

Detecting and estimating (Neanderthal) ancestry using the *admixr* R package

A little bit of theory & practical demo/tutorial in R

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Demo #1

1. EIGENSTRAT file format
2. *admixr* R package

Detecting admixture
(i.e. testing "treeness")
using f -statistics

2010: Neanderthal “draft” genome

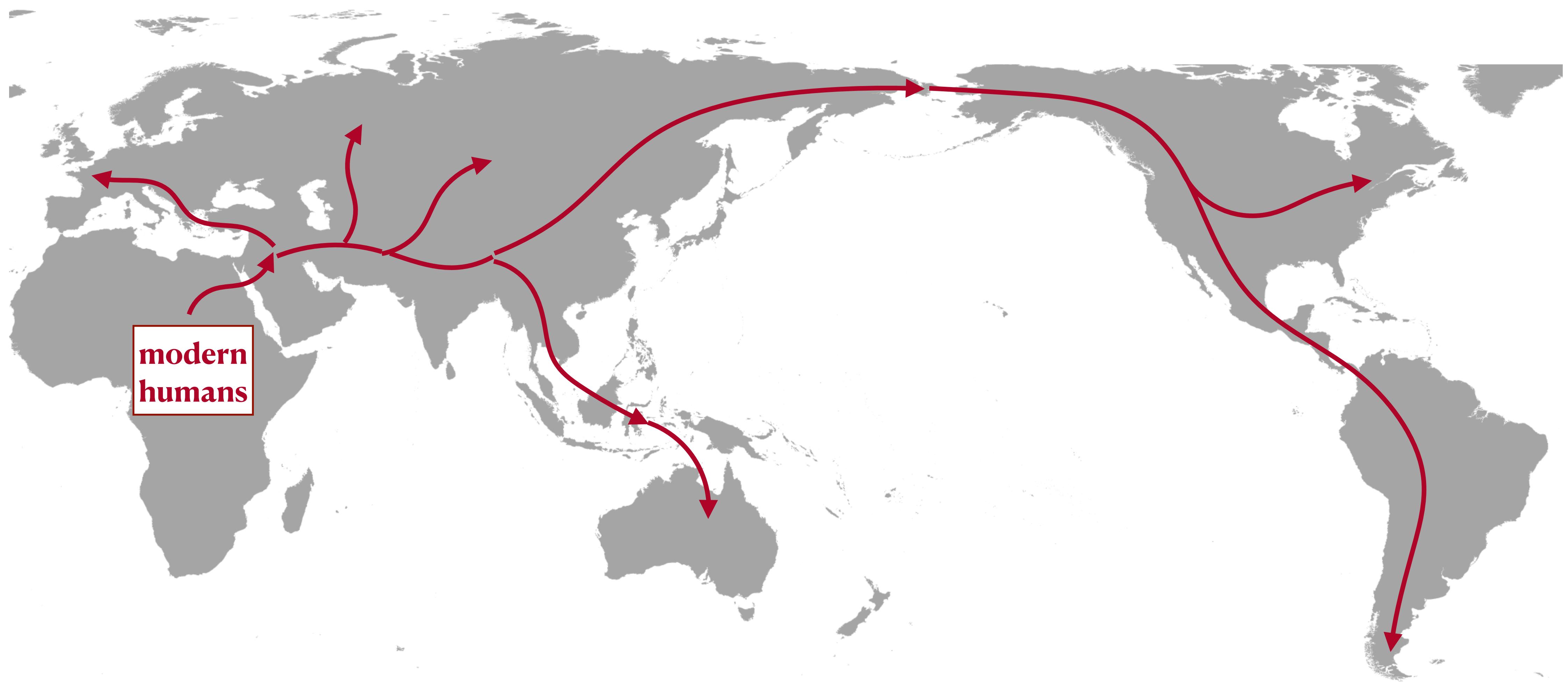


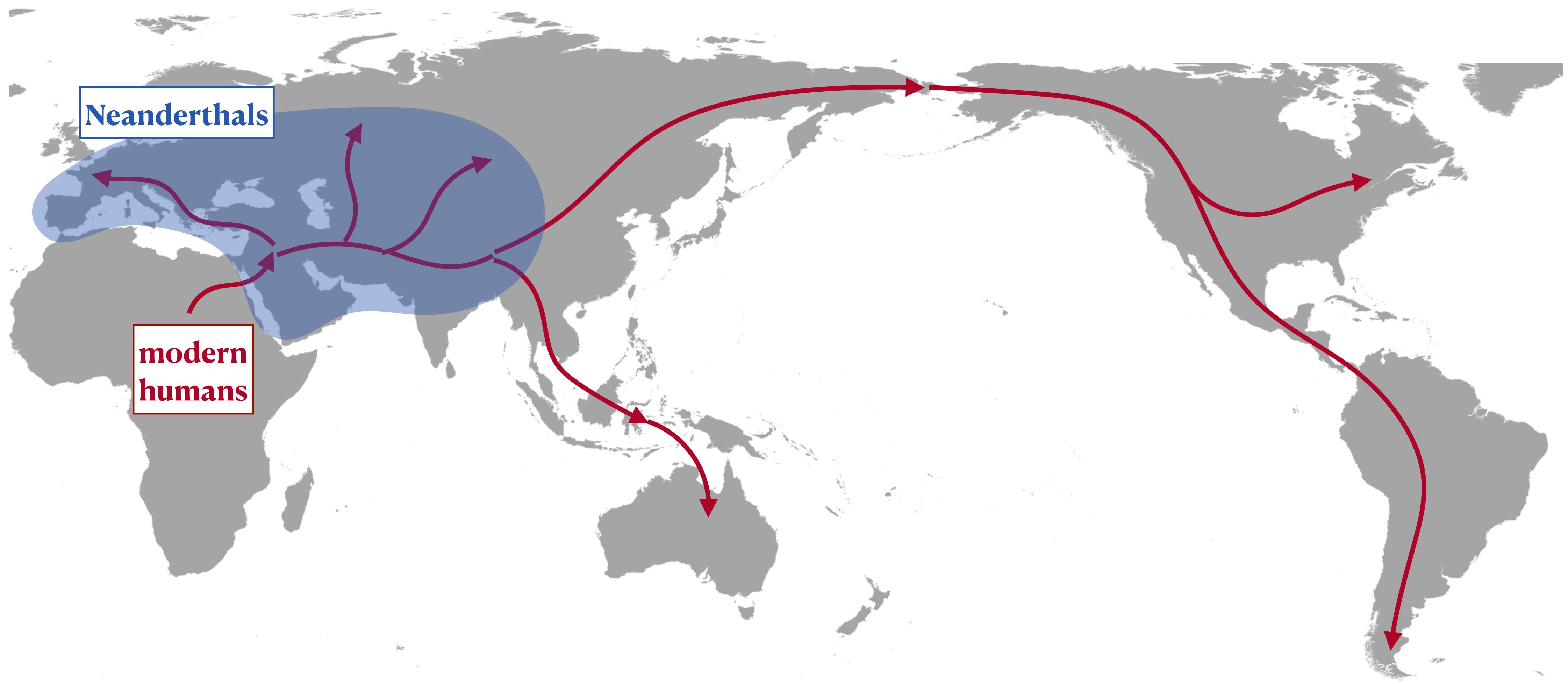
- ~1.3X coverage of the whole genome (later genomes at 30-40X)

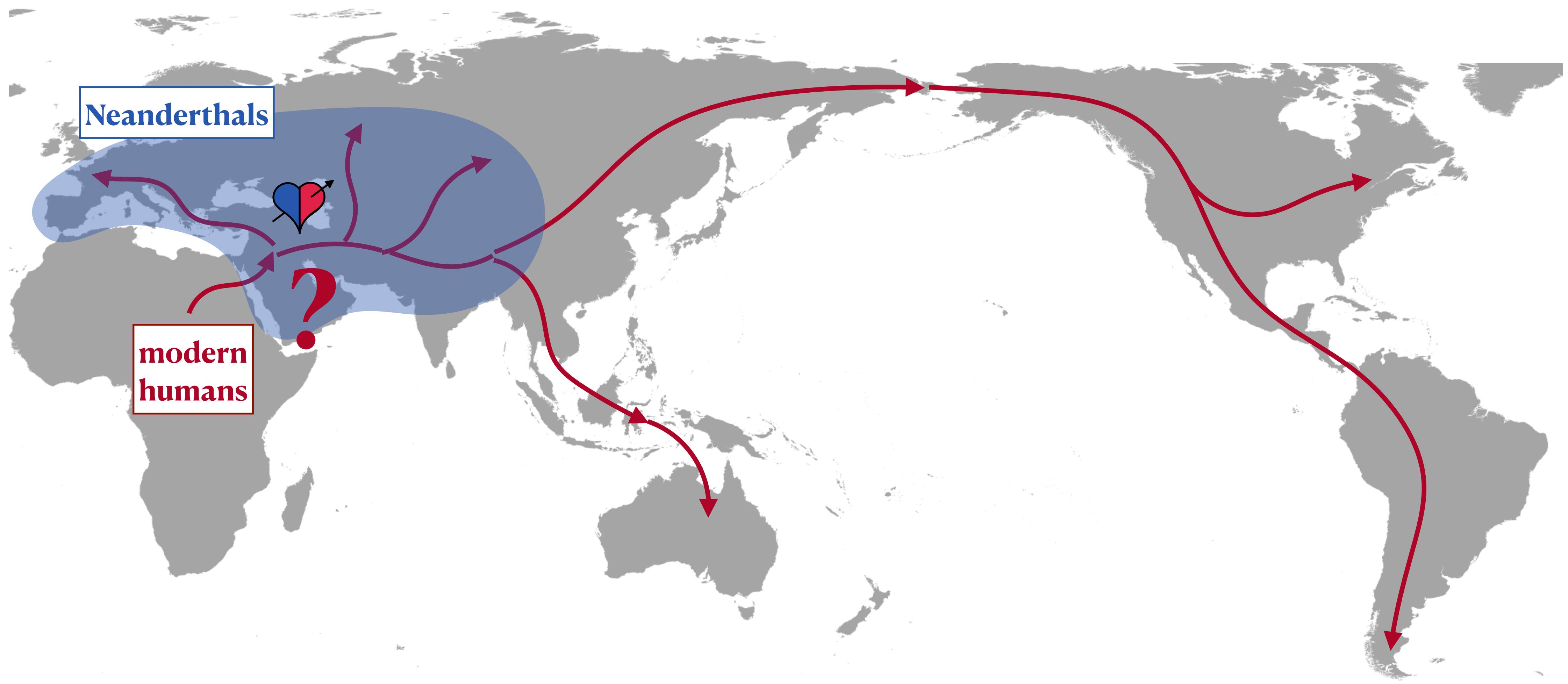




**modern
humans**







Detecting admixture

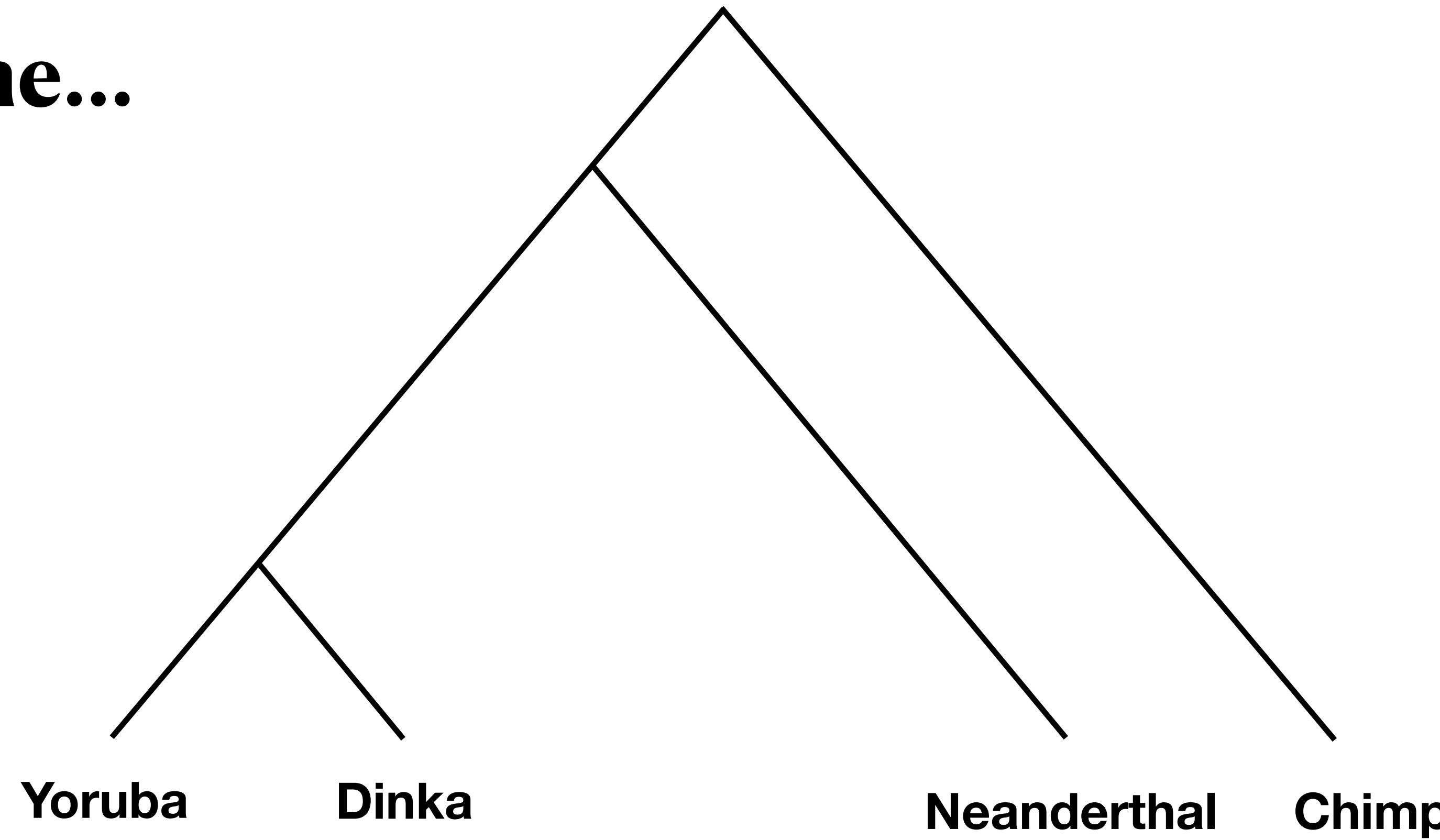
Four-population test — f_4 statistic (*D* statistic)

Detecting admixture

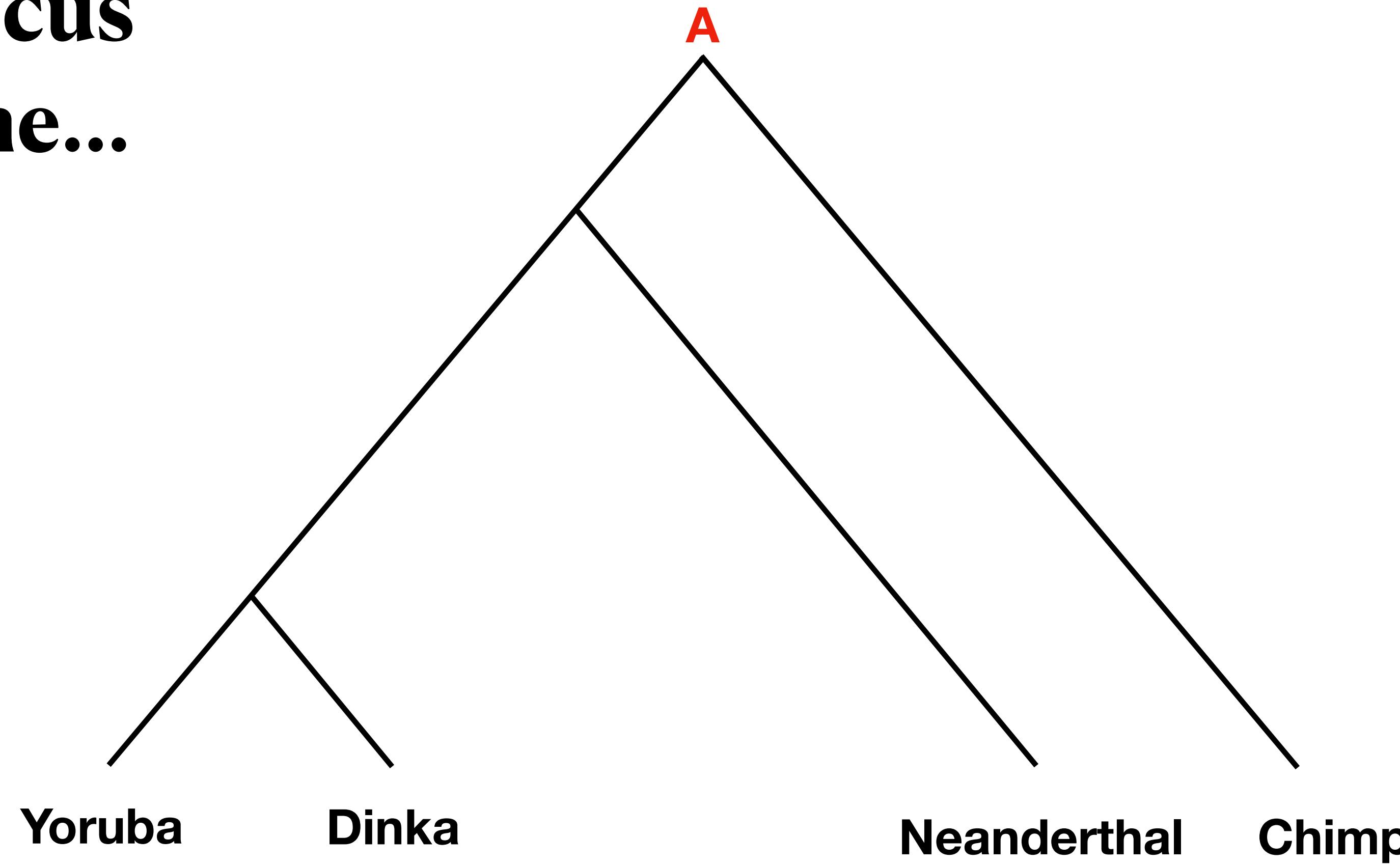
Four-population test – f_4 statistic (*D statistic*)

Compares the counts of BABA vs ABBA sites
between four samples (genomes)

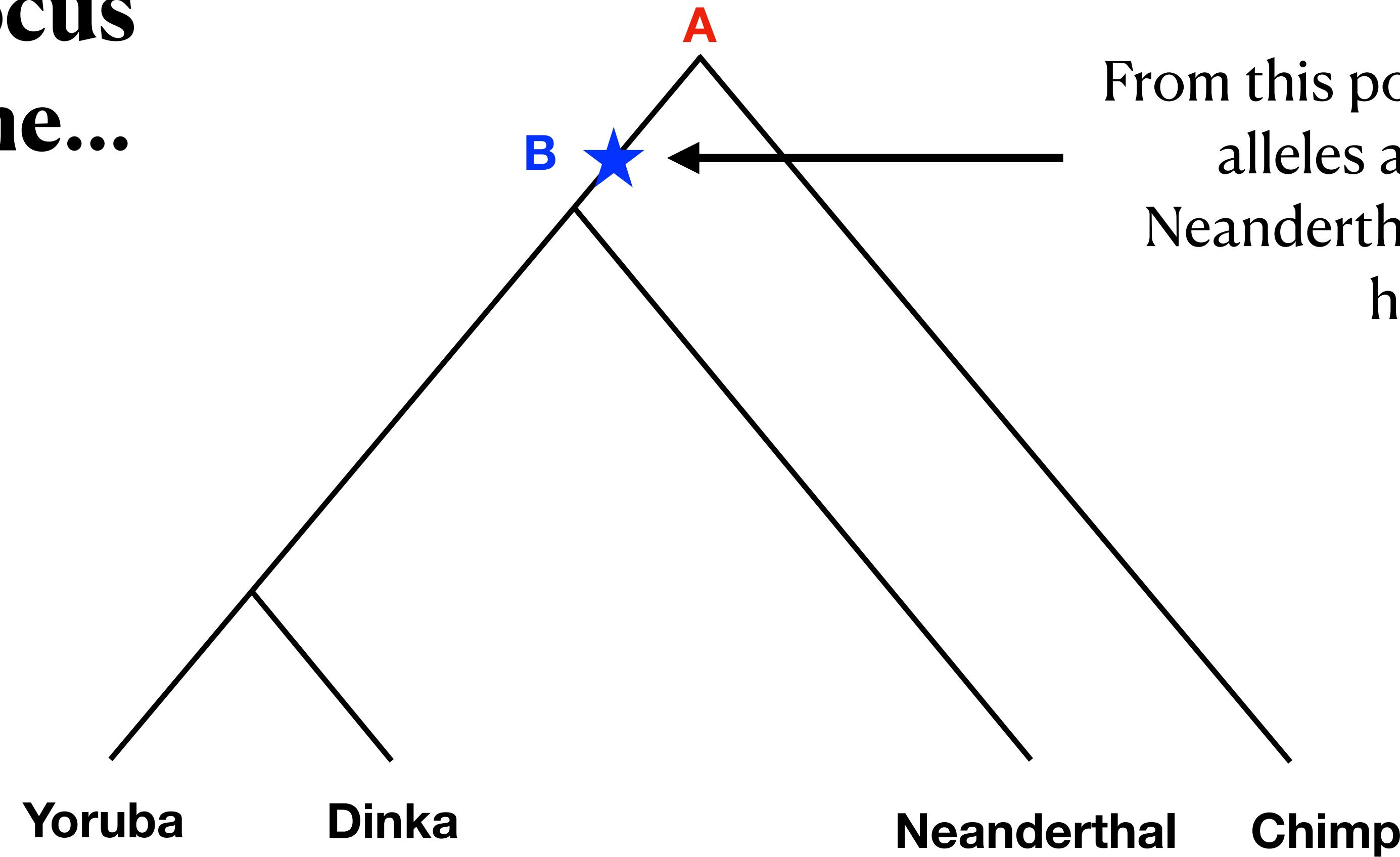
**At a single locus
in the genome...**



**At a single locus
in the genome...**

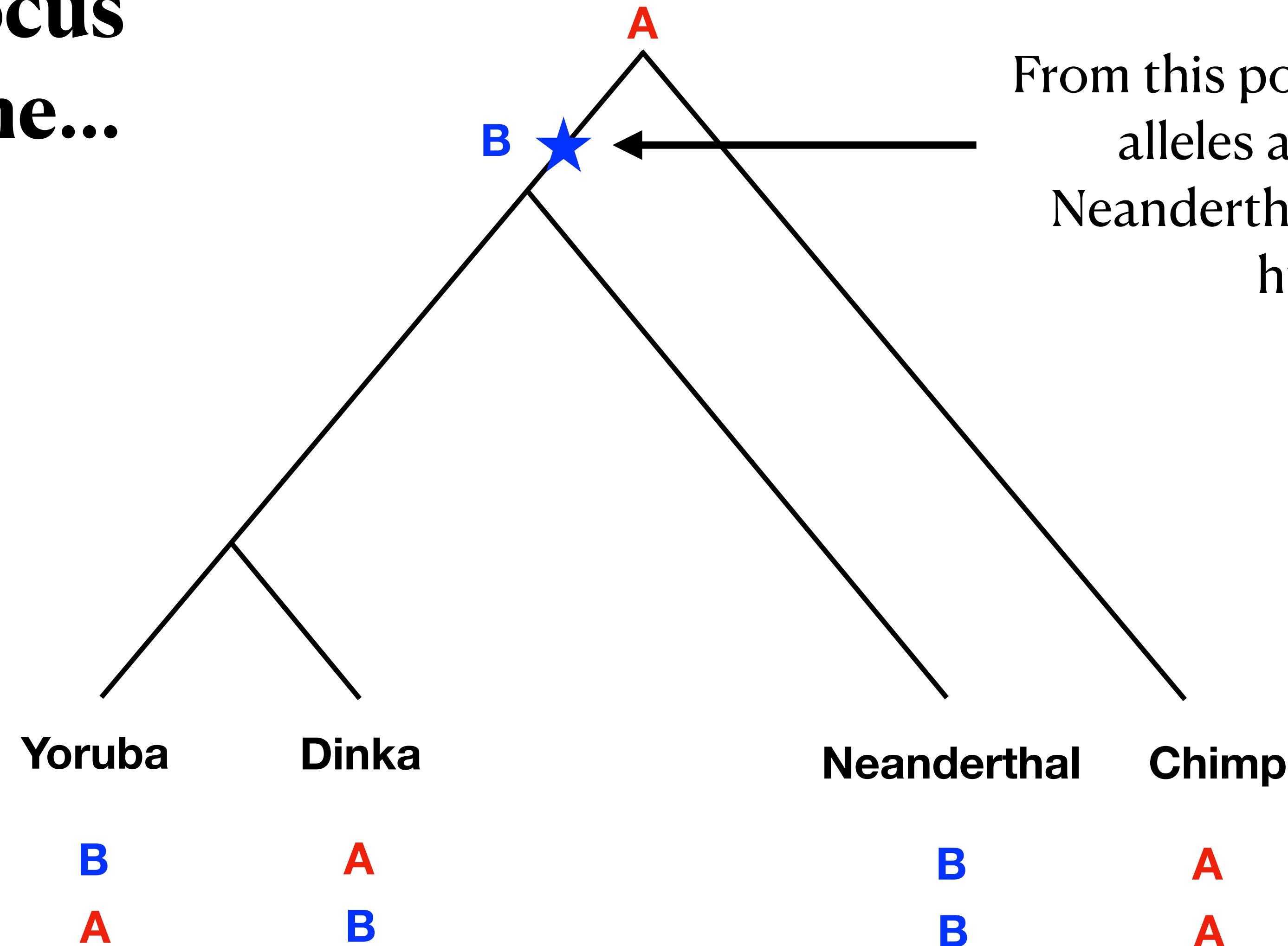


**At a single locus
in the genome...**



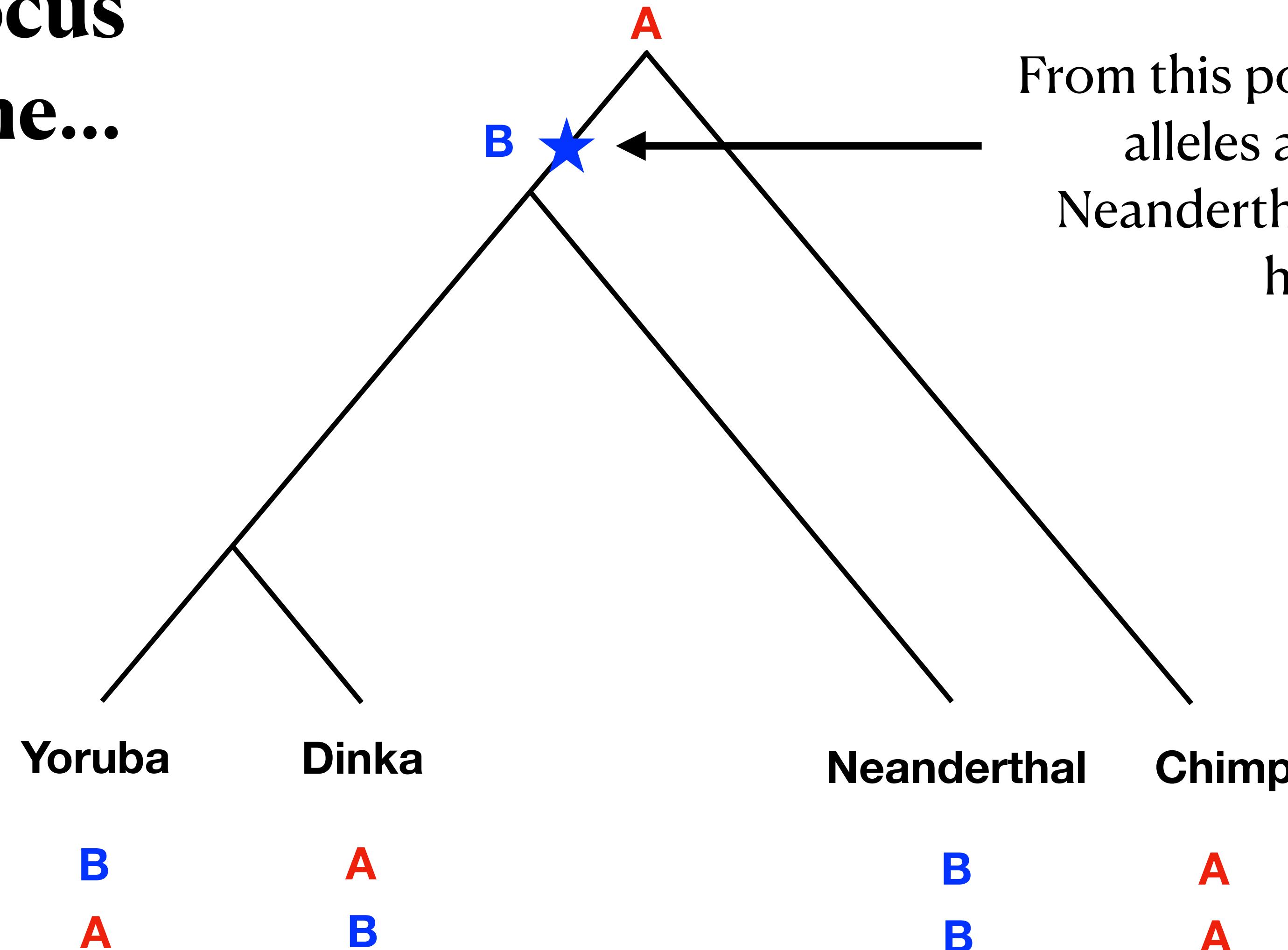
From this point, both **B** and **A** alleles are present in Neanderthals and modern humans

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in the genome...**



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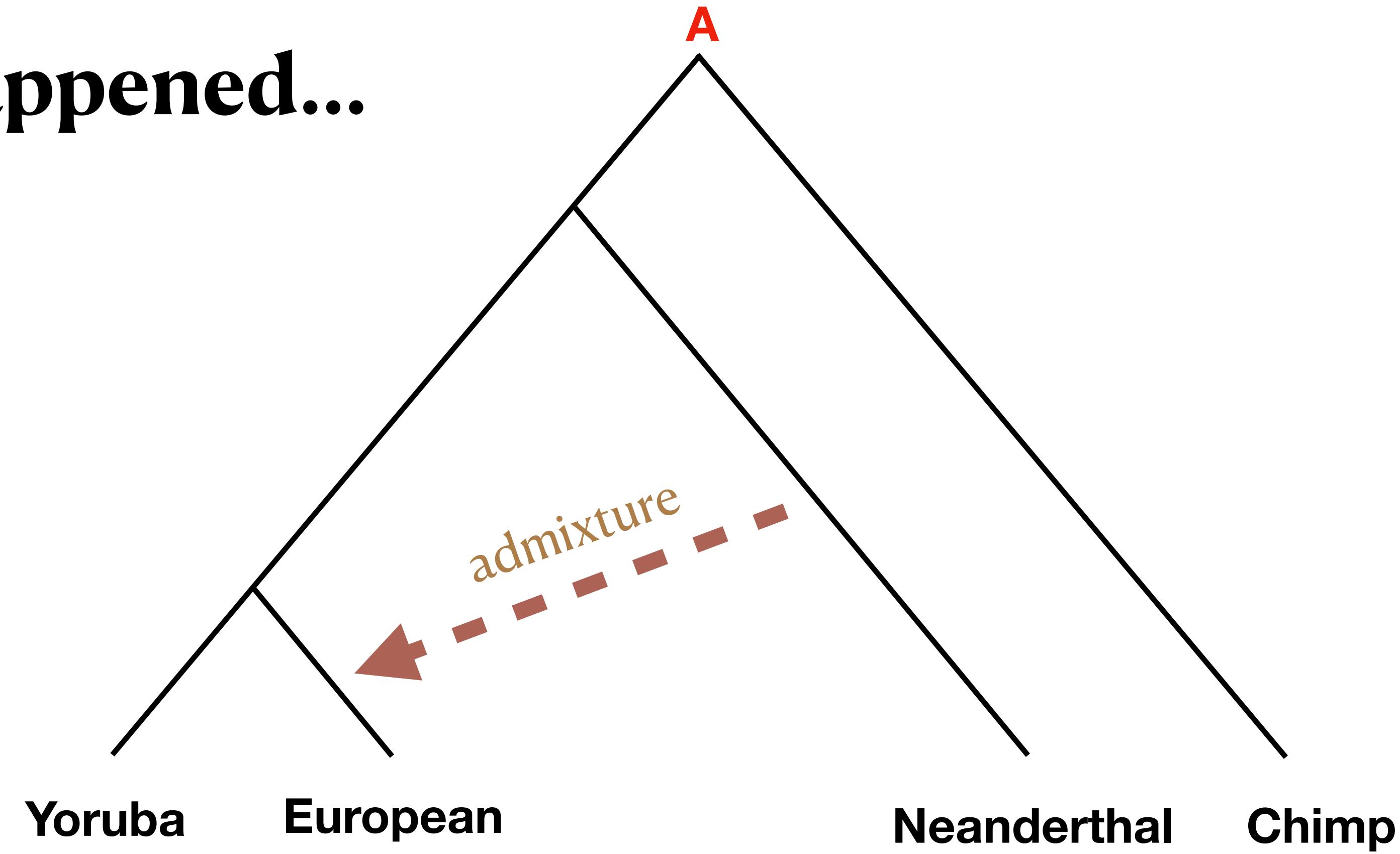
At a single locus
in the genome...



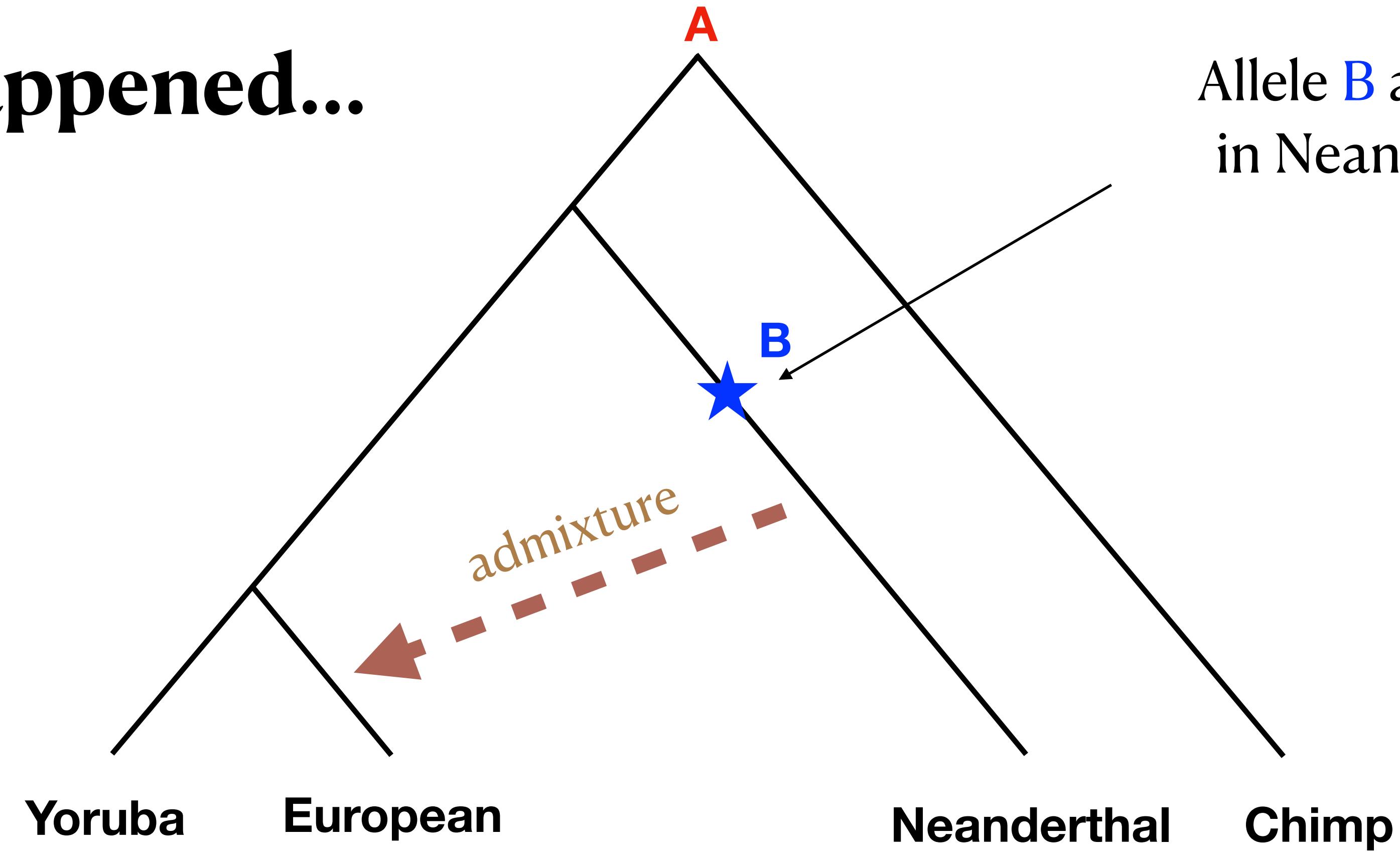
From this point, both **B** and **A** alleles are present in Neanderthals and modern humans

Data consistent with the tree: $f_4 = (\# \text{ BABA} - \# \text{ ABBA}) \sim 0$

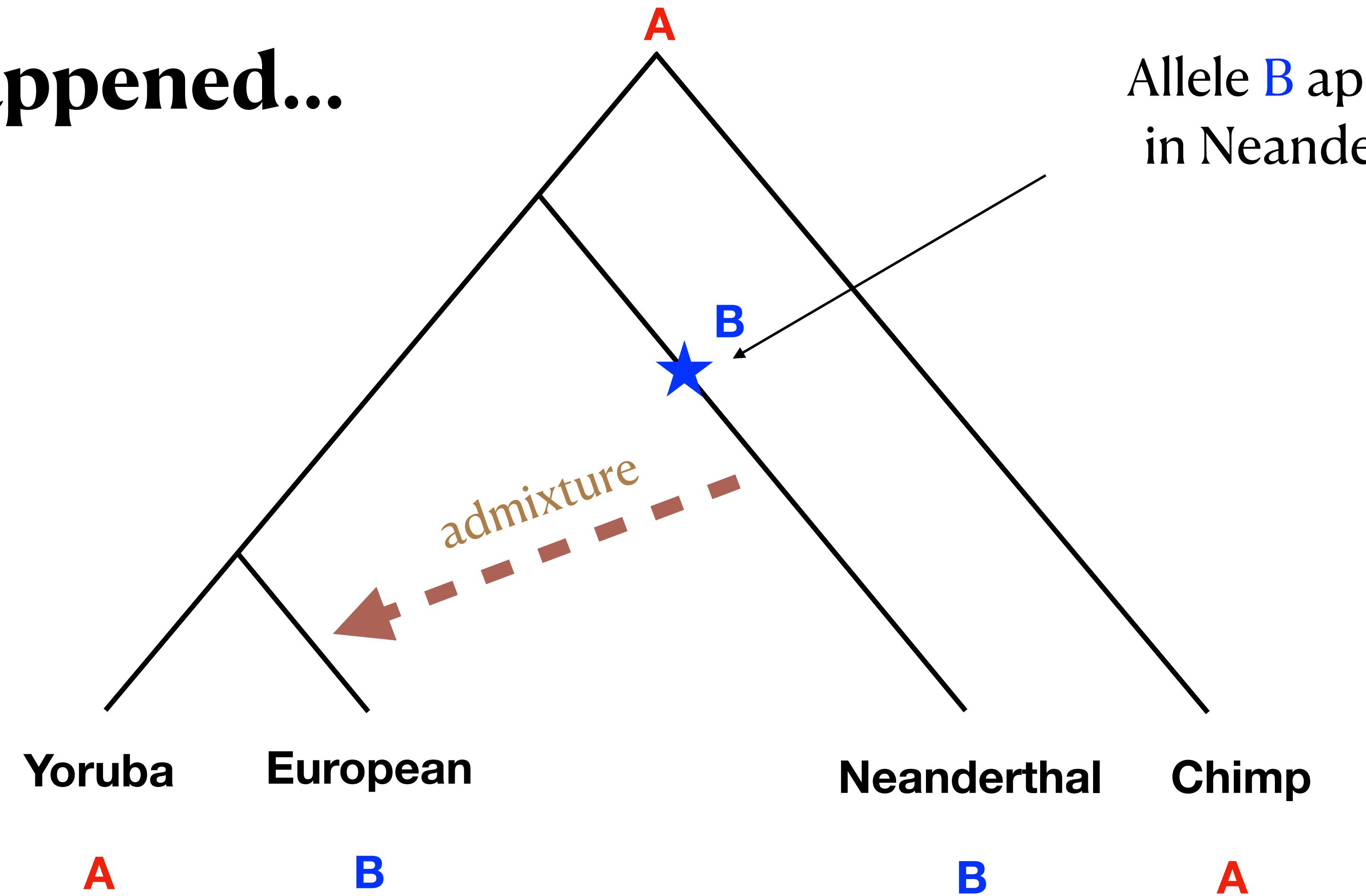
**Assume that
admixture happened...**



**Assume that
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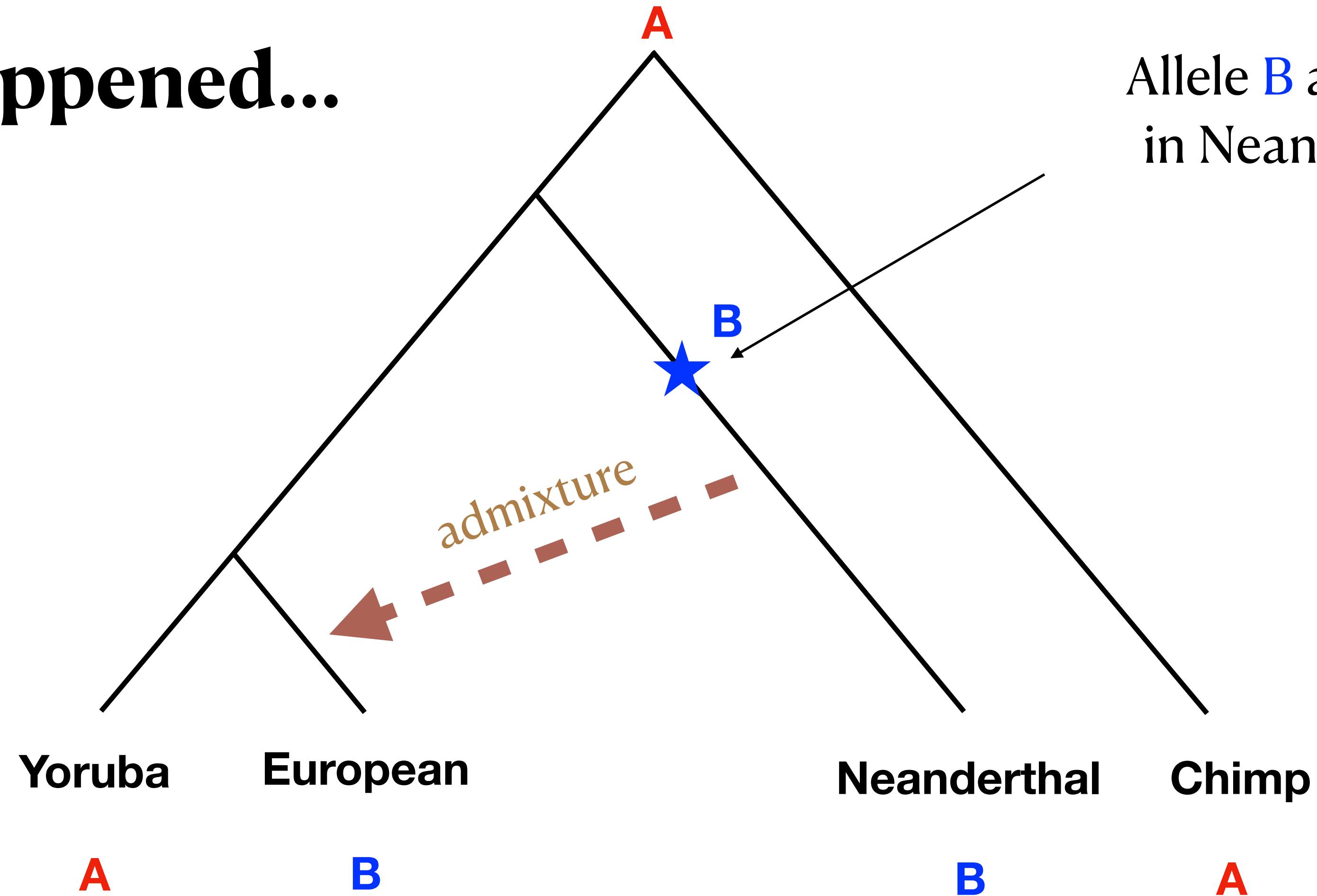


**Assume that
admixture happened...**



Allele B appeared
in Neanderthals

**Assume that
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Allele B appeared
in Neanderthals

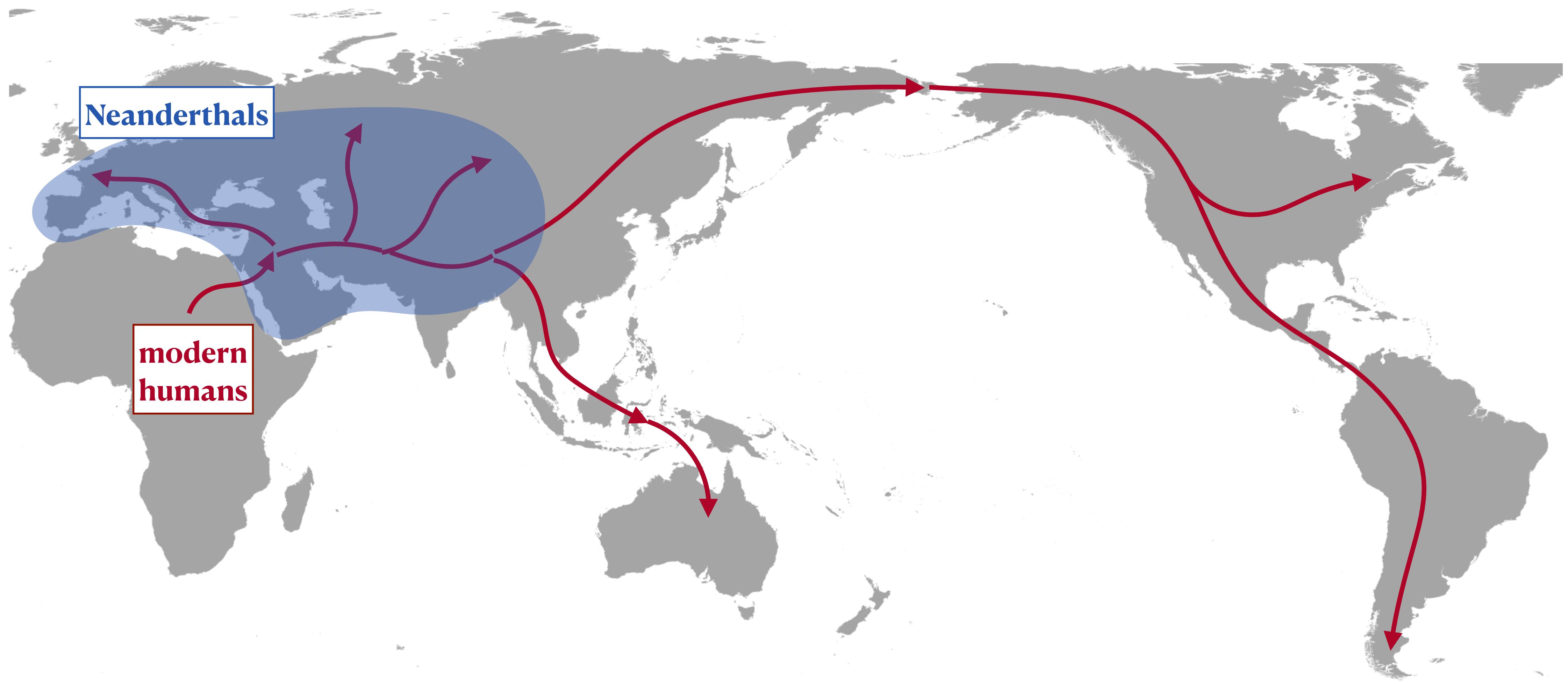
Introgression: $f_4 = (\# \text{ BABA} - \# \text{ABBA}) < 0$

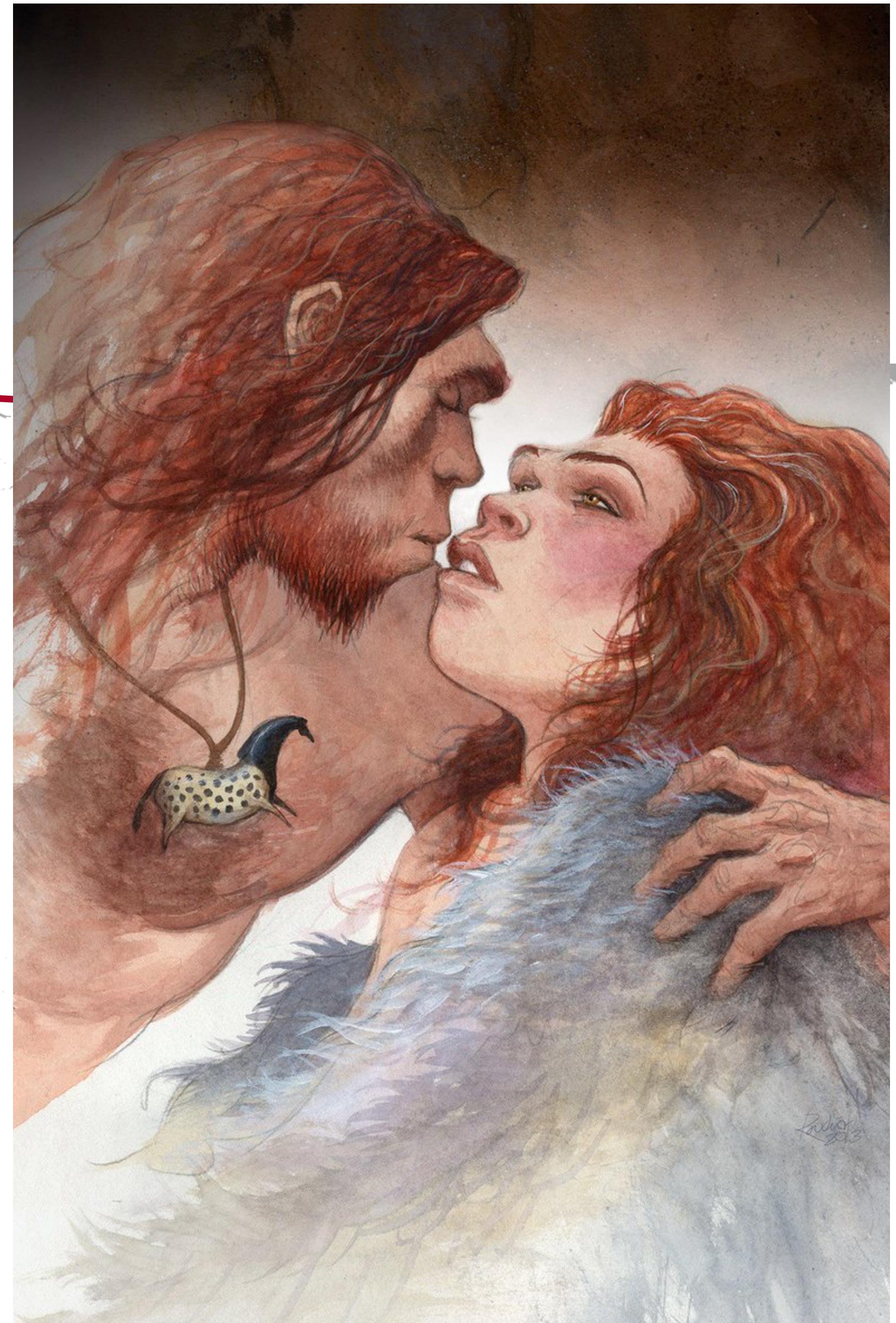
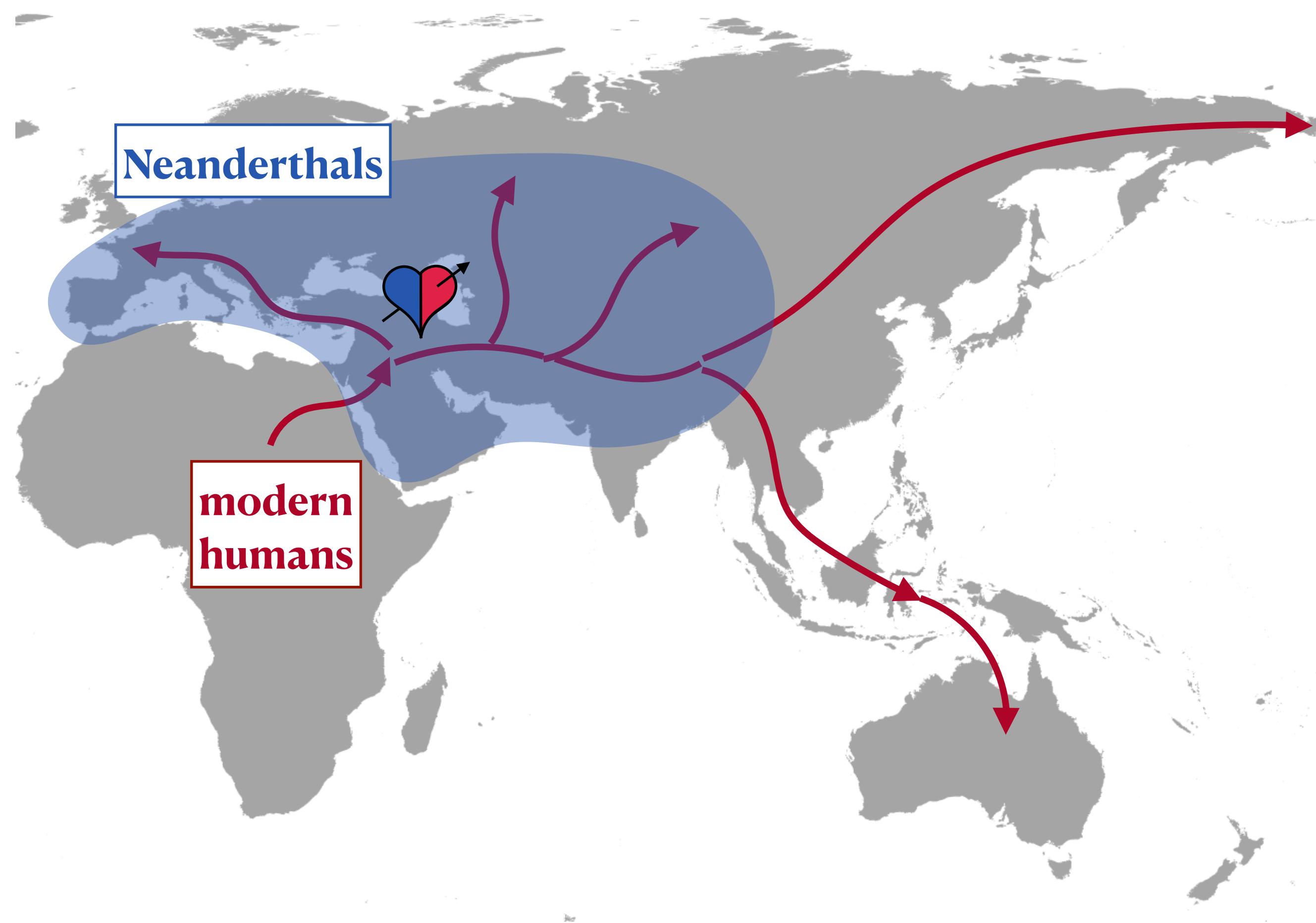
(the sign can flip if we flip Yoruba and European)



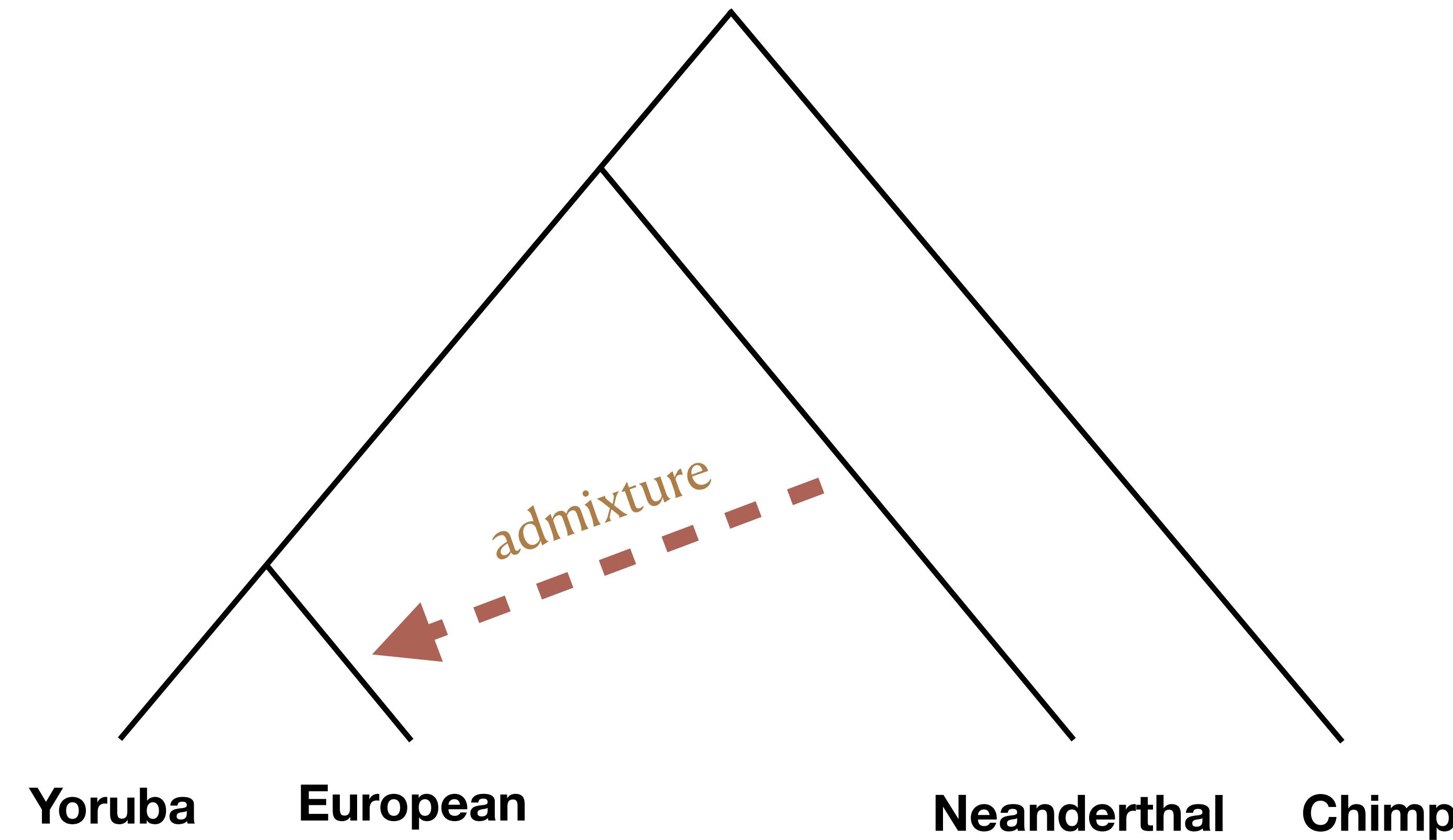
Demo #2

Performing admixture tests using *admixr*



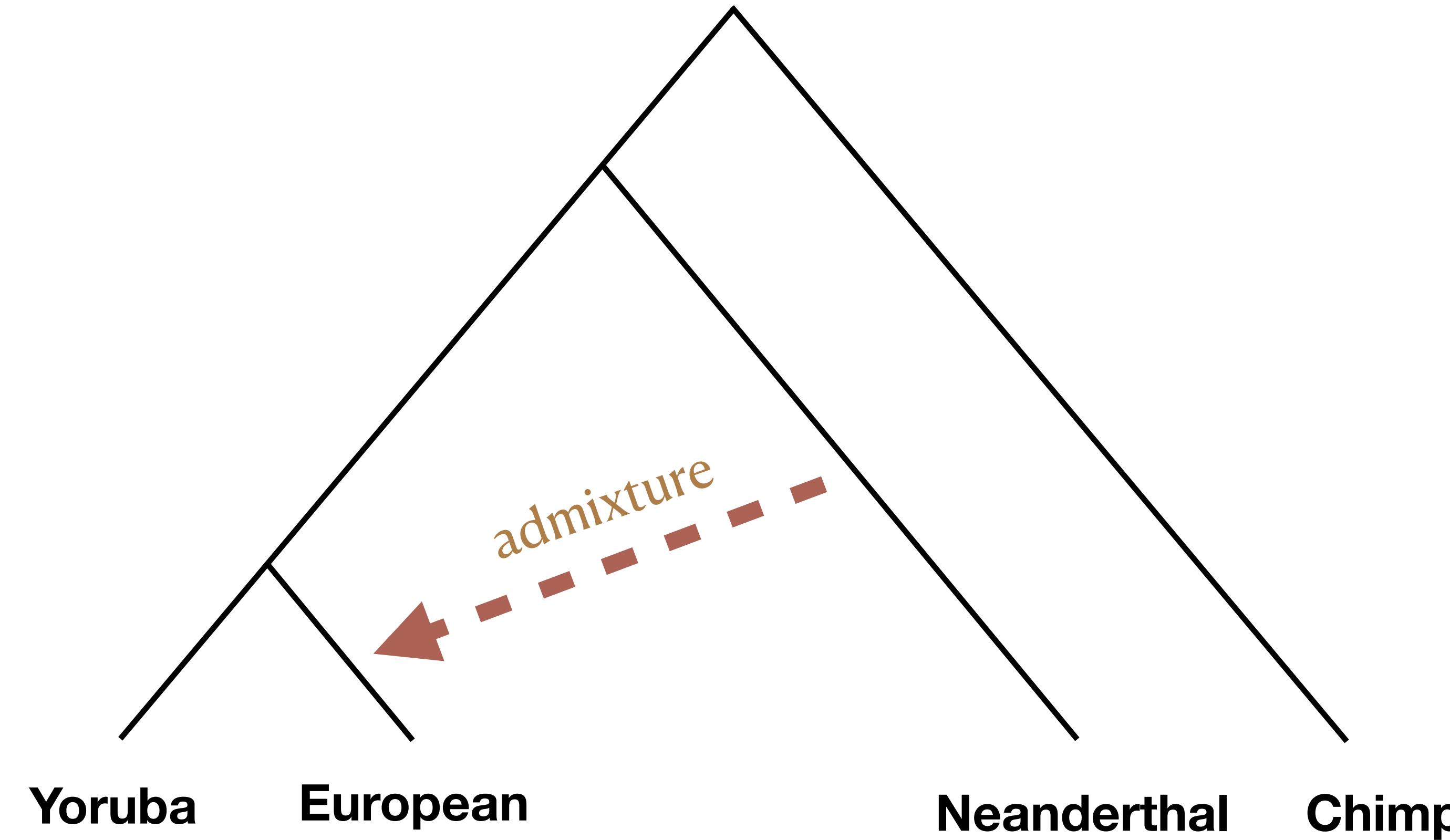


Detecting admixture



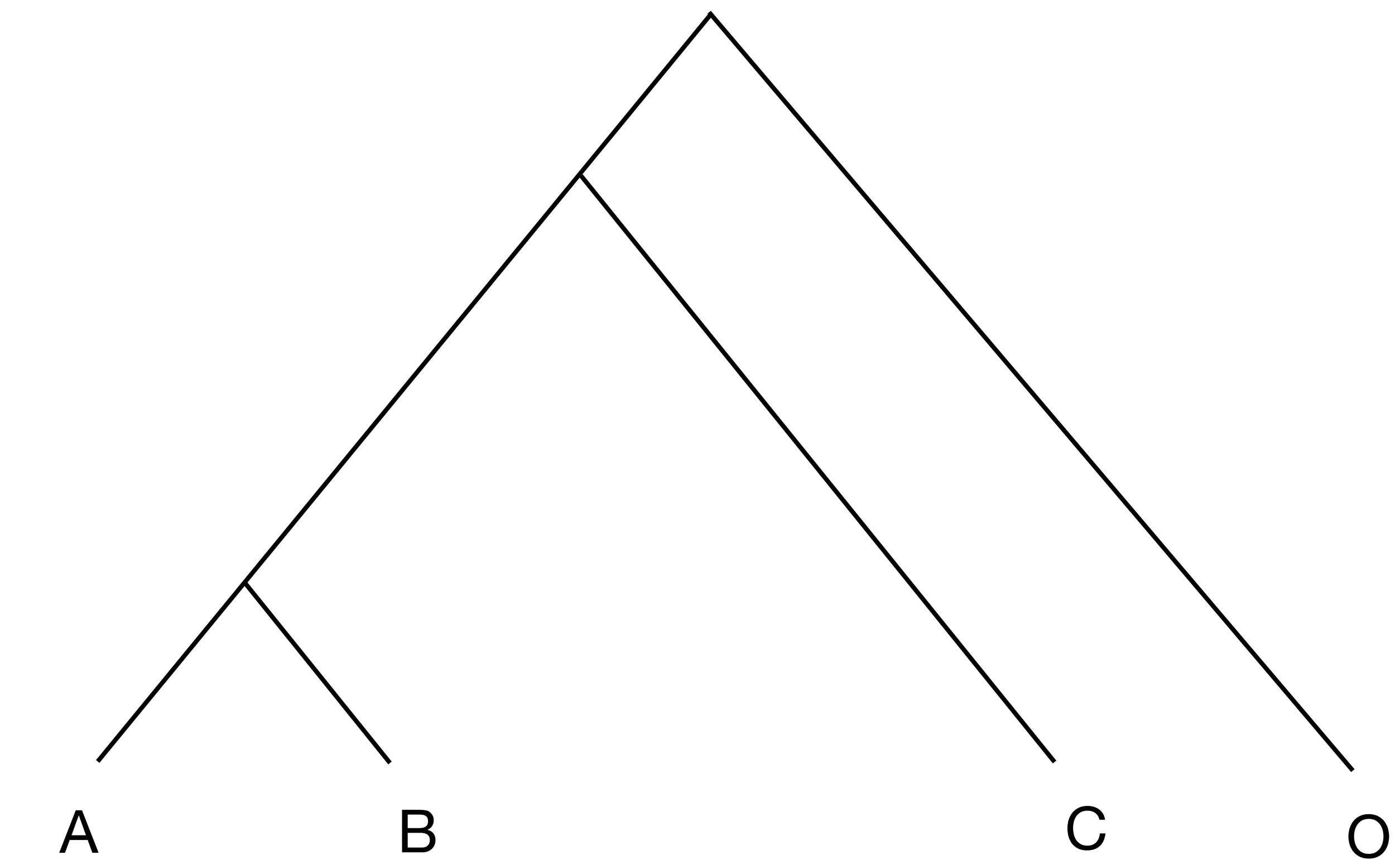
Introgression: $f_4 = (\# \text{ BABA} - \# \text{ ABBA}) < 0$

Detecting admixture proportion?



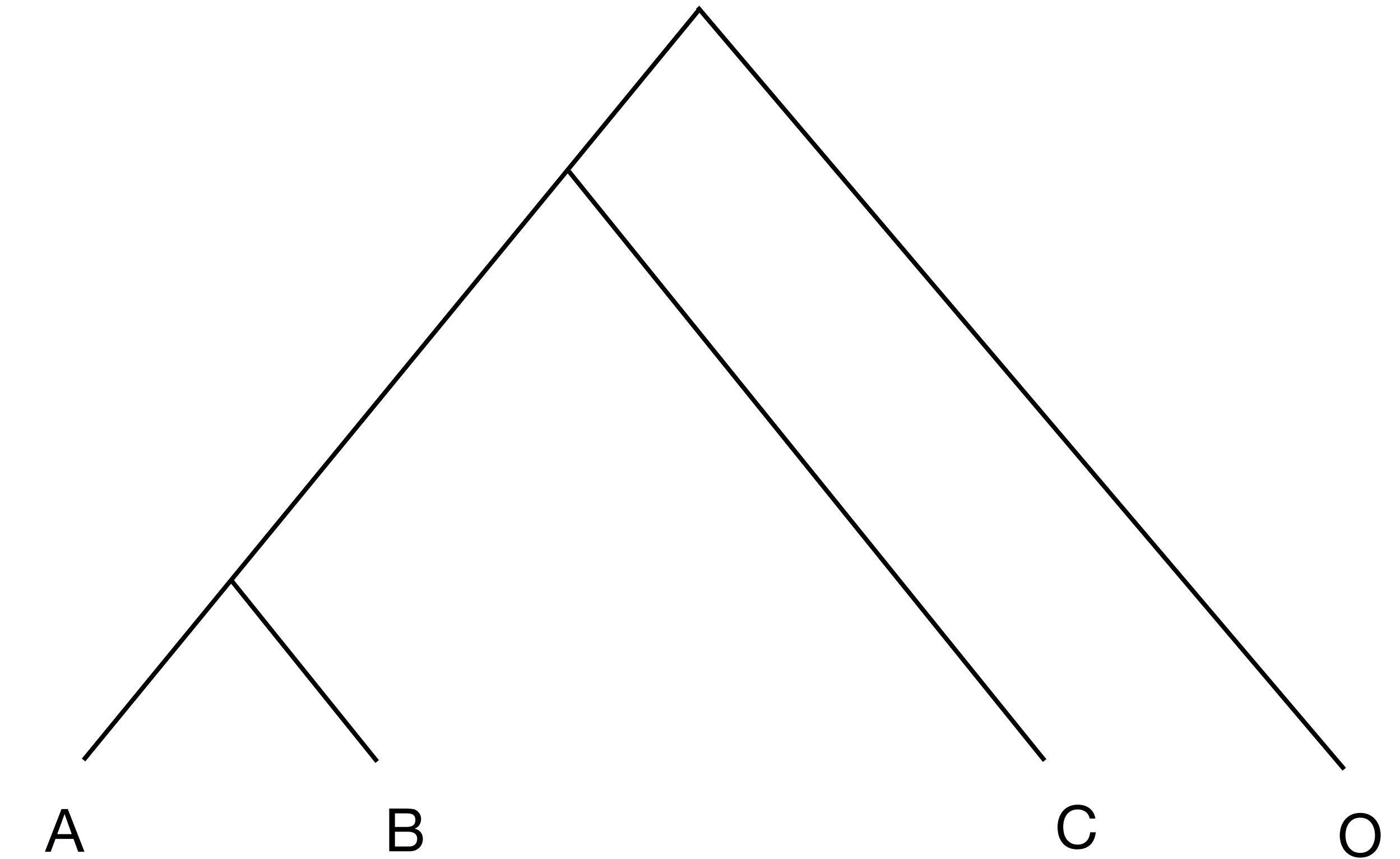
Introgression: $f_4 = (\# \text{ BABA} - \# \text{ ABBA}) < 0$

f_4 -ratio statistic: two possible paths for an admixed sample



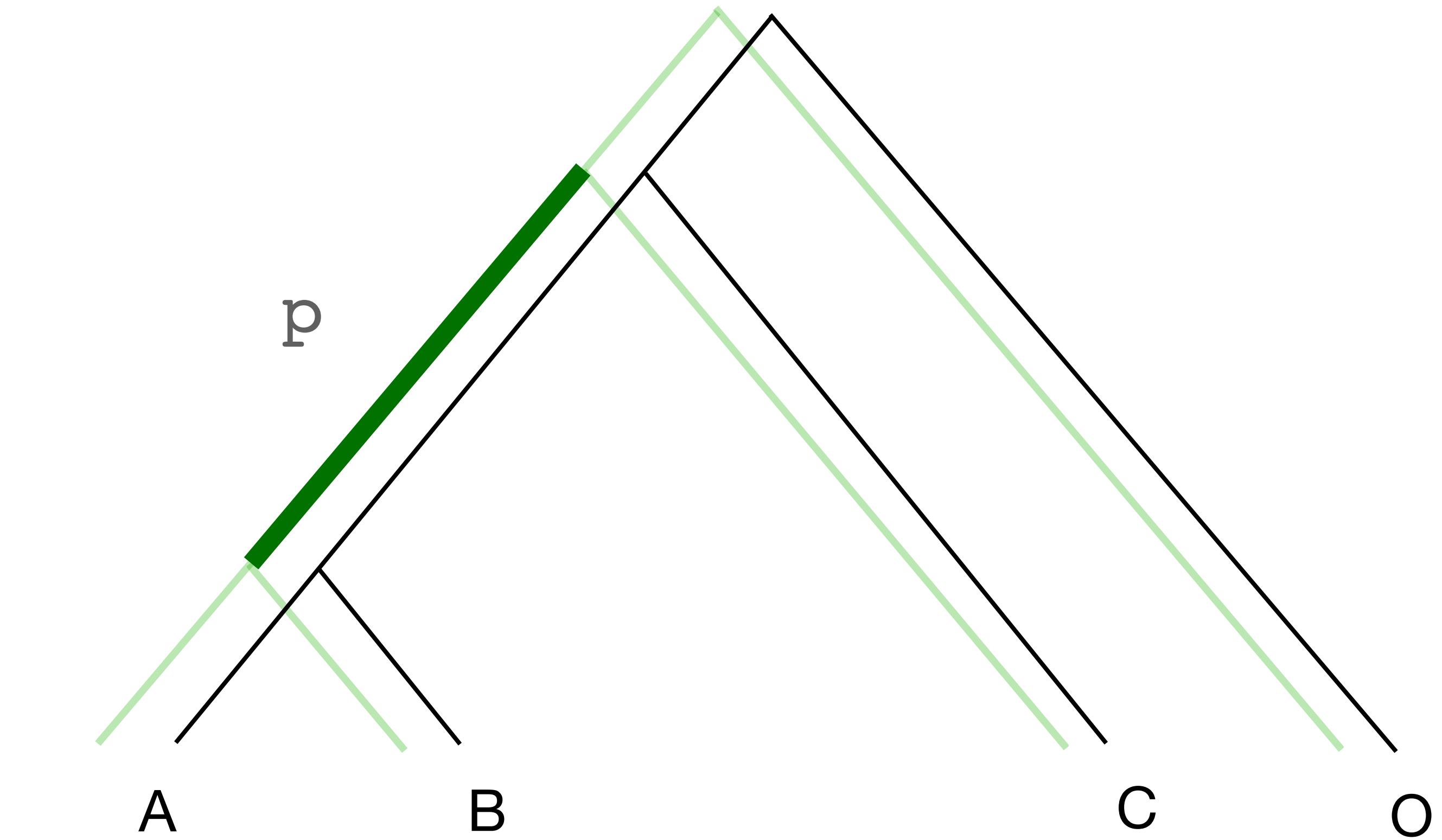
f_4 -ratio statistic: two possible paths for an admixed sample

$$f_4(C, B; A, O)$$



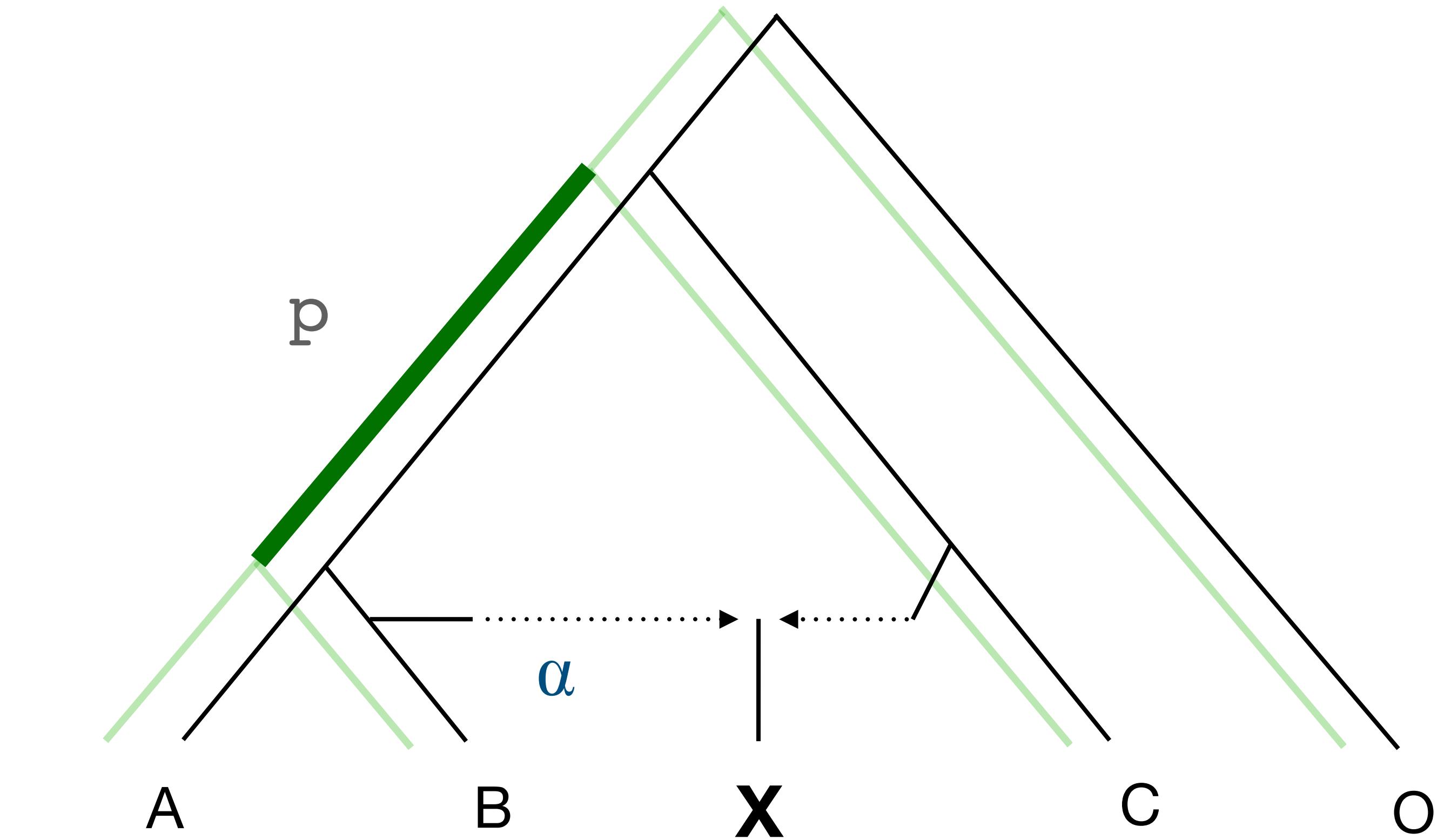
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$$p = f_4(C, B; A, O)$$



f_4 -ratio statistic: two possible paths for an admixed sample

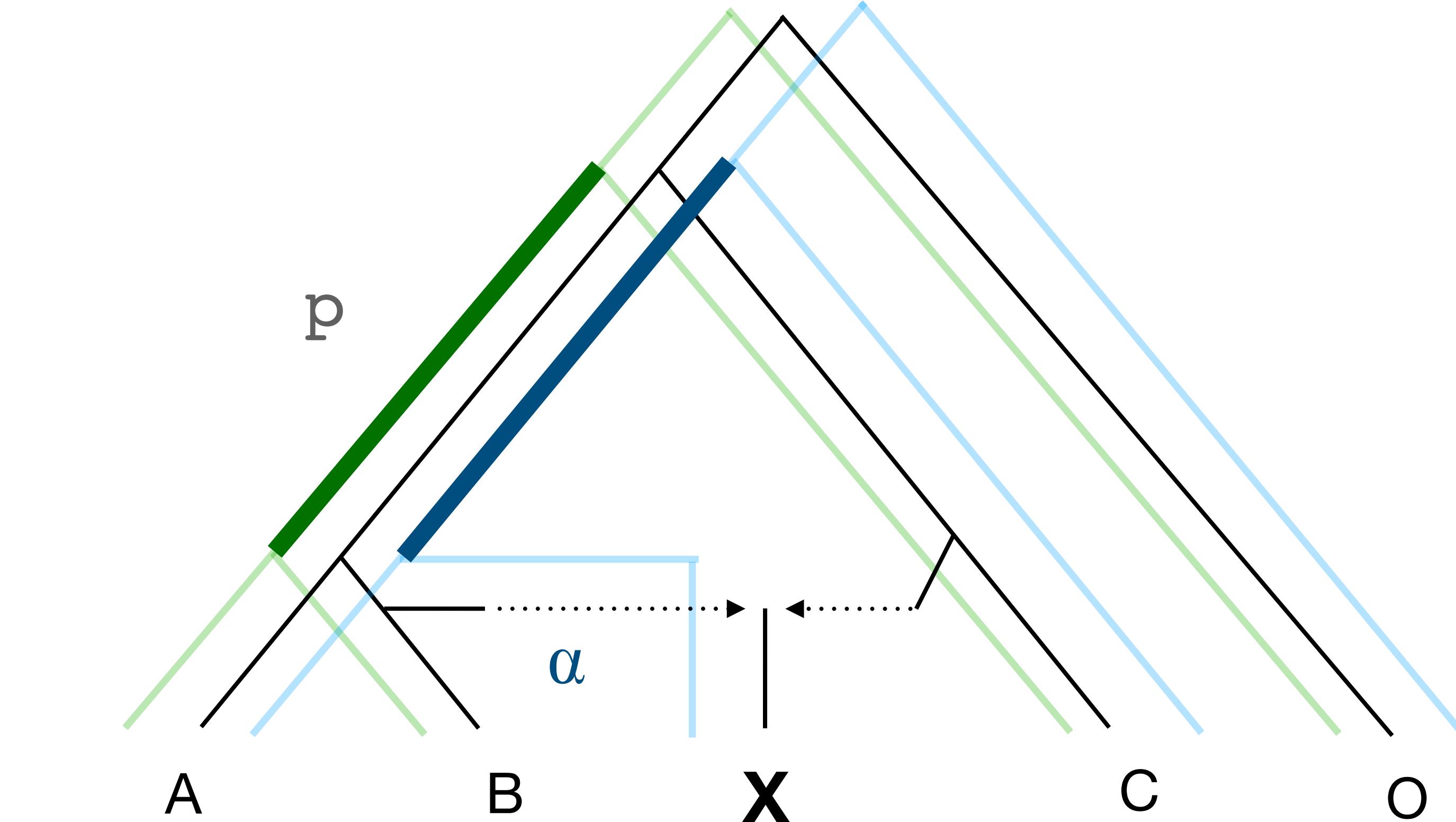
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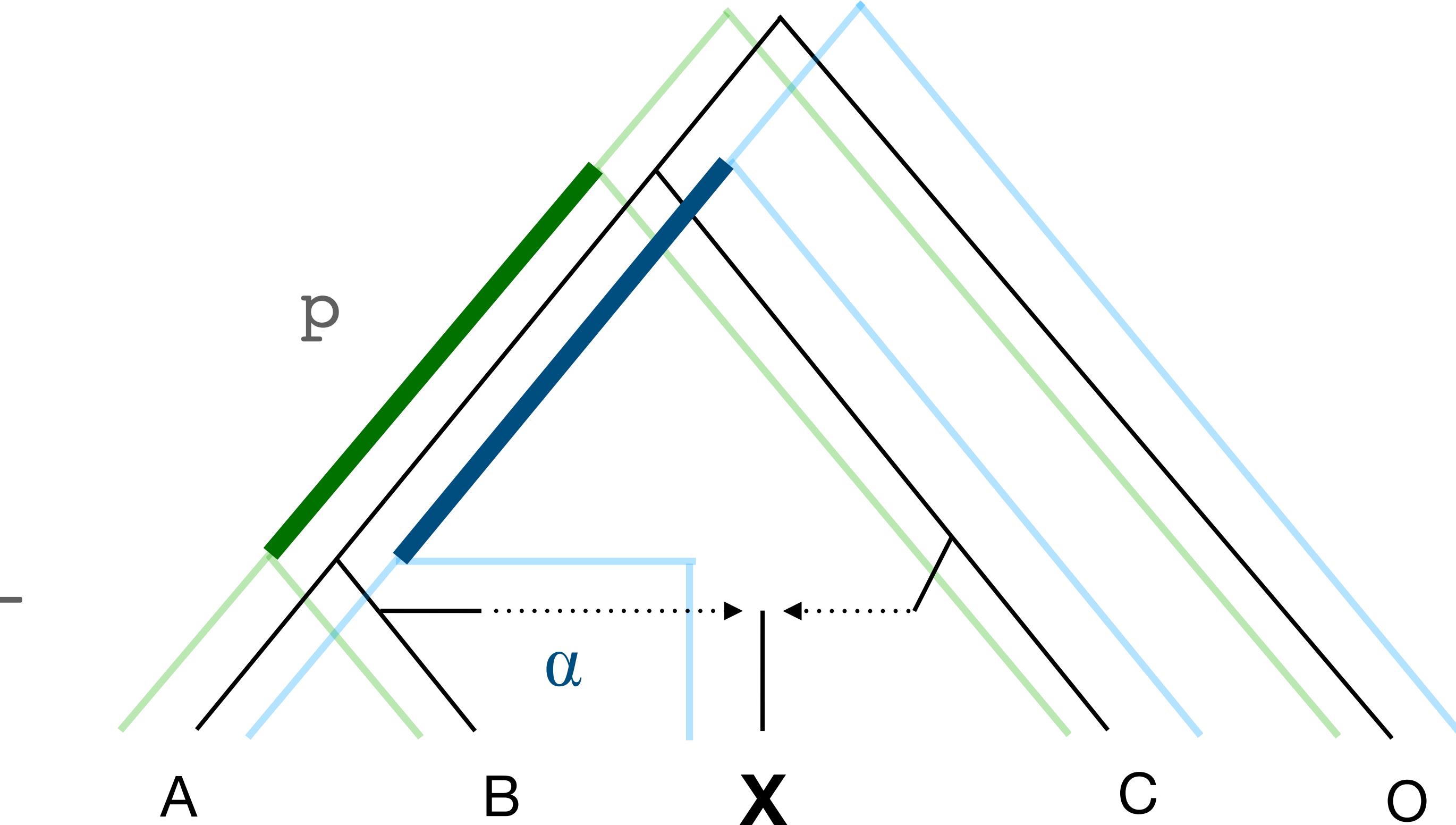
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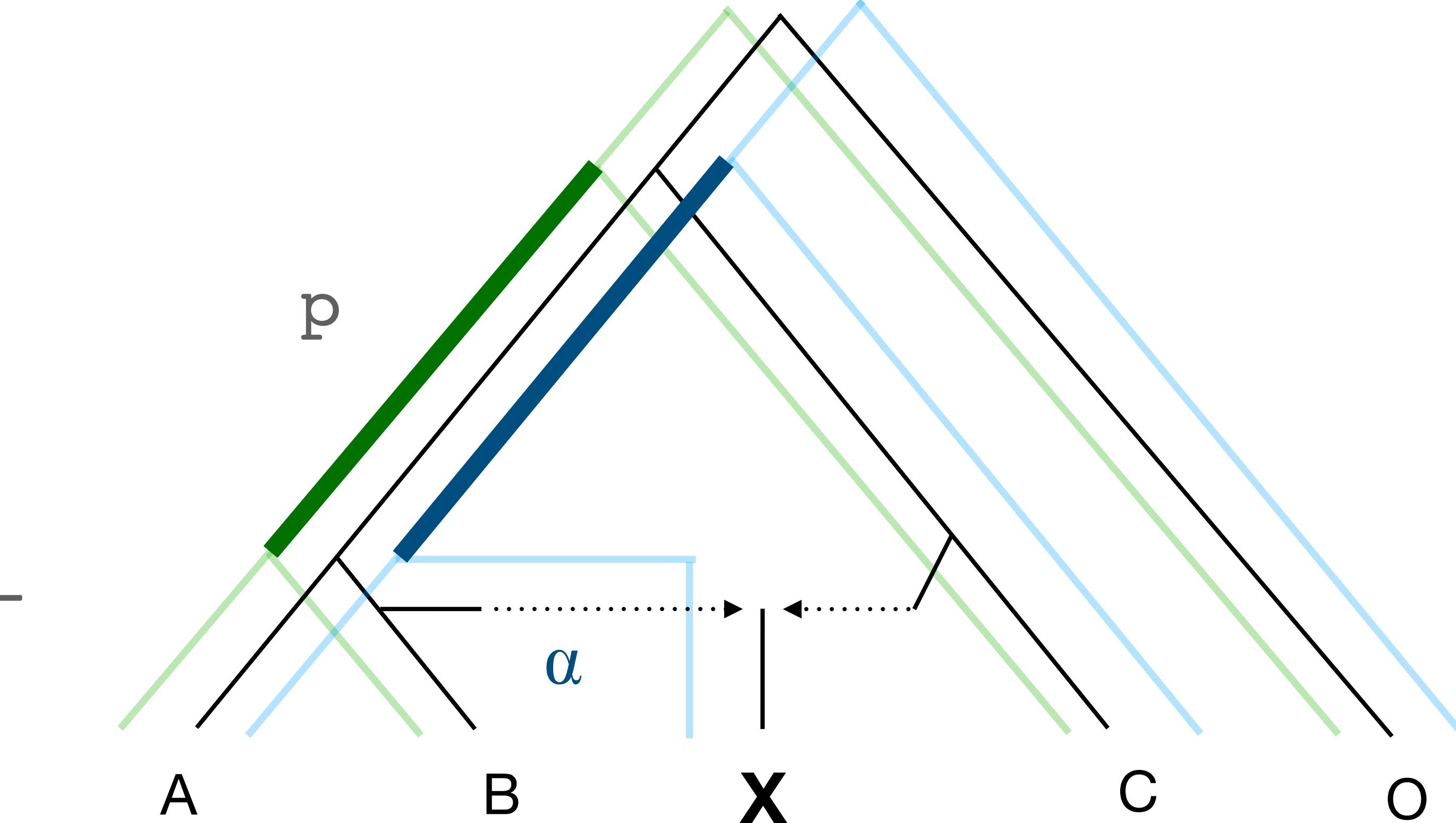


f_4 -ratio statistic: two possible paths for an admixed sample

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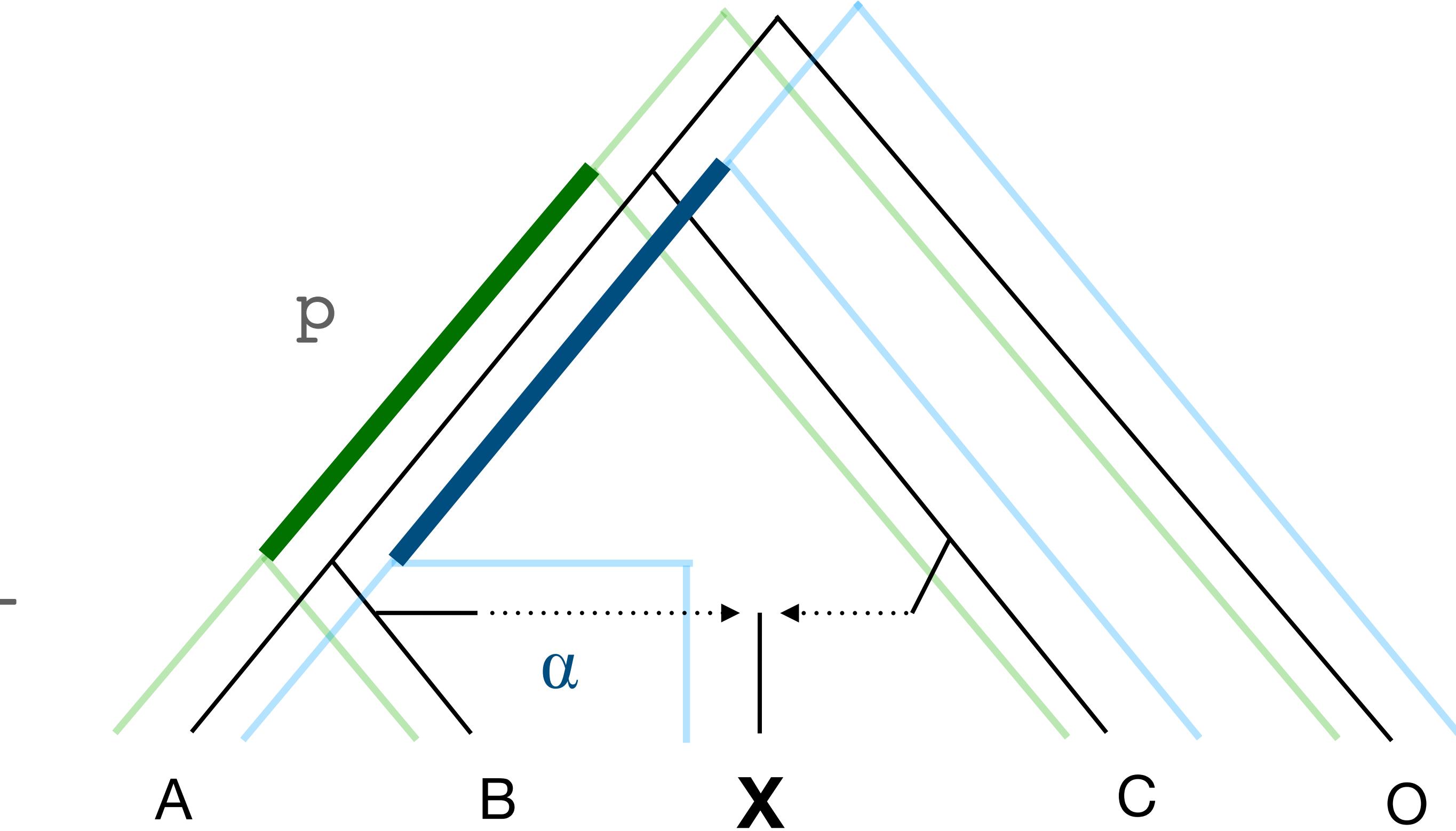
$$\alpha p = f_4(C, X; A, O)$$

$$\frac{\alpha p}{p} = \frac{f_4(C, X; A, O)}{f_4(C, B; A, O)}$$



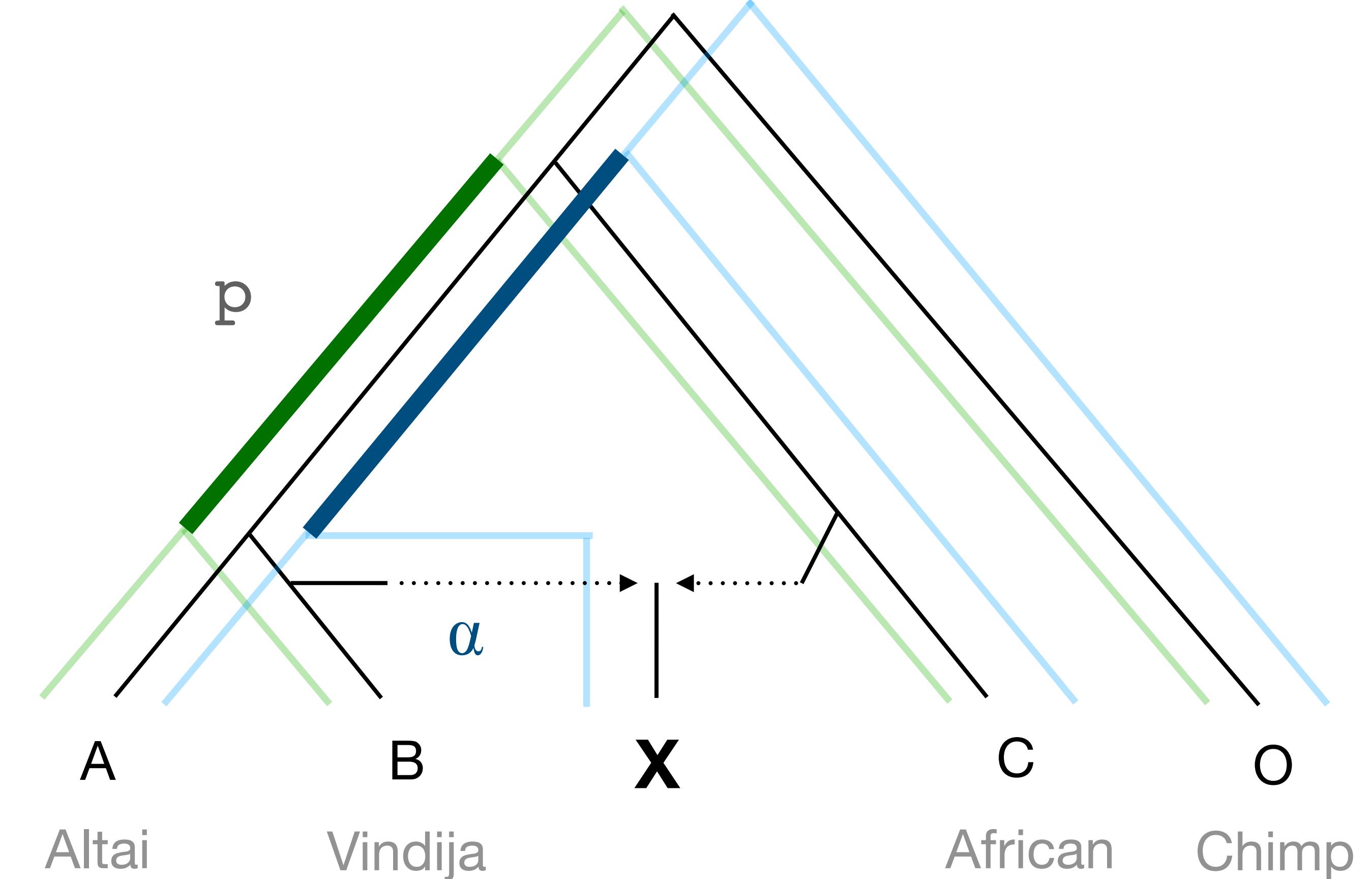
f_4 -ratio statistic: two possible paths for an admixed sample

$$p = f_4(C, B; A, O)$$
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f_4 -ratio statistic: two possible paths for an admixed sample

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f_4 -ratio statistic: two possible paths for an admixed sample

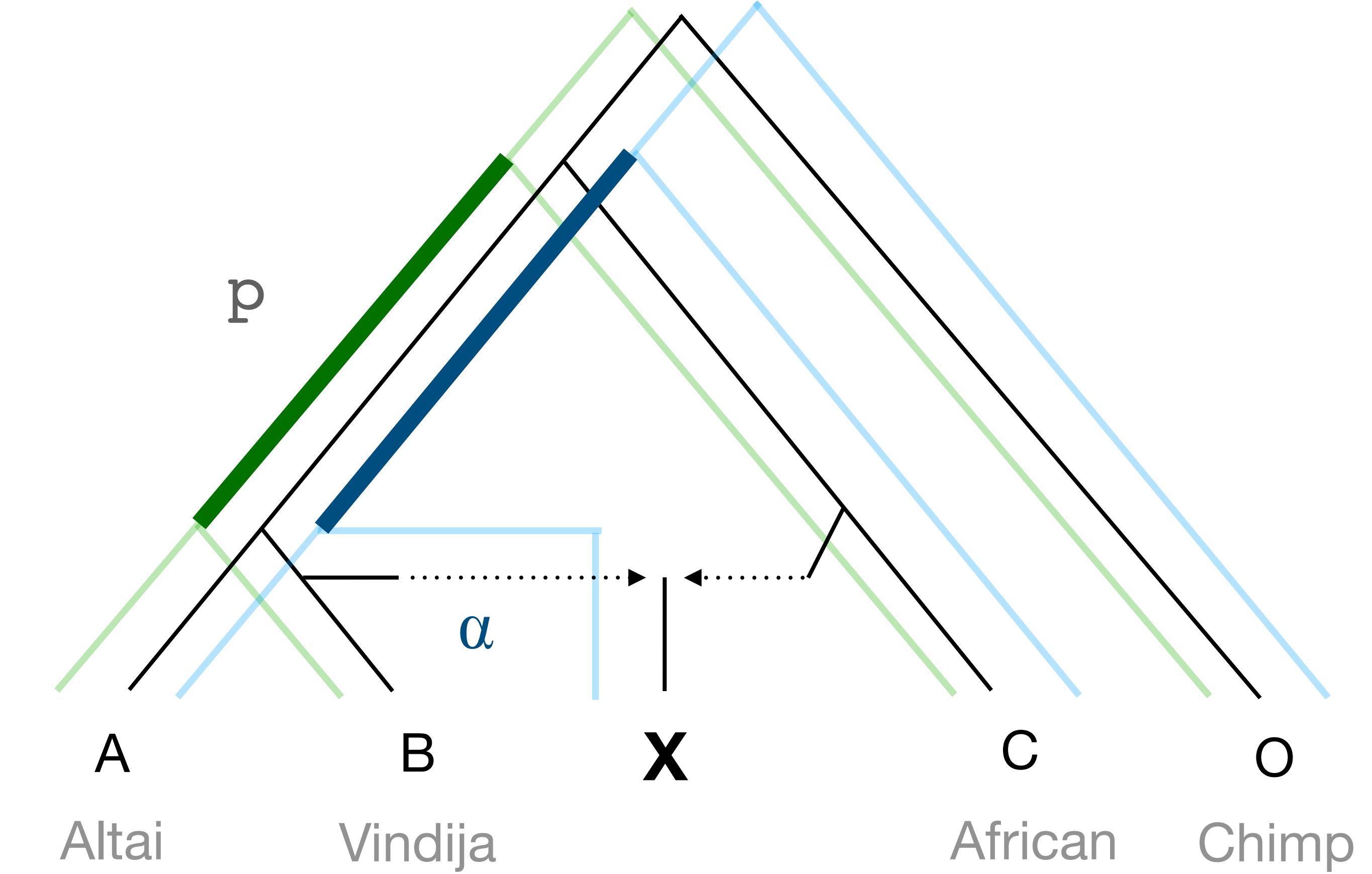
$$p = f_4(C, B; A, O)$$
$$\alpha p = f_4(C, X; A, O)$$
$$\alpha = \frac{\alpha p}{p} = \frac{f_4(C, X; A, O)}{f_4(C, B; A, O)}$$

$f_4(\text{African}, X; \text{Altai}, \text{Chimp})$

(C)

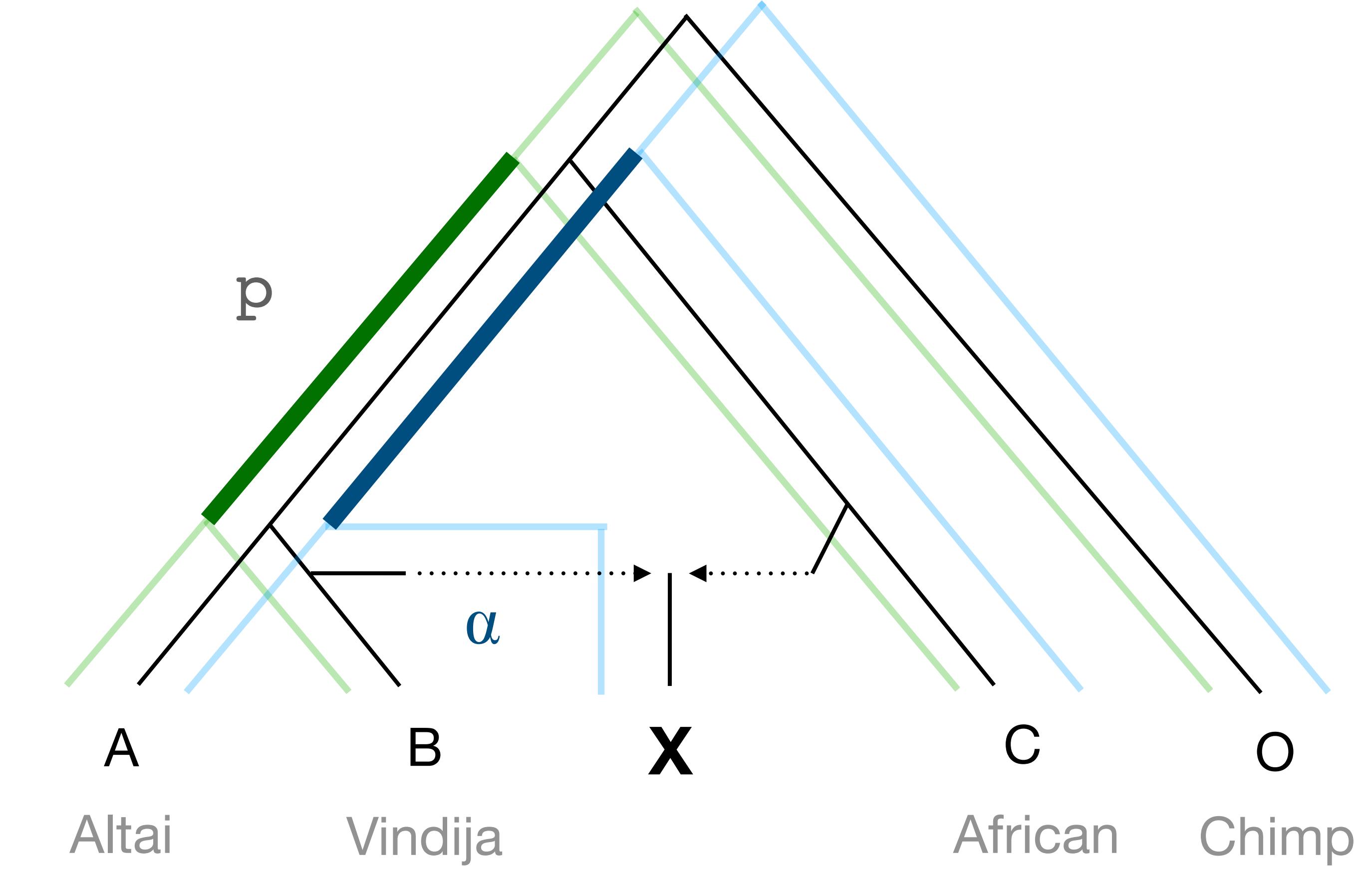
(A)

(O)



f_4 -ratio statistic: two possible paths for an admixed sample

$$p = f_4(C, B; A, O)$$
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$$f_4(\text{African}, X; \text{Altai}, \text{Chimp}) / f_4(\text{African}, \text{Vindija}; \text{Altai}, \text{Chimp})$$

(C)

(A)

(O)

(C)

(B)

(A)

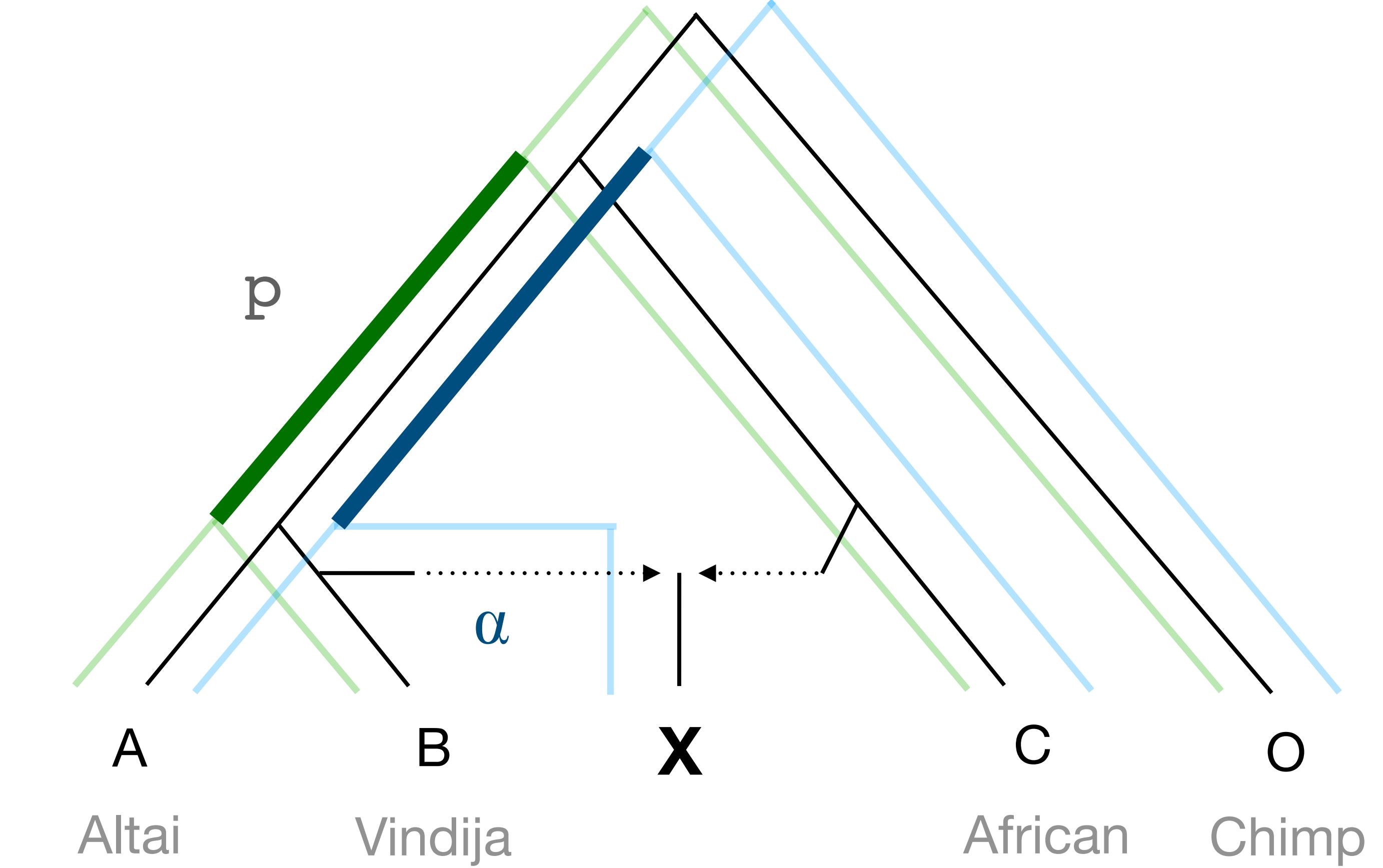
(O)

f_4 -ratio statistic: two possible paths for an admixed sample

$$p = f_4(C, B; A, O)$$

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(C)

(A)

(O)

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(B)

(A)

(O)

$f_4(\text{African, X; Altai, Chimp}) / f_4(\text{African, Vindija; Altai, Chimp})$

We are comparing
the rate of allele **sharing of X with one Neanderthal**,
with
the rate of **sharing between two Neanderthals**

$f_4(\text{African}, \mathbf{X}; \text{Altai}, \text{Chimp}) / f_4(\text{African}, \mathbf{Vindija}; \text{Altai}, \text{Chimp})$

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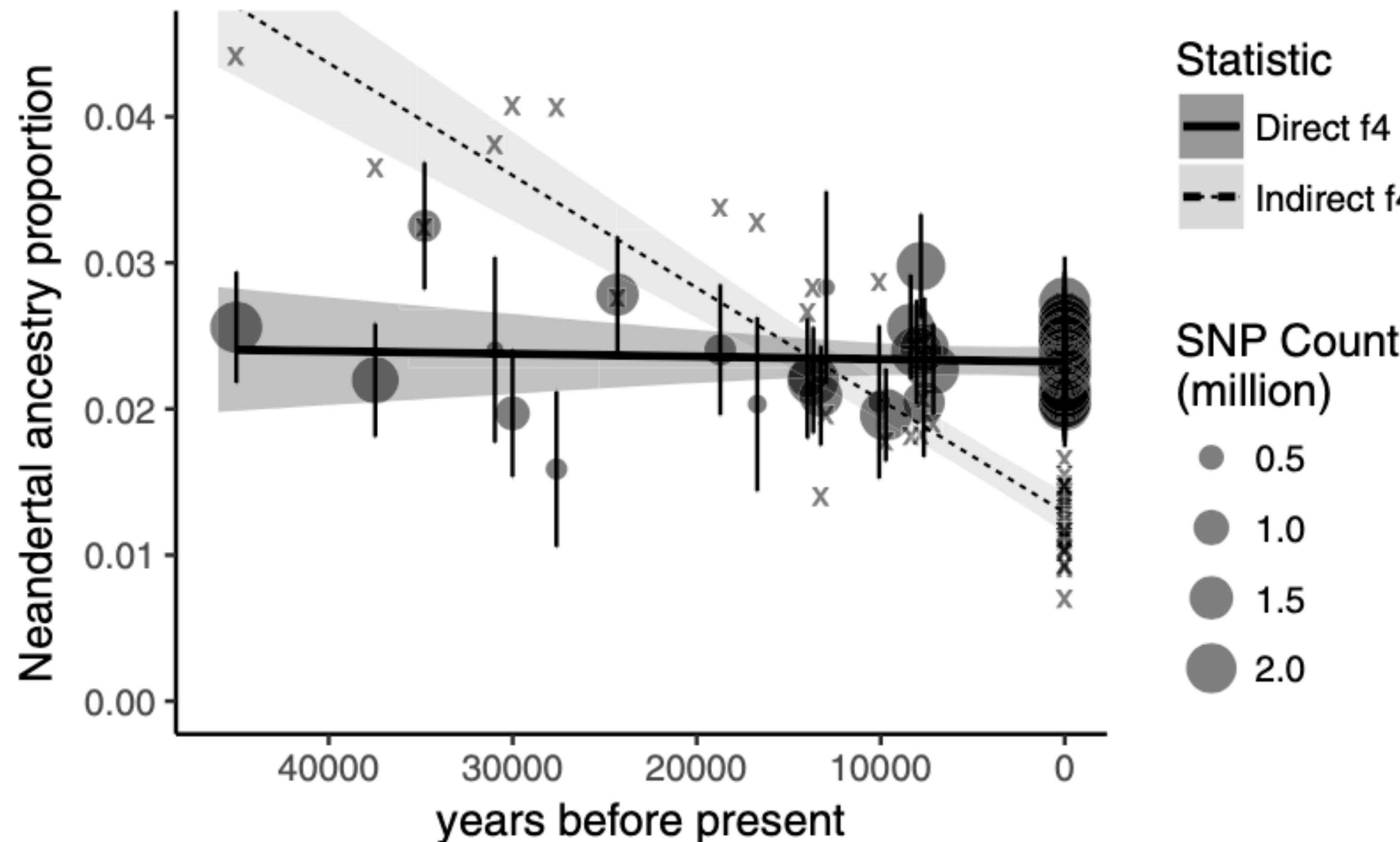
$$f_4(\text{African, X; Altai, Chimp}) / f_4(\text{African, Vindija; Altai, Chimp})$$

B	A	B	A	B	A	B	A
A	B	B	A	A	B	B	A

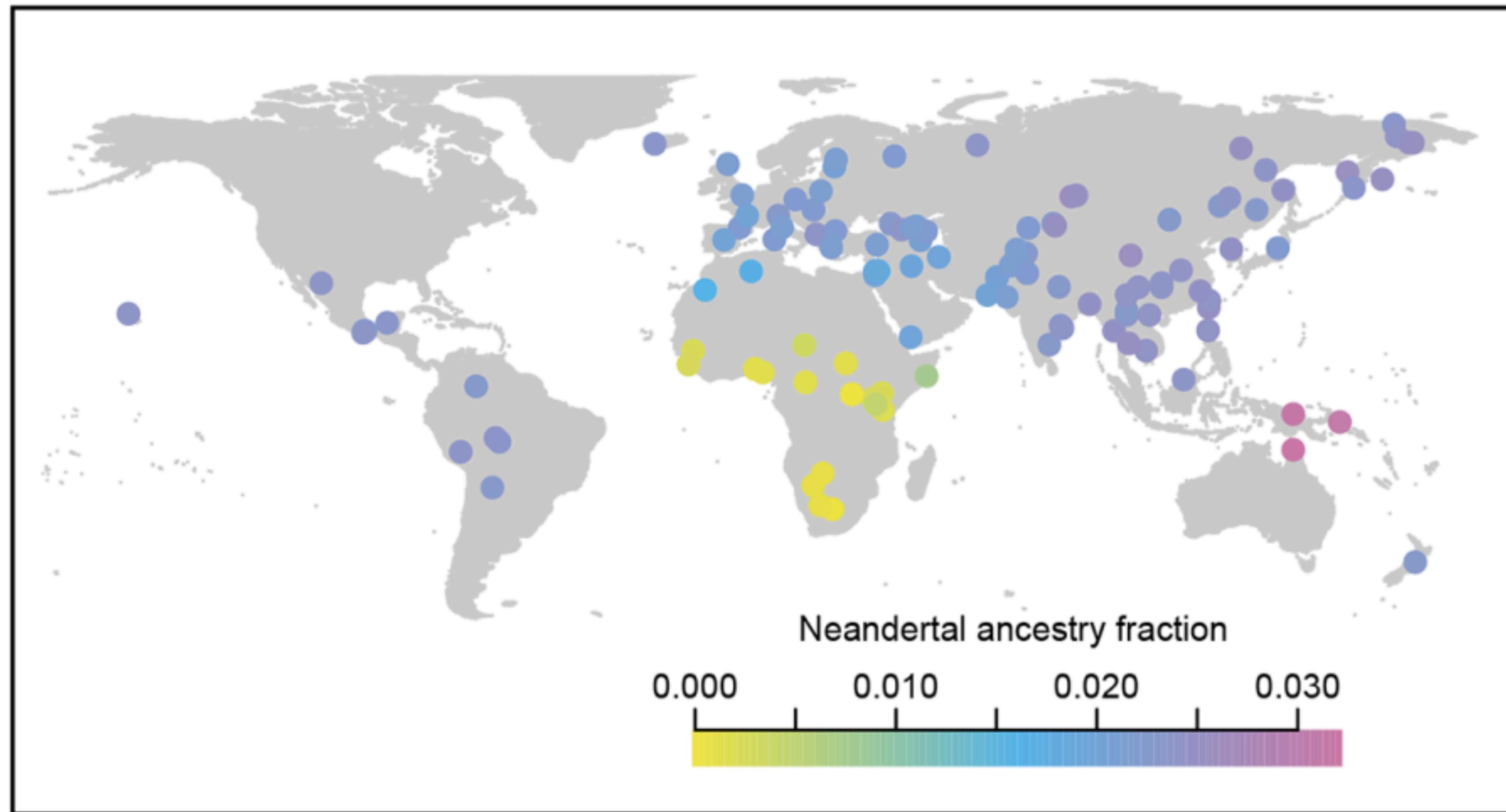
Demo #3

Estimating Neanderthal ancestry
proportions using *admixr*

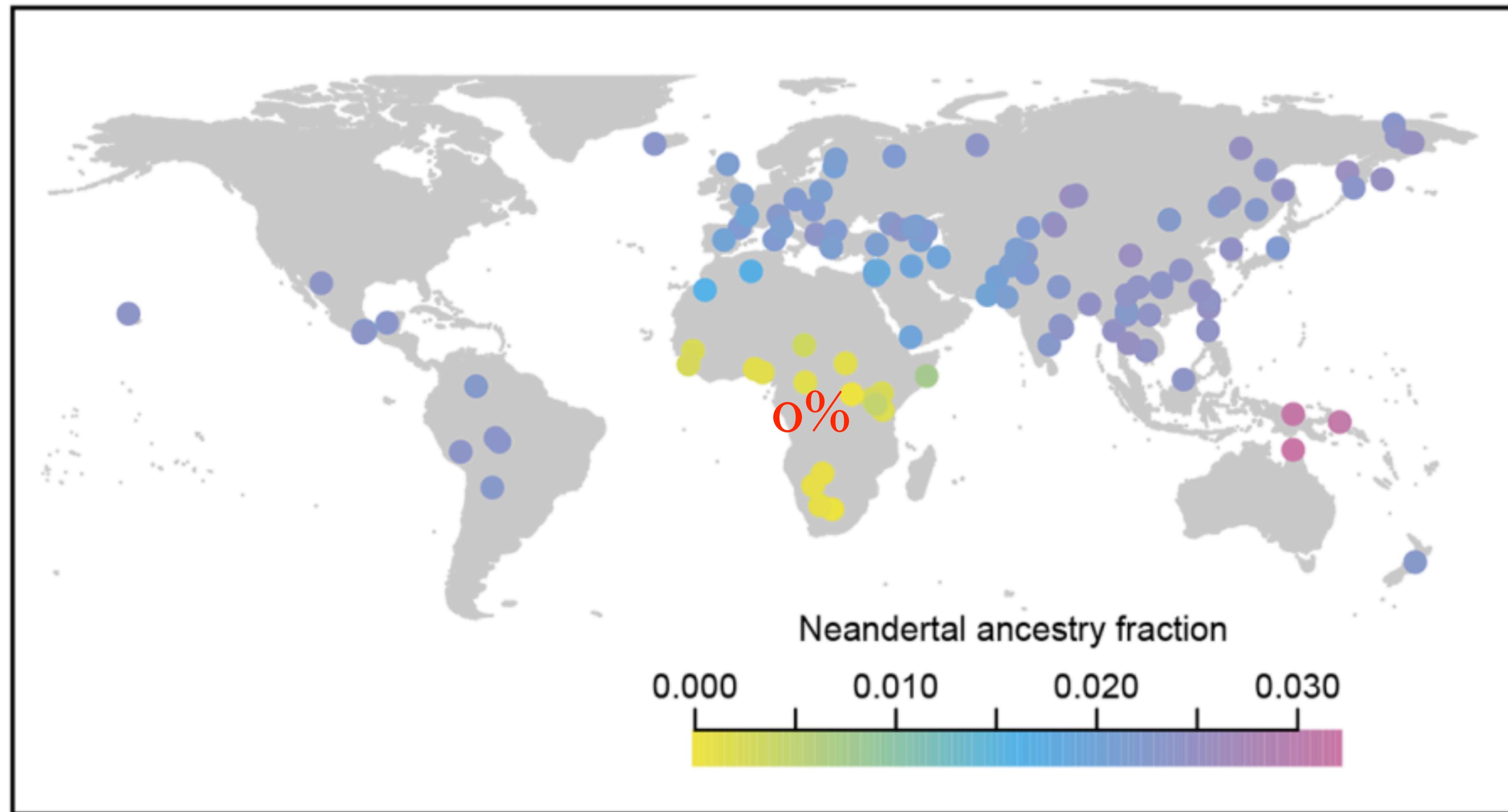
Neanderthal ancestry in Europe over time



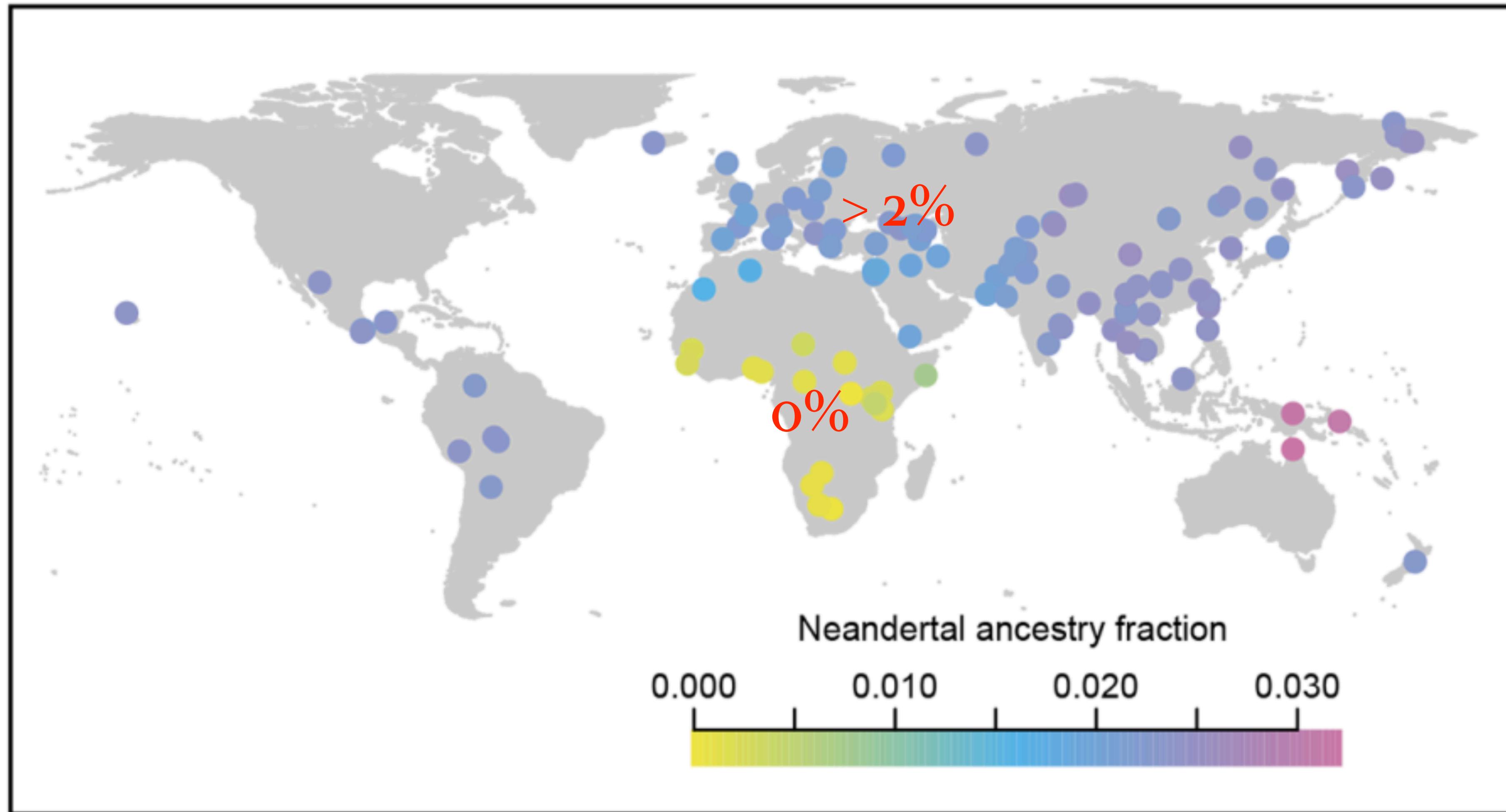
Geographic distribution of Neanderthal ancestry in the world



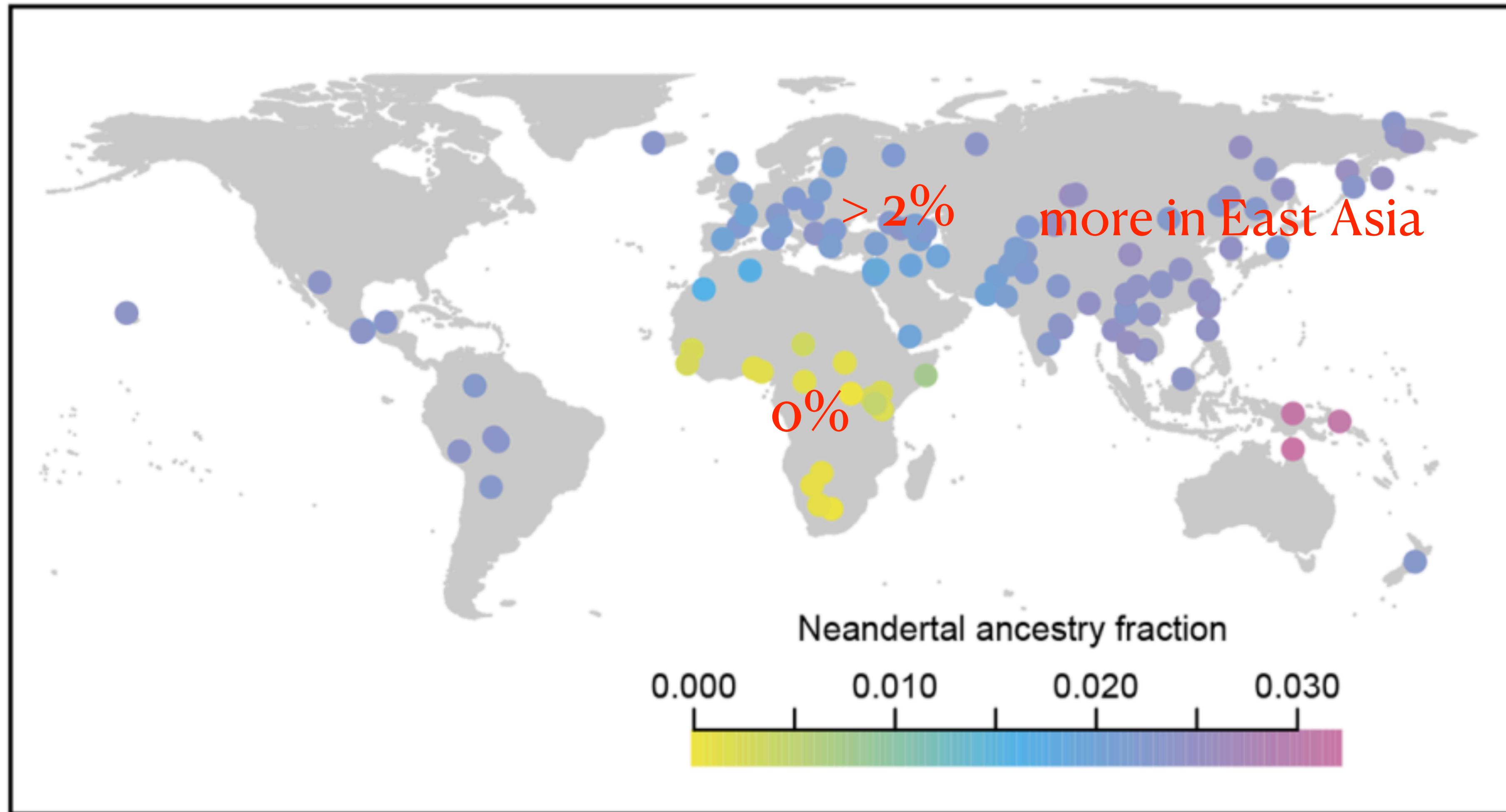
Geographic distribution of Neanderthal ancestry in the world



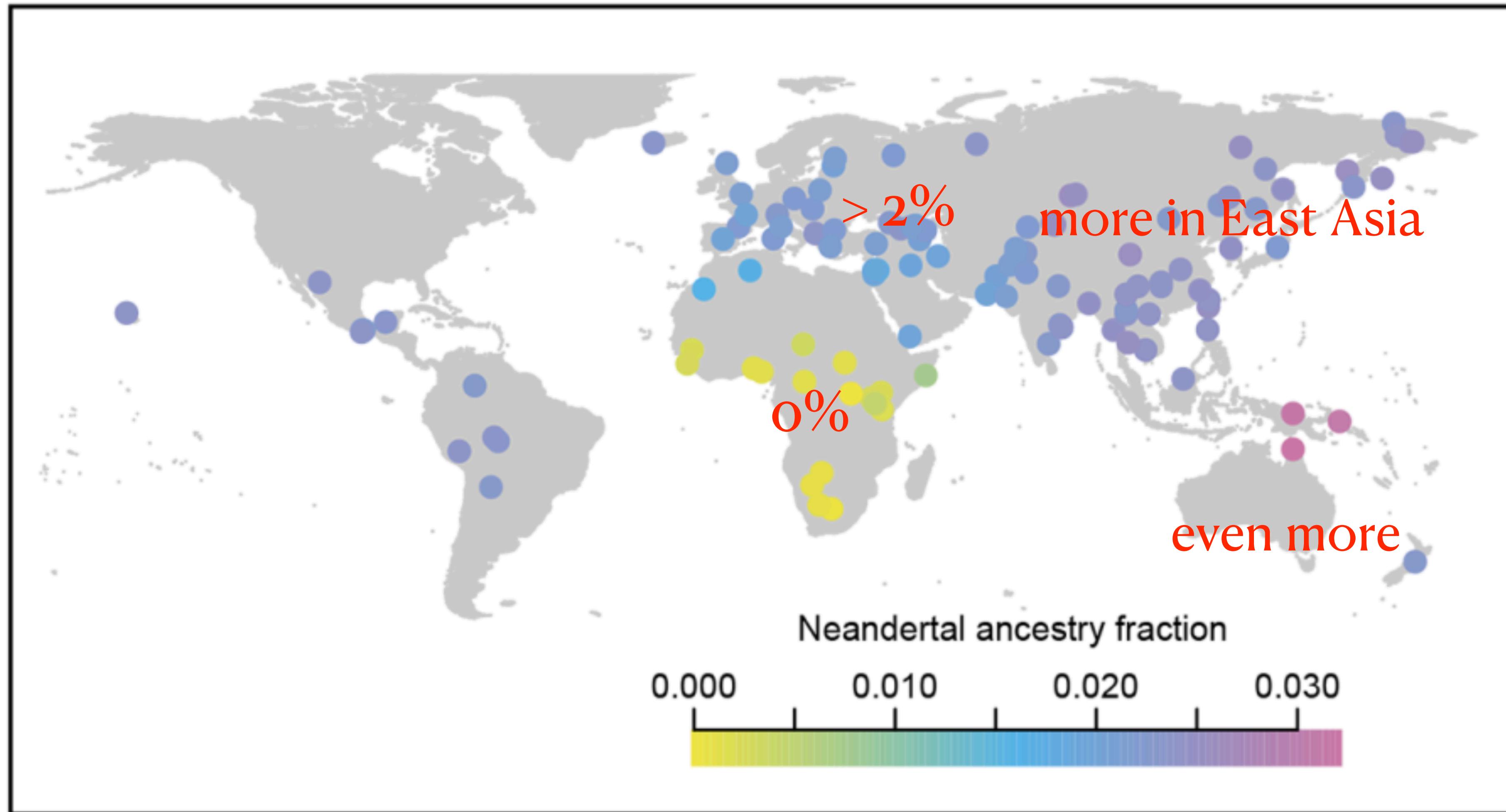
Geographic distribution of Neanderthal ancestry in the world



Geographic distribution of Neanderthal ancestry in the world



Geographic distribution of Neanderthal ancestry in the world



Exercises?

1. Try changing the order of samples in a simple f_4 or D calculation and convince yourselves that many orderings (which ones?) return the same result, or differ up to a sign. Why is that?
2. Run the "outgroup" f_3 statistic on the data we used in this lecture. You can use the example code from the "official" *admixr* tutorial [1].
3. What happens when you change the African in the f_4 -ratio calculation (use Africans listed in the data/samples.tsv table and replace the Dinka).
 - Do you see the same amount of Neanderthal ancestry in, say, French individual even with different Africans? Compare what you found with the results shown in Fig. S4 of [2].
4. Try to reproduce Fig. S2A or Fig. S6 from [2] using f_4 or D statistic.

[1] <https://bodkan.net/admixr/articles/tutorial.html#f3-statistic-1>

[2] Petr *et al.* (PNAS 2019)

References

Ancient Admixture in Human History, Patterson *et al.* (GENETICS 2012)

Admixture, Population Structure, and F-Statistics Benjamin M. Peter (GENETICS 2016)

***admixr*—R package for reproducible analyses using ADMIXTOOLS**, Petr *et al.* (Bioinformatics 2019)
& the tutorial at <https://www.bodkan.net/admixr>

R for Data Science, Wickham and Grolemund - <https://r4ds.had.co.nz/> (O'Reilly 2017)