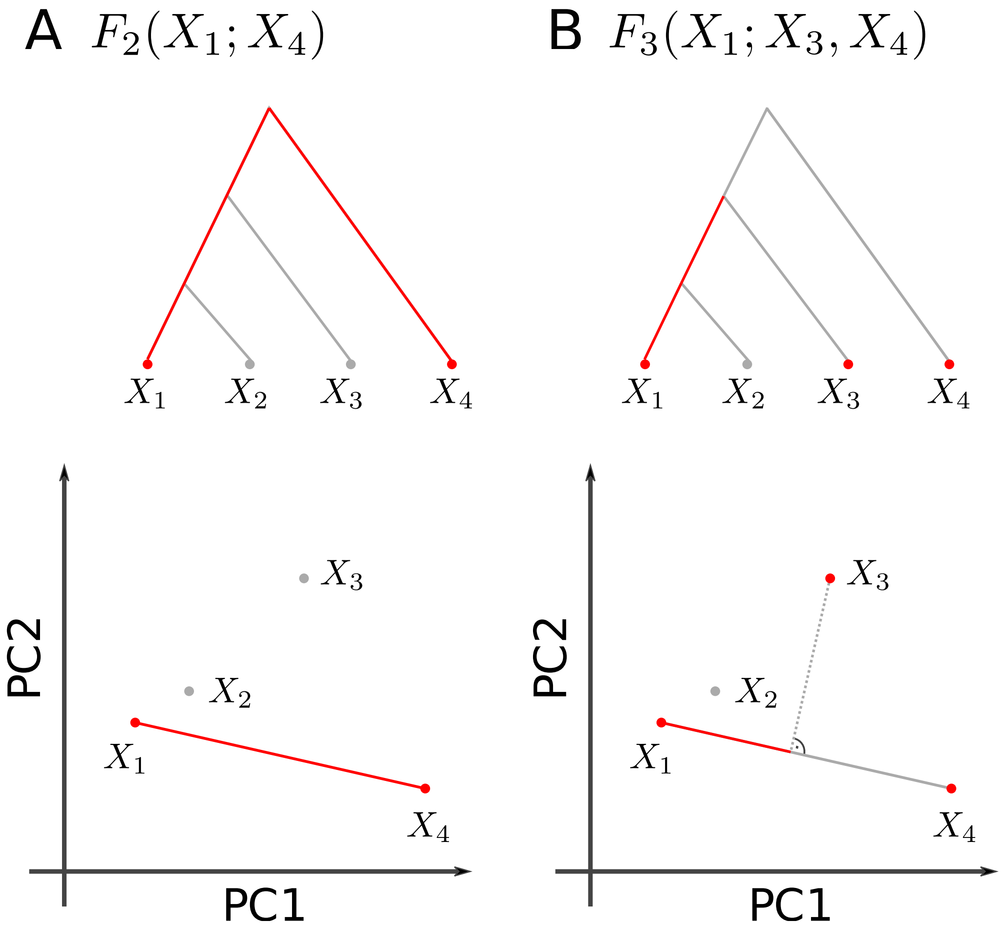

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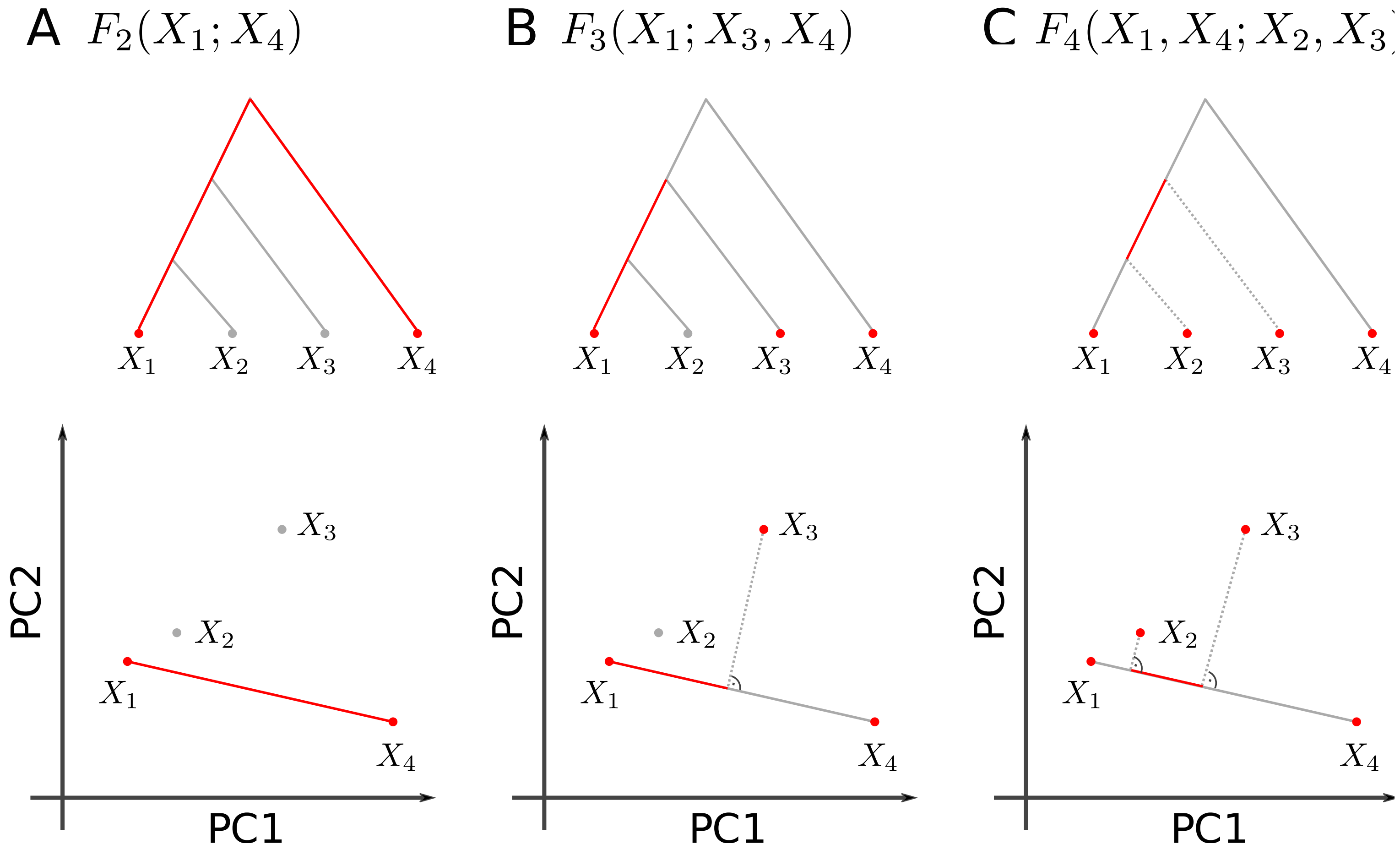

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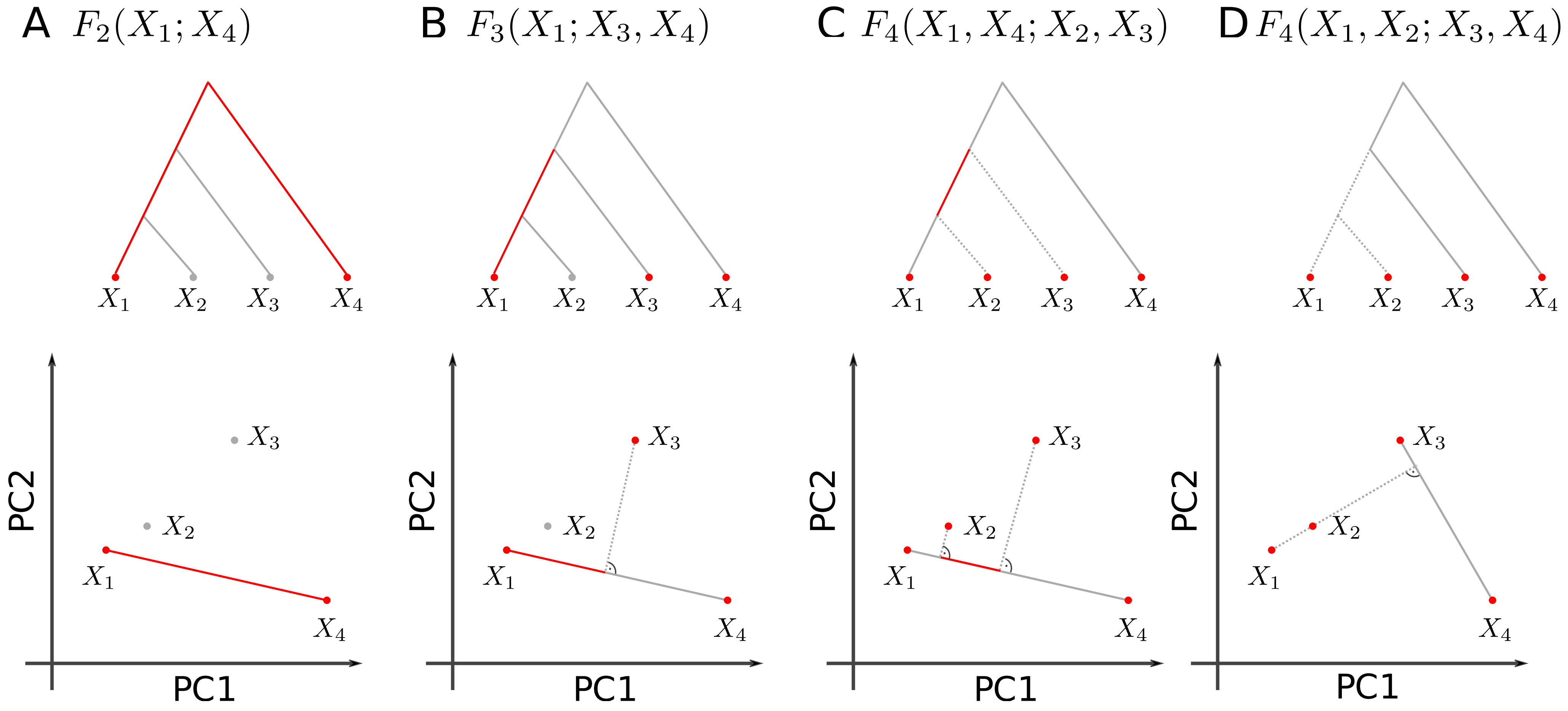

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