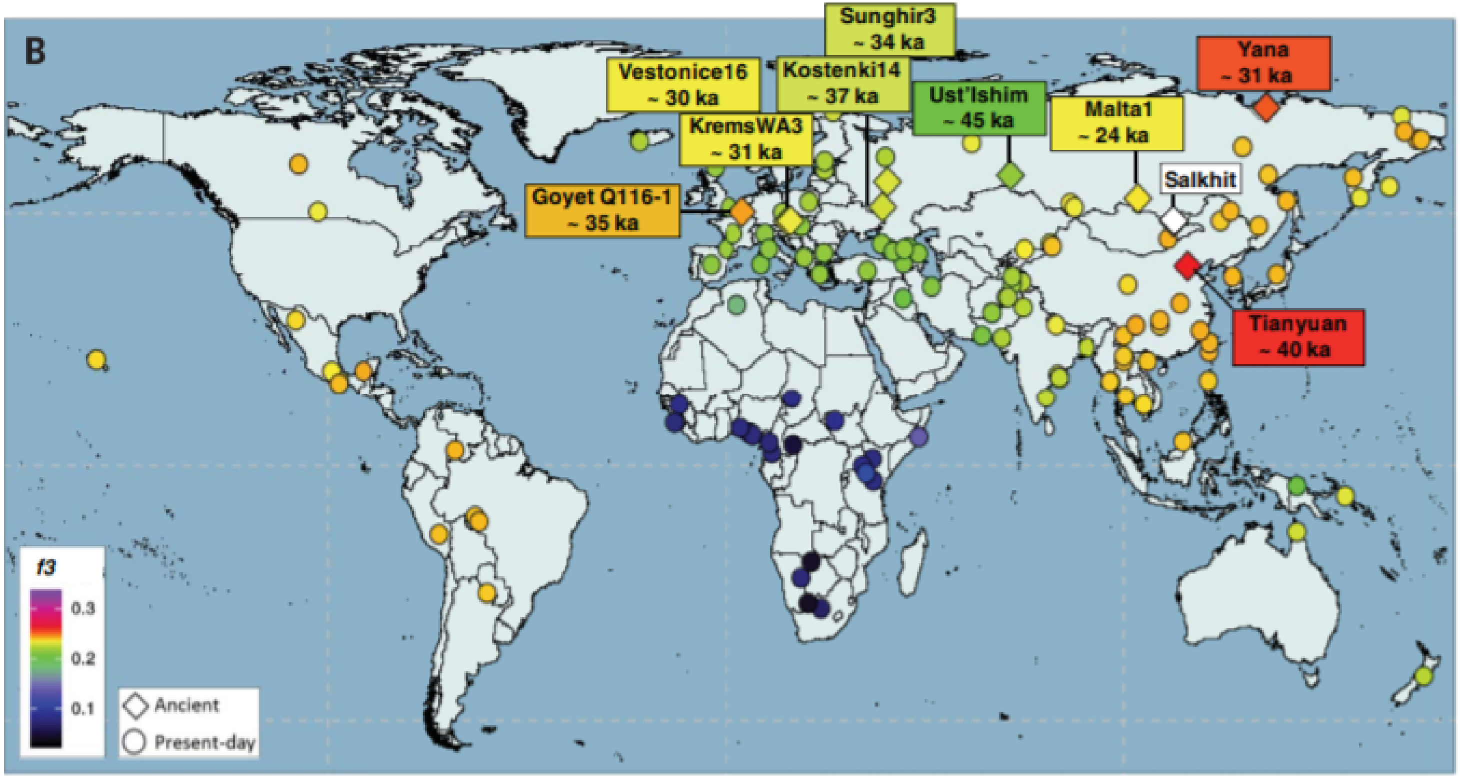
F-statistics and Population Structure

Benjamin Peter, MPI for Evolutionary Anthropology

Motivation: Ancient DNA



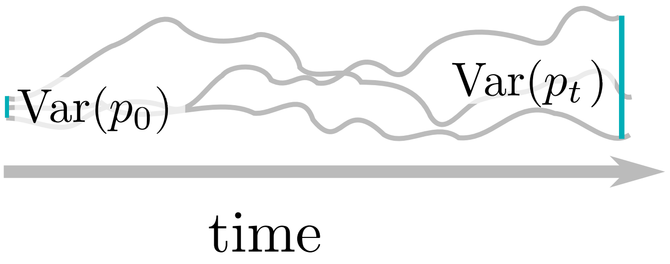
Setup

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

Measuring Genetic Drift

Measuring Genetic Drift

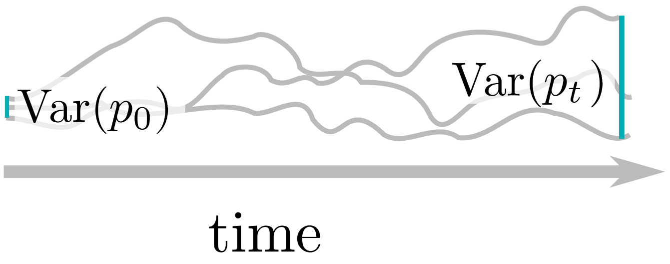
Decay of Heterozygosity

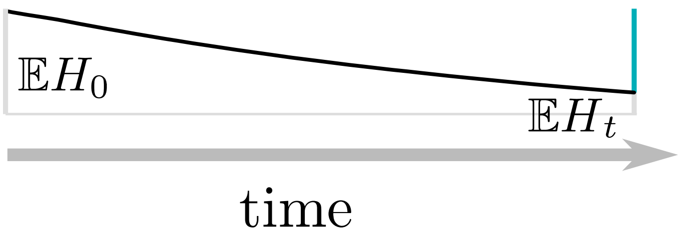


Measuring Genetic Drift

Decay of Heterozygosity

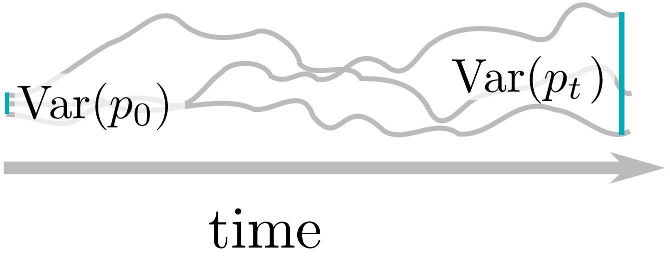
Change in Allele Frequency



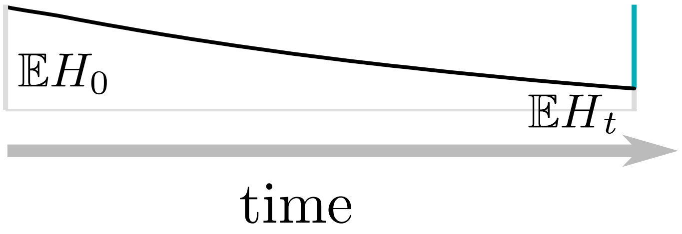


Measuring Genetic Drift

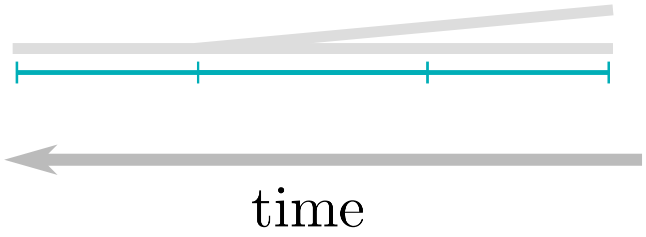
Decay of Heterozygosity



Change in Allele Frequency

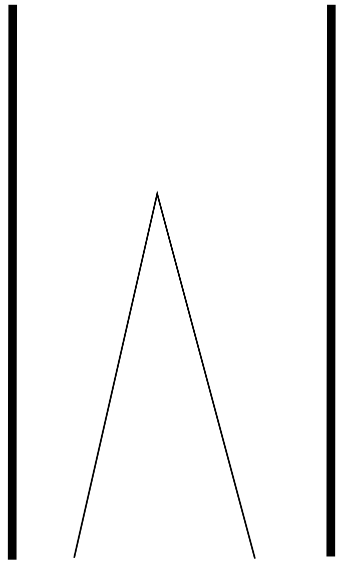


Coalescence rates



Pairwise differences

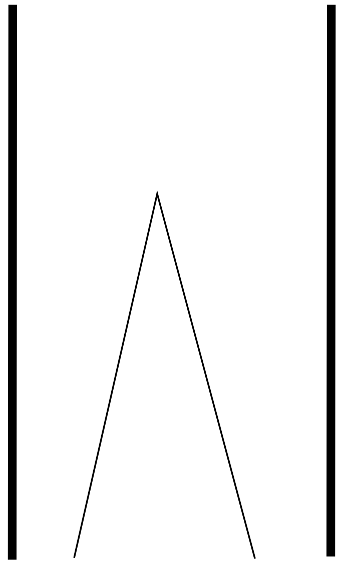
$$\mathbb{E}[\pi] = 4N\mu = \theta$$

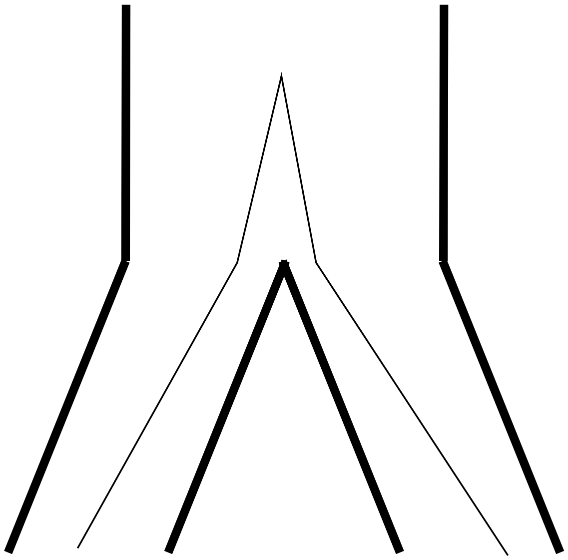


Pairwise differences

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

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



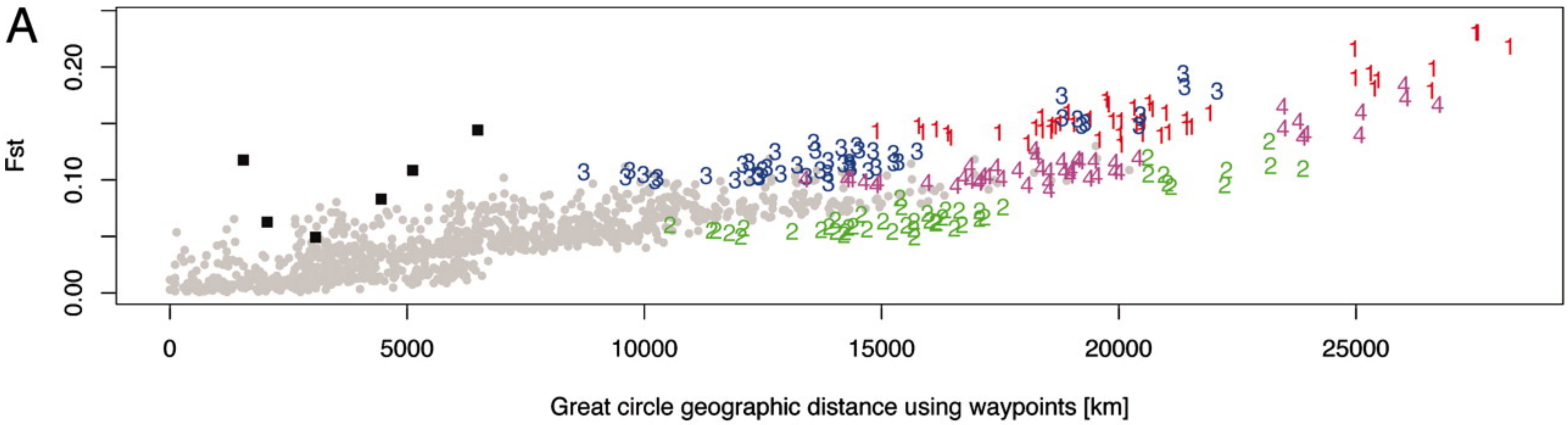


Fixation Index F_{ST}

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

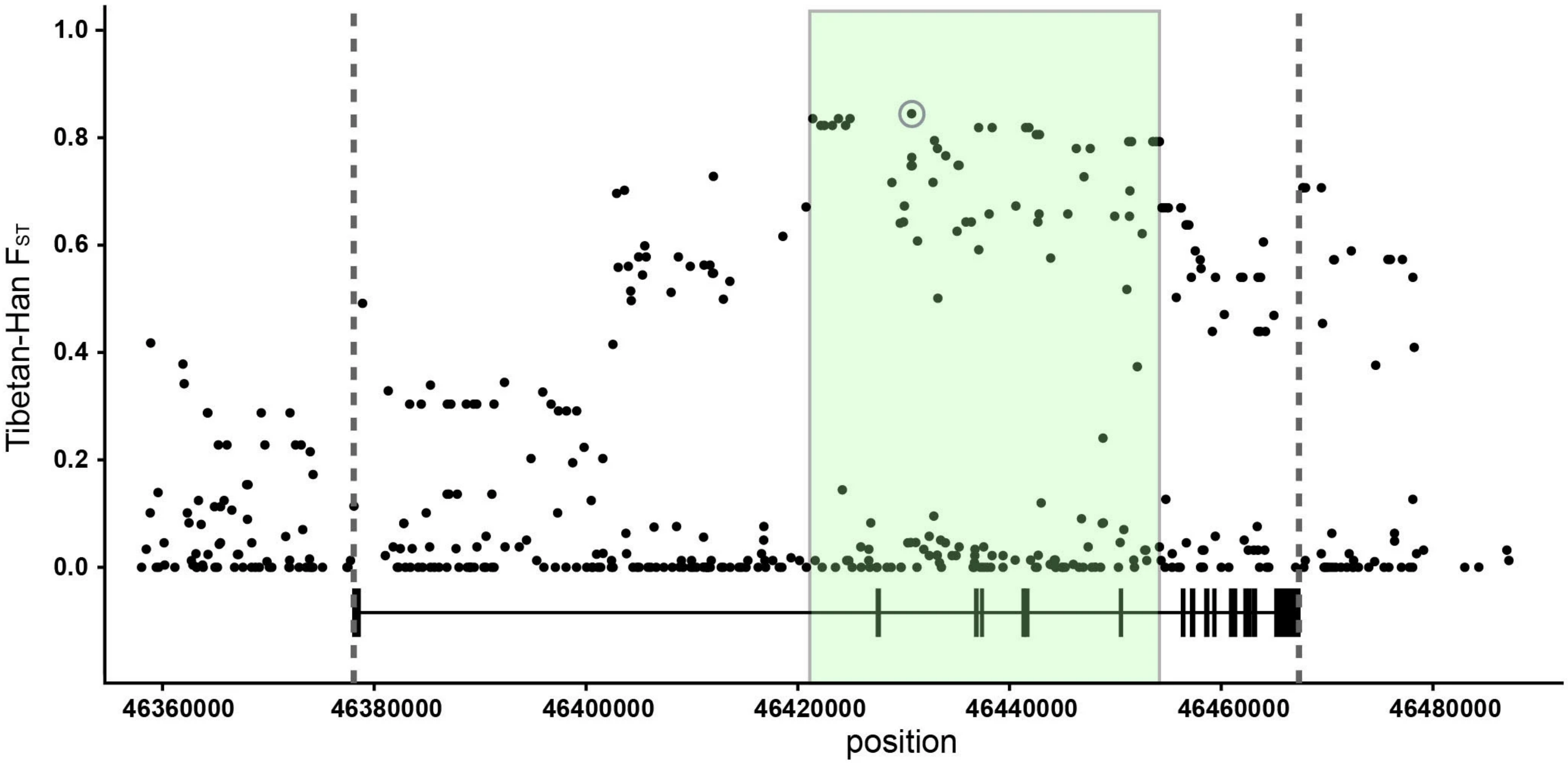
- F_{ST} is a correlation coefficient
- Between 0 and 1
- Hierarchical partitioning (AMOVA)
- Many estimators exist
  - Hudson (1991)
  - Weir & Cockerham (1984)

Fixation Index F_{ST}



Ramachandran et al. 2005

F_{ST} Outliers



Huerta-Sanchez et al. 2014

F_2-statistic

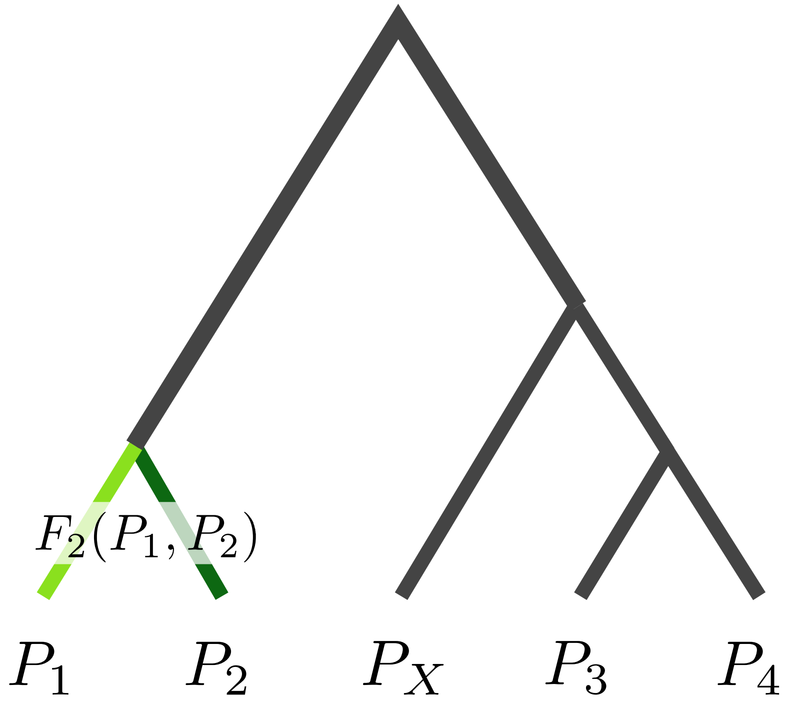
$$F_{ST}(P_1, P_2) = \frac{\pi_{12} - \frac{\pi_1 + \pi_2}{2}}{\pi_{12}}$$

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

$$\begin{aligned} F_2(P_1, P_2) &= 2\pi_{12} - \pi_1 - \pi_2 \\ &= \sum_l (p_{1l} - p_{2l})^2 \end{aligned}$$

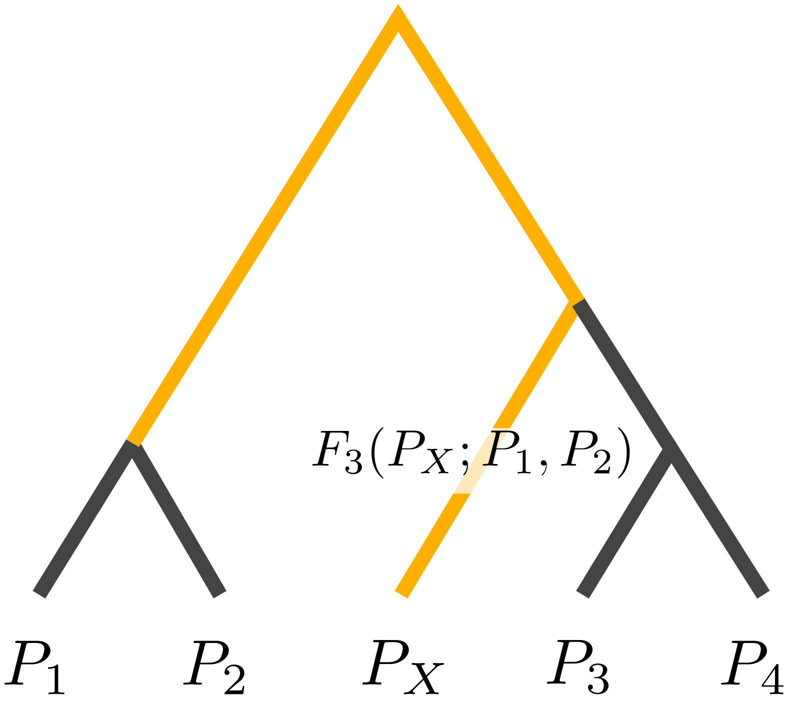
- F_2 is a covariance
- Bigger than 0
- Tree-additive
- Testing for treeness

Tree-additive



F_3-statistic

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



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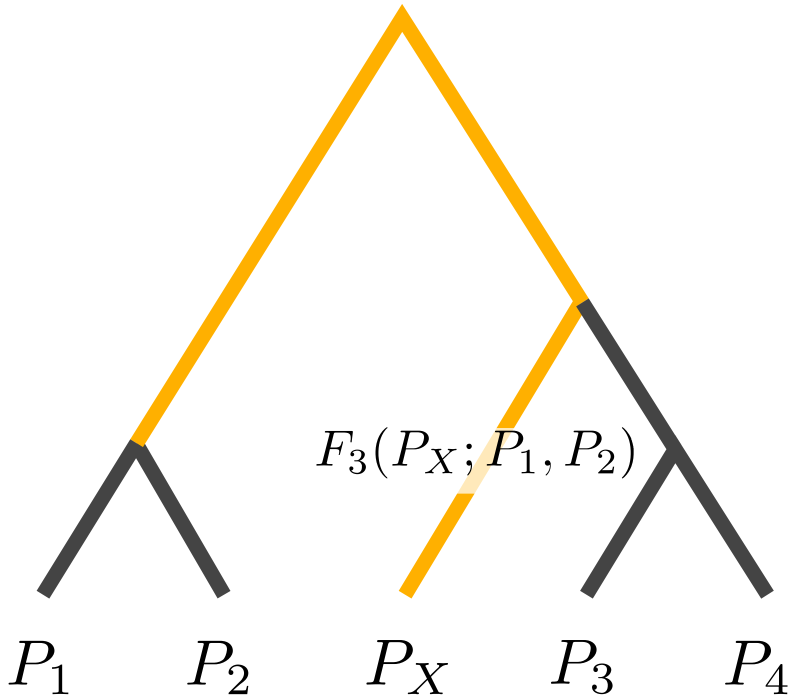
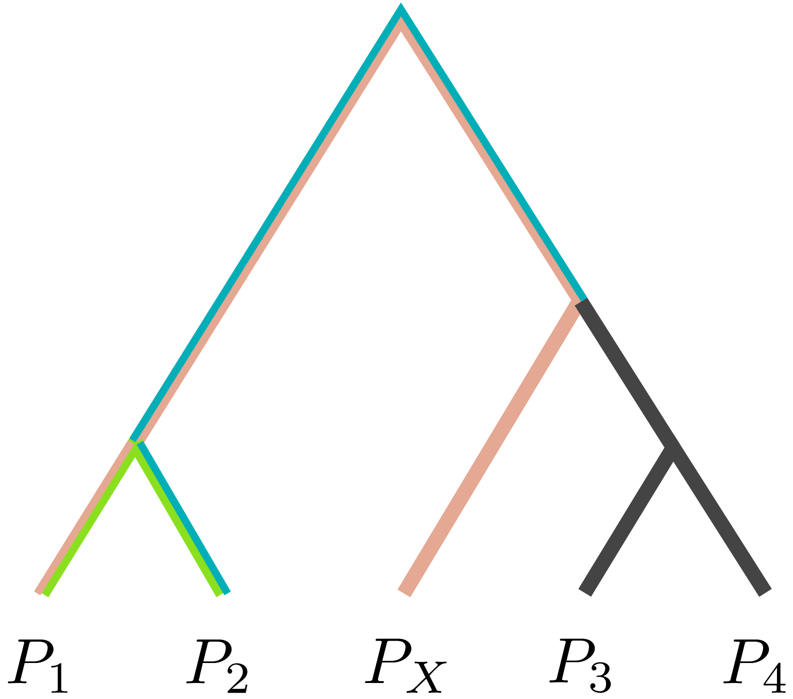
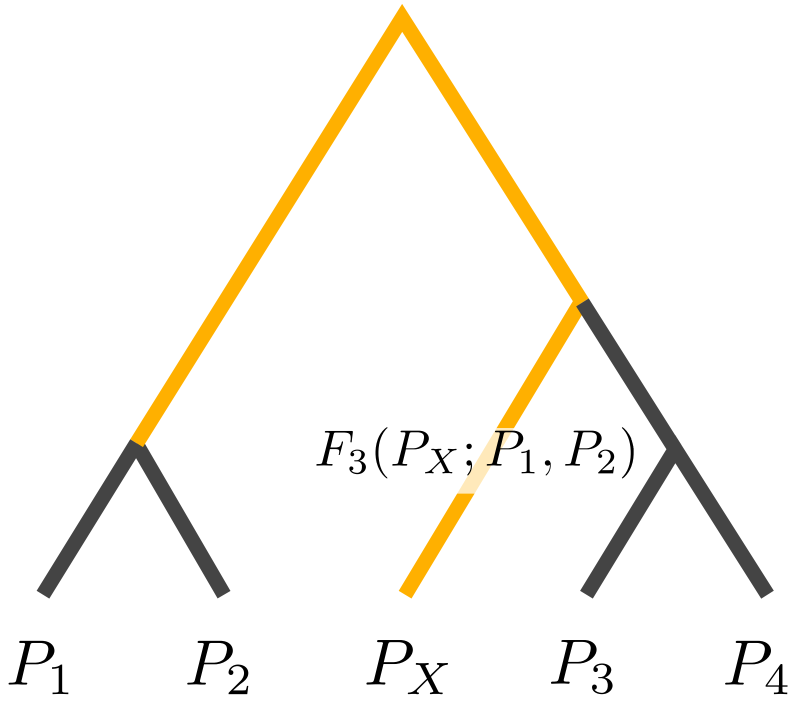
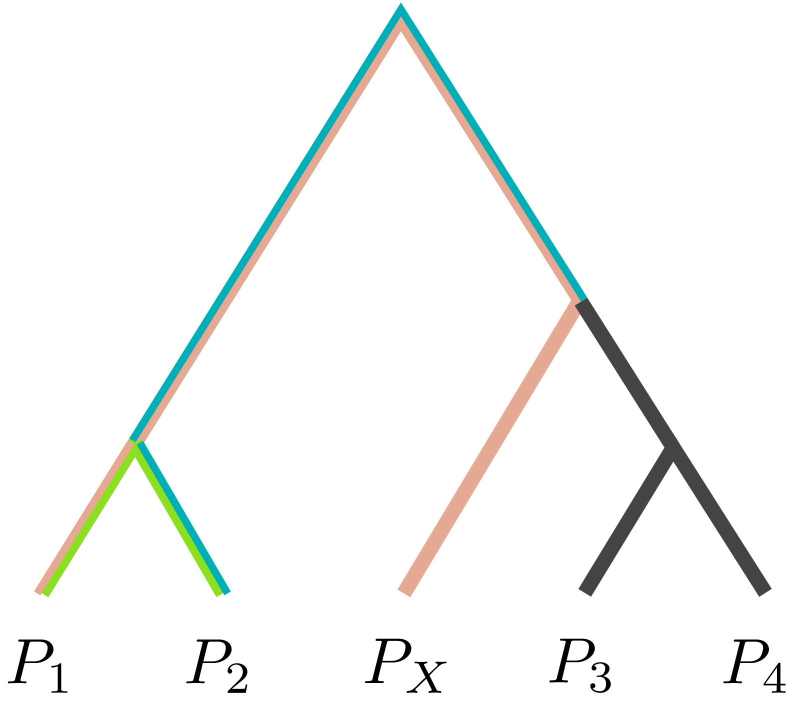




F_3-statistic

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





F_3 -statistic equations

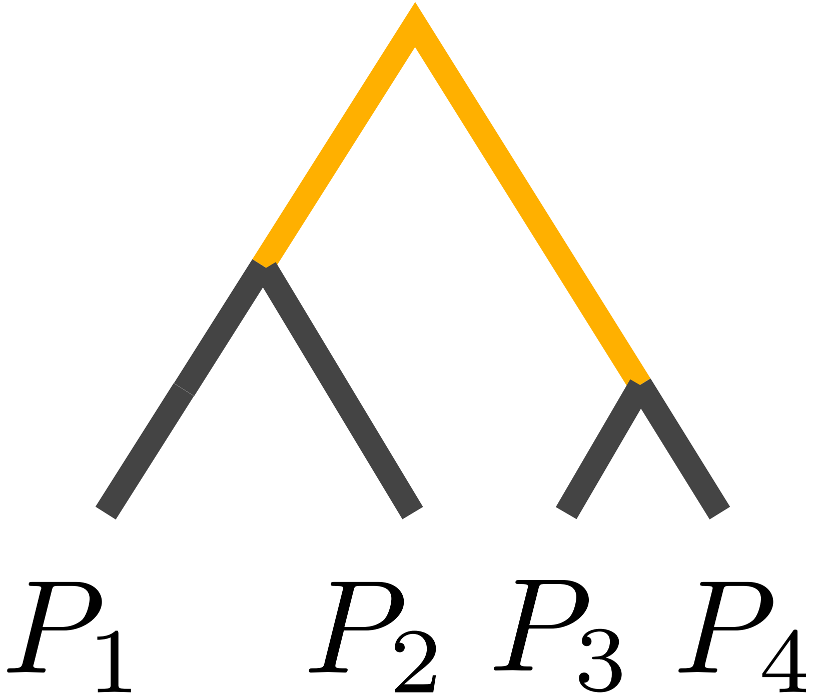
$$F_3(P_X; P_1, P_2) = \frac{1}{2}\left(F_2(P_X, P_1) + F_2(P_X, P_2) - F_2(P_1, P_2)\right)$$

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

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

(Branch)-F_4-statistic

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

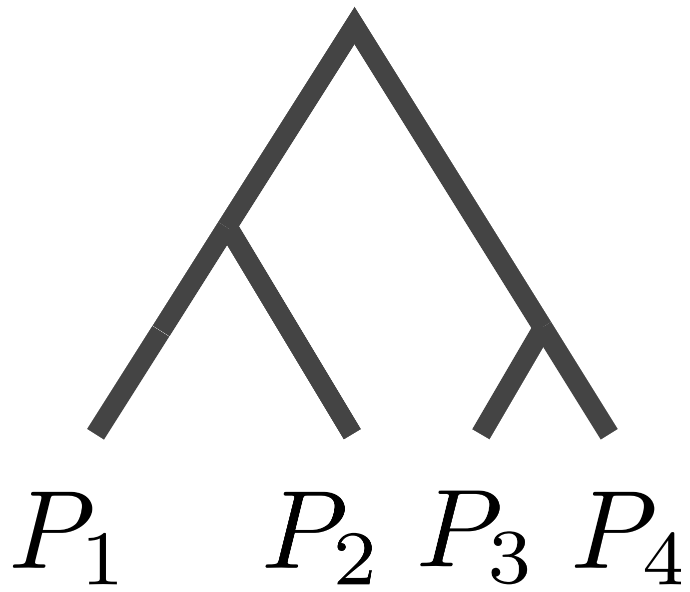


What if we reorder the arguments?

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

(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

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

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

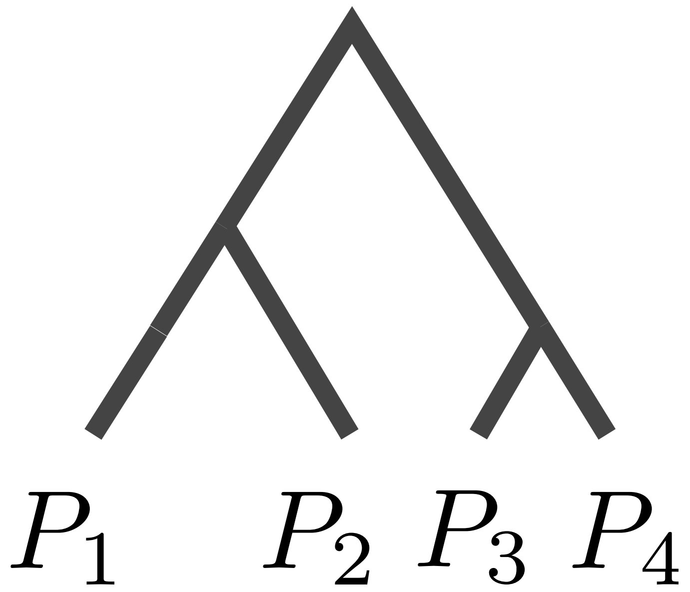
$$F_4^{(T)}(P_1, P_2; P_3, P_4) = \pi_{13} + \pi_{24} - \pi_{14} - \pi_{23}$$

Testing Treeness

If data is generated from a tree:

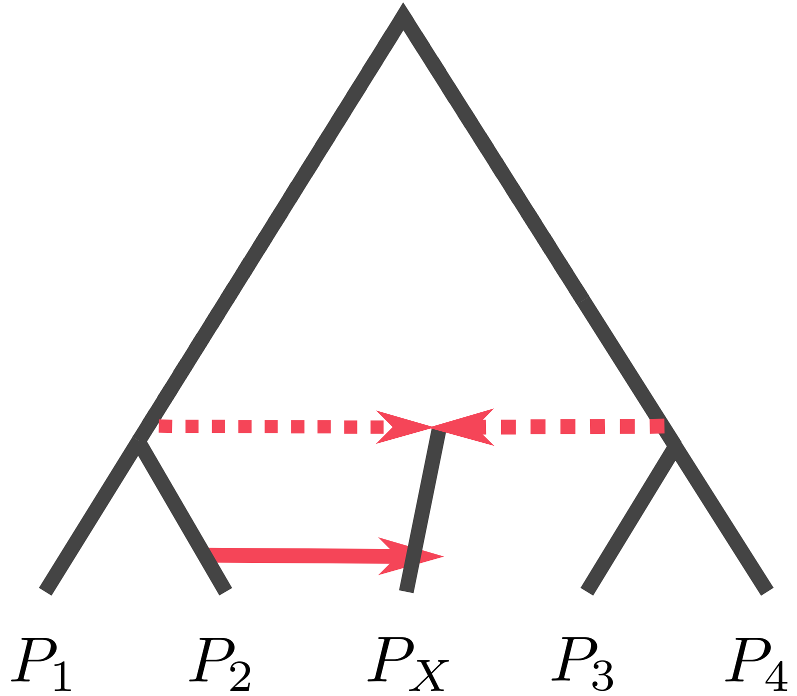
$$F_3(P_3; P_1; P_2) \geq 0$$

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



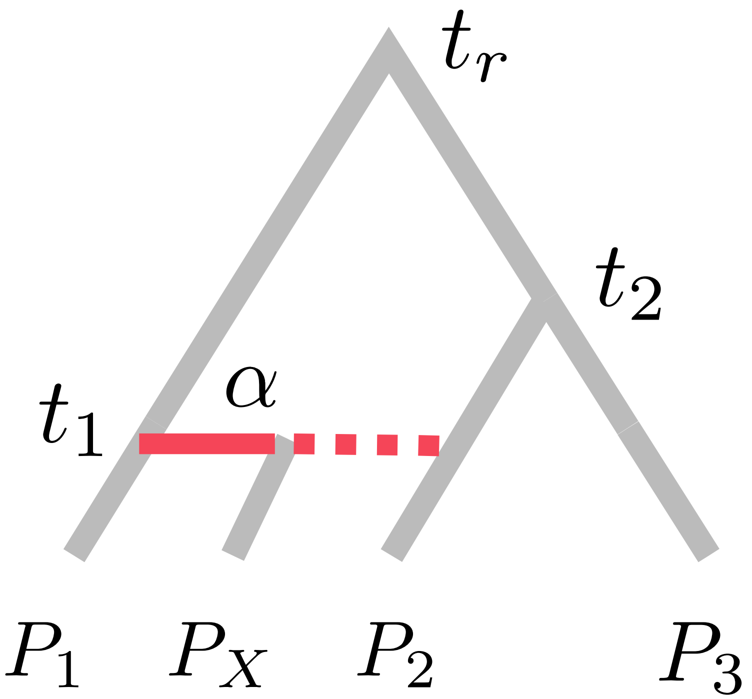
Buneman 1974

Admixture Graphs



F3 in an admixture graph

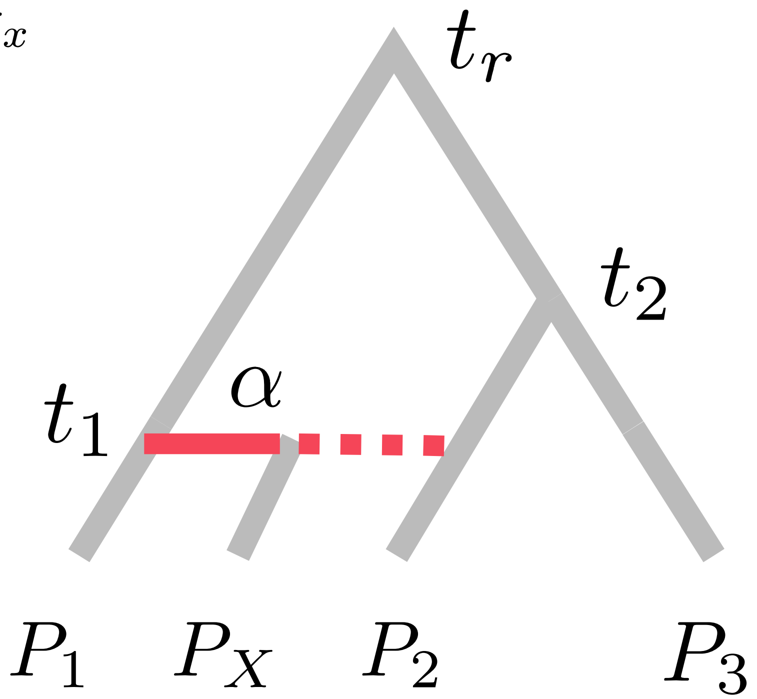
$$F_3(P_X; P_1, P_2) \approx \theta\left[t_1 - 2\alpha(1-\alpha)t_r\right]$$



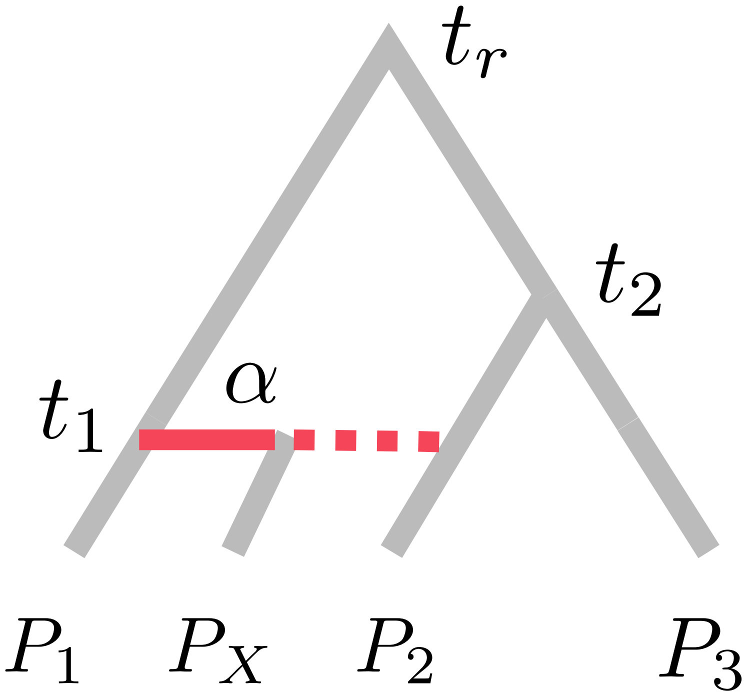
F3 in an admixture graph

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

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

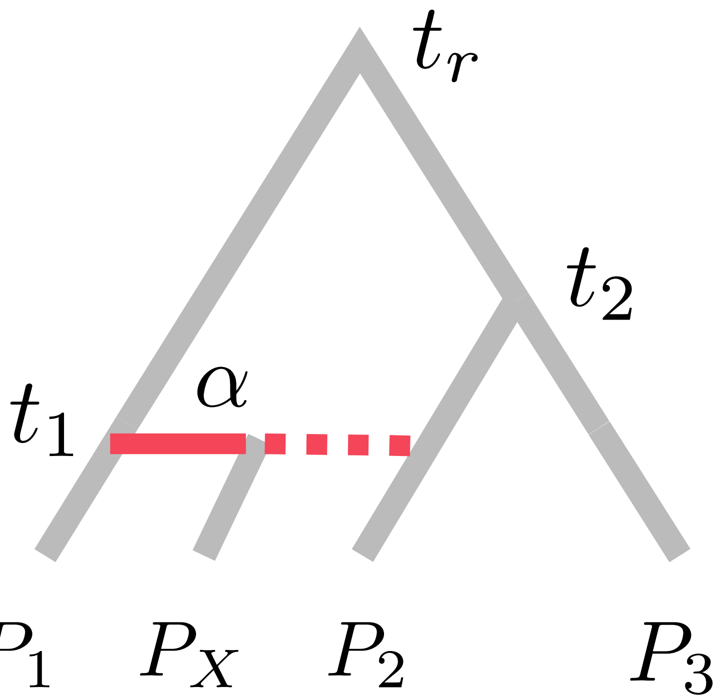


F4 in an admixture graph



F4 in an admixture graph

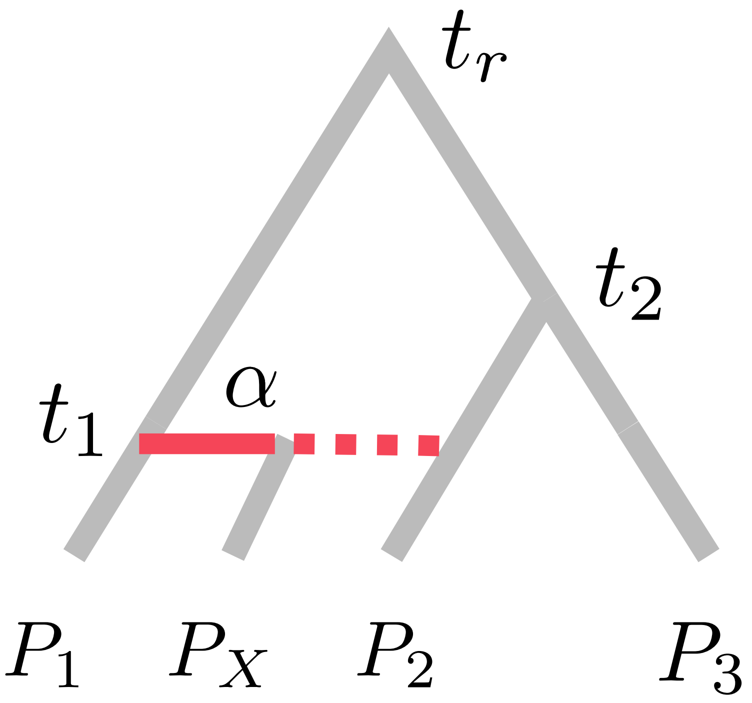
$$F_4^{(T)}(P_1, P_X; P_2, P_3) = \pi_{12} + \pi_{3x} - \pi_{13} - \pi_{2x}$$



F4 in an admixture graph

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

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

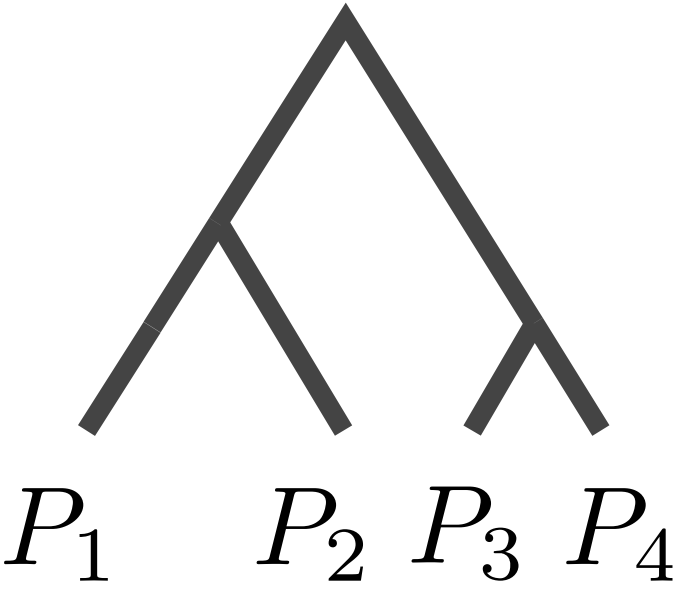


D-statistic

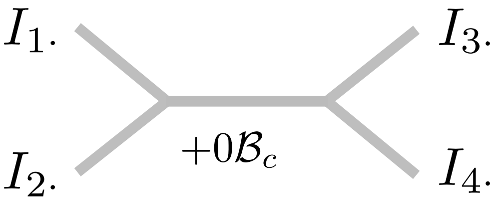
$$D = \frac{\mathrm{BABA} - \mathrm{ABBA}}{\mathrm{BABA} + \mathrm{ABBA}}$$

- D-statistic and F4 are closely related

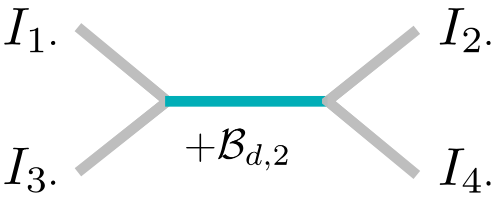
$$F_4^{(T)}(P_1, P_2; P_3, P_4) = \pi_{13} + \pi_{24} - \pi_{14} - \pi_{23}$$



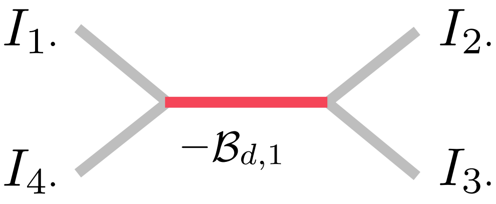
concordant



BABA-genealogy



ABBA-genealogy



F4-ratio

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