

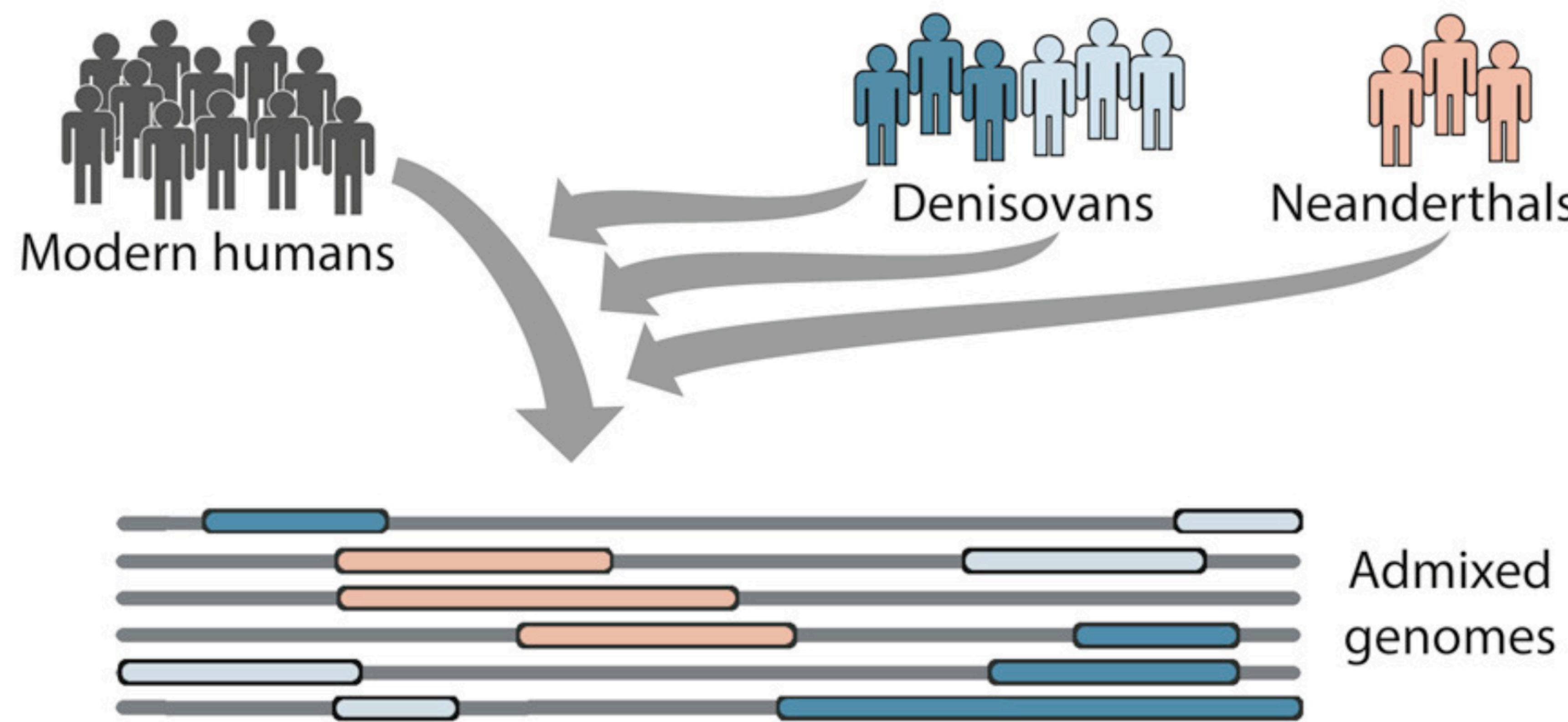
The Evolutionary History of Neanderthal and Denisovan Y chromosomes

Evolutionary Genetics of Humans and Other Primates Journal Club

Martin Petr & Janet Kelso

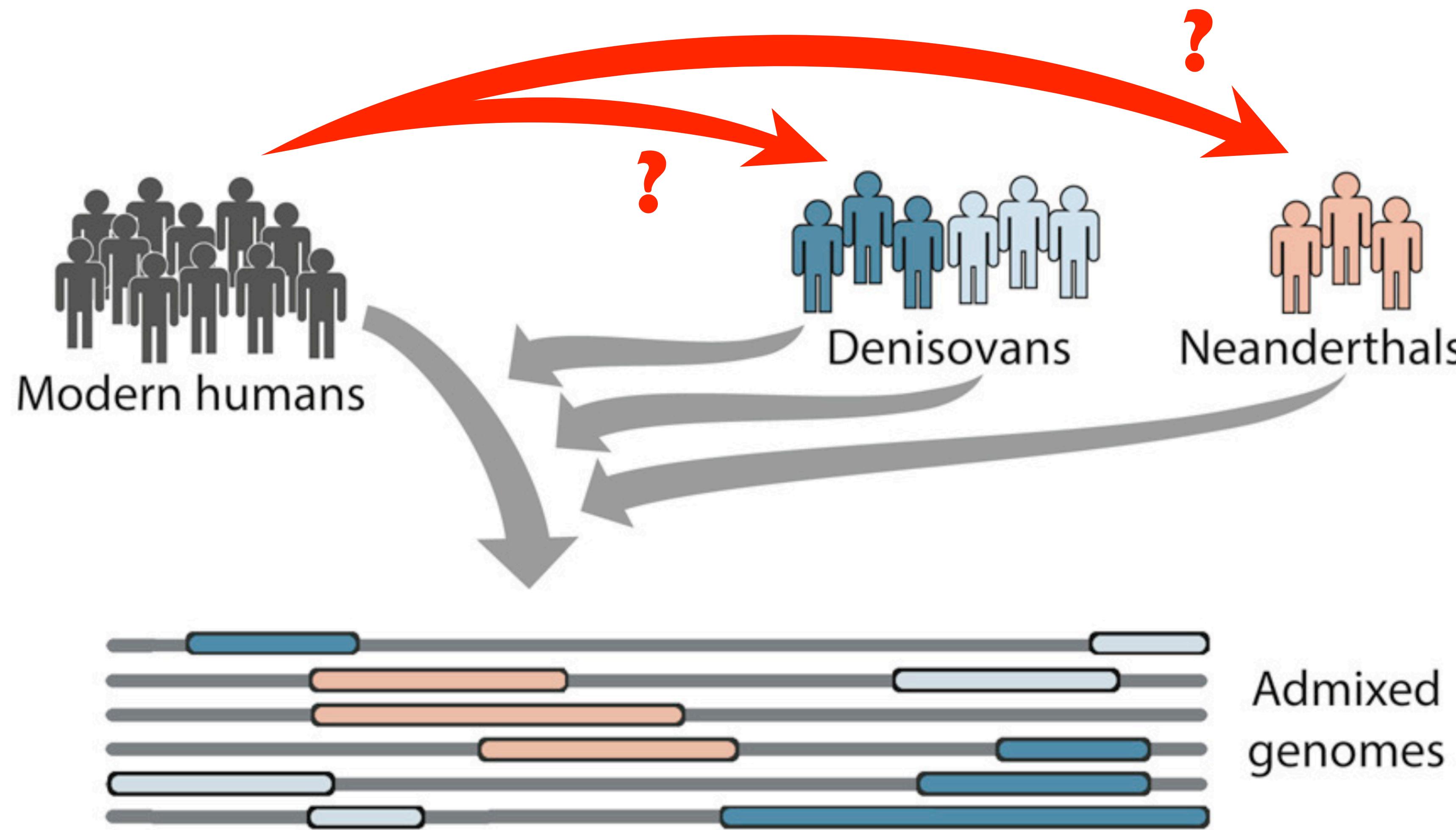
Minerva Research Group for Bioinformatics
Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany

Admixture from archaic humans into modern humans



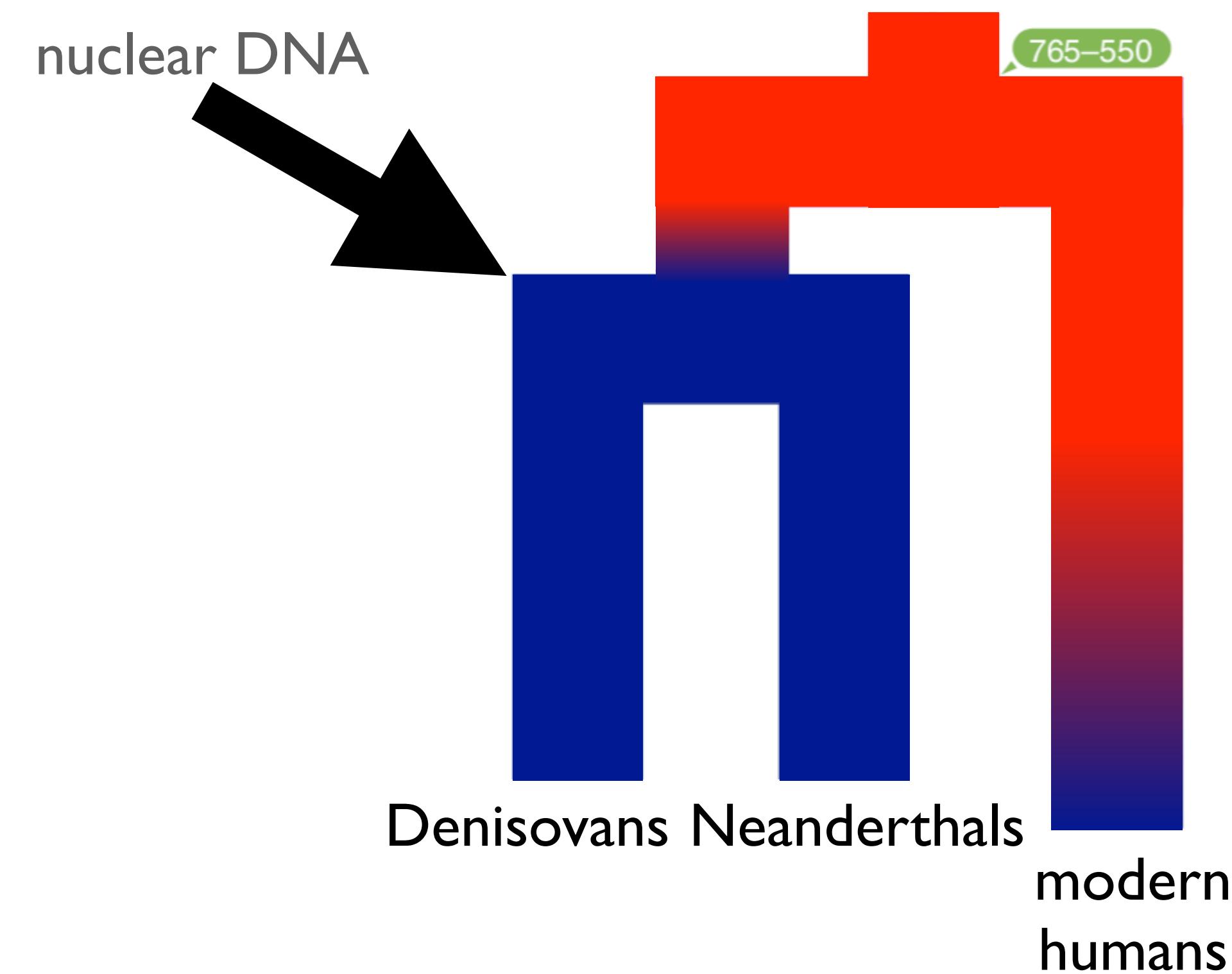
modified from Browning *et al.* (Cell, 2018)

Admixture from modern humans into archaic humans



modified from Browning *et al.* (Cell, 2018)

Nuclear vs mitochondrial DNA discrepancy

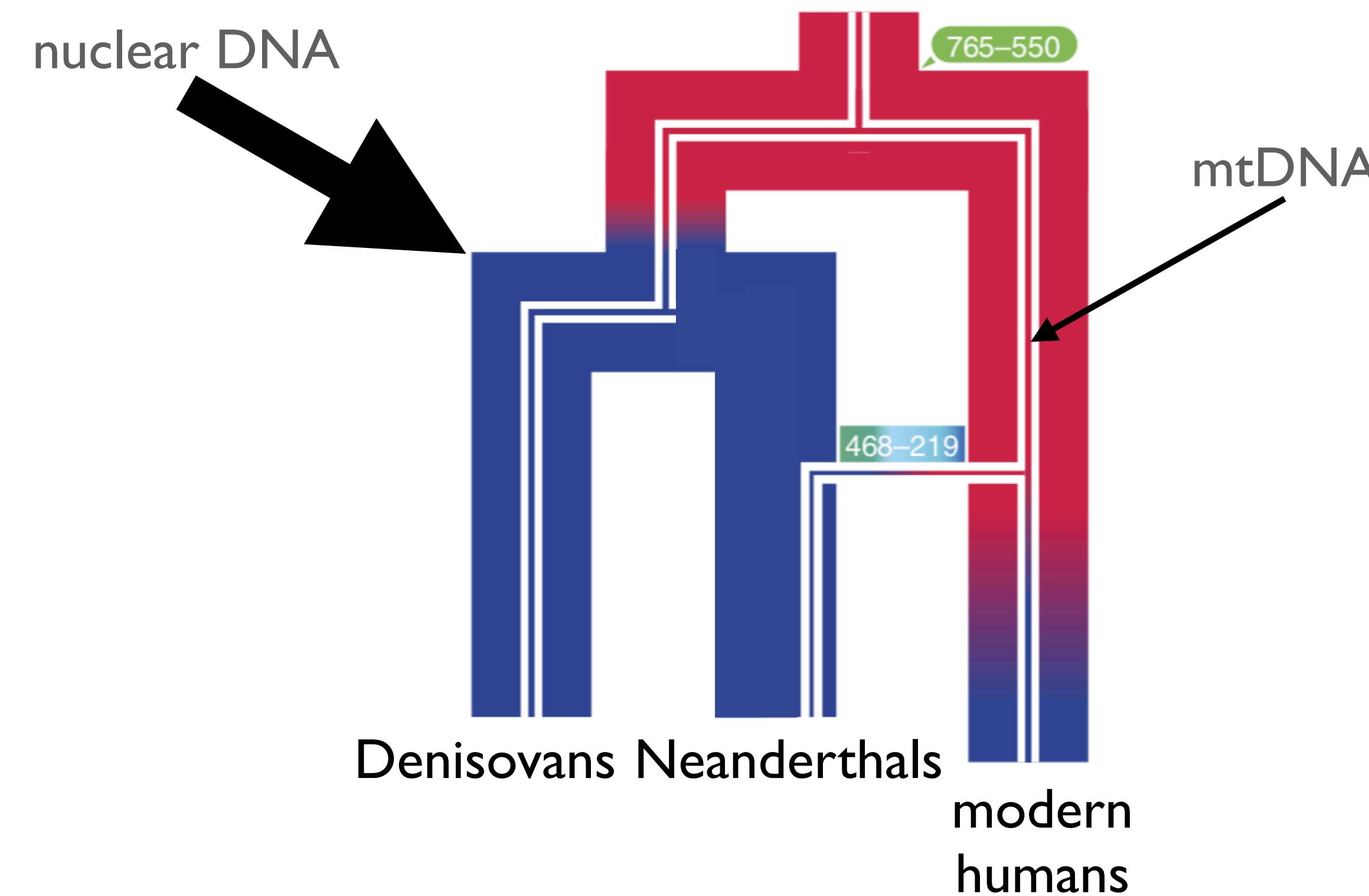


Meyer *et al.* (Nature, 2014)

Meyer *et al.* (Nature, 2016)

modified from Posth *et al.* (Nat Comm, 2017)

Nuclear vs mitochondrial DNA discrepancy

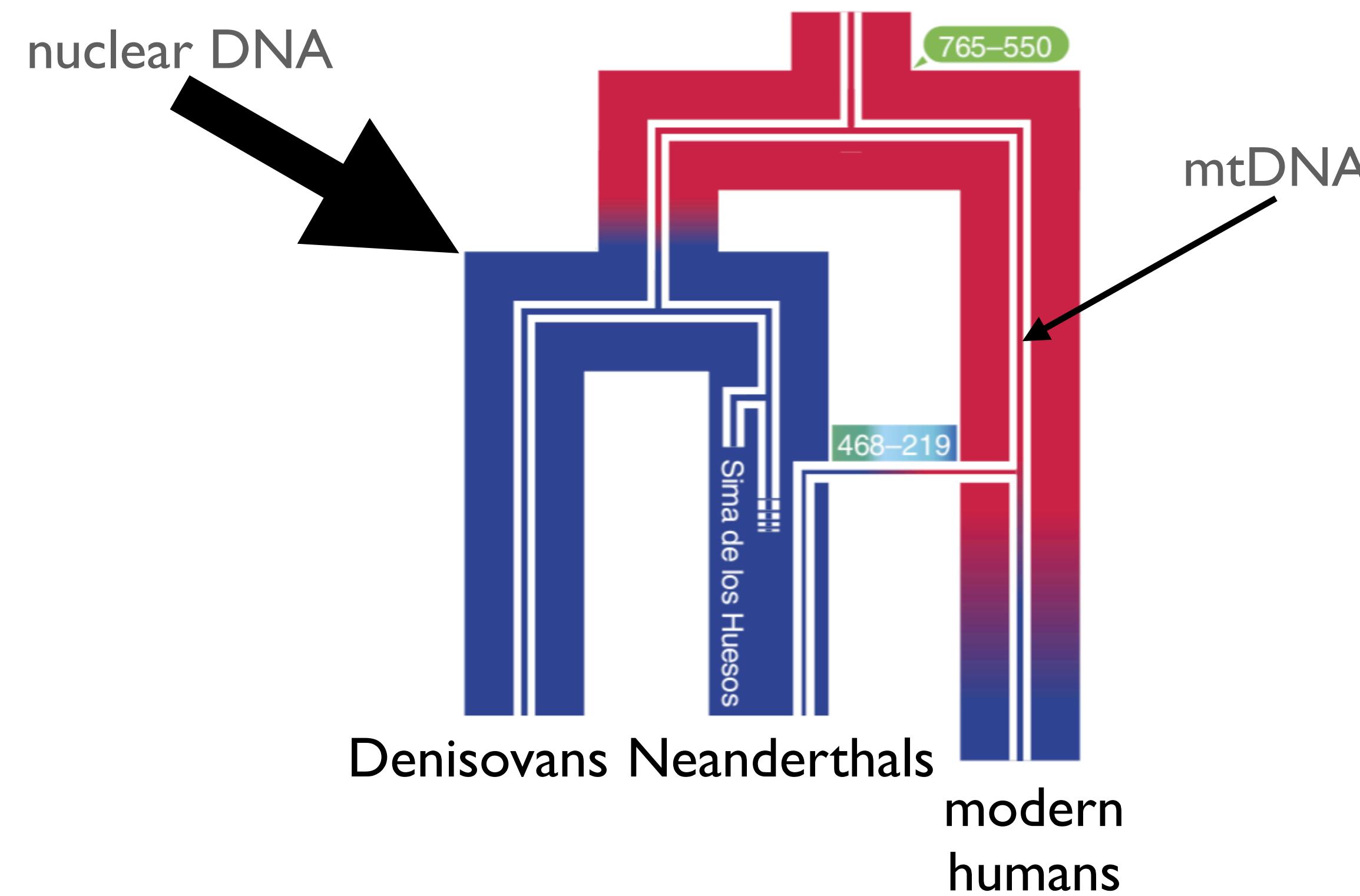


Meyer *et al.* (Nature, 2014)

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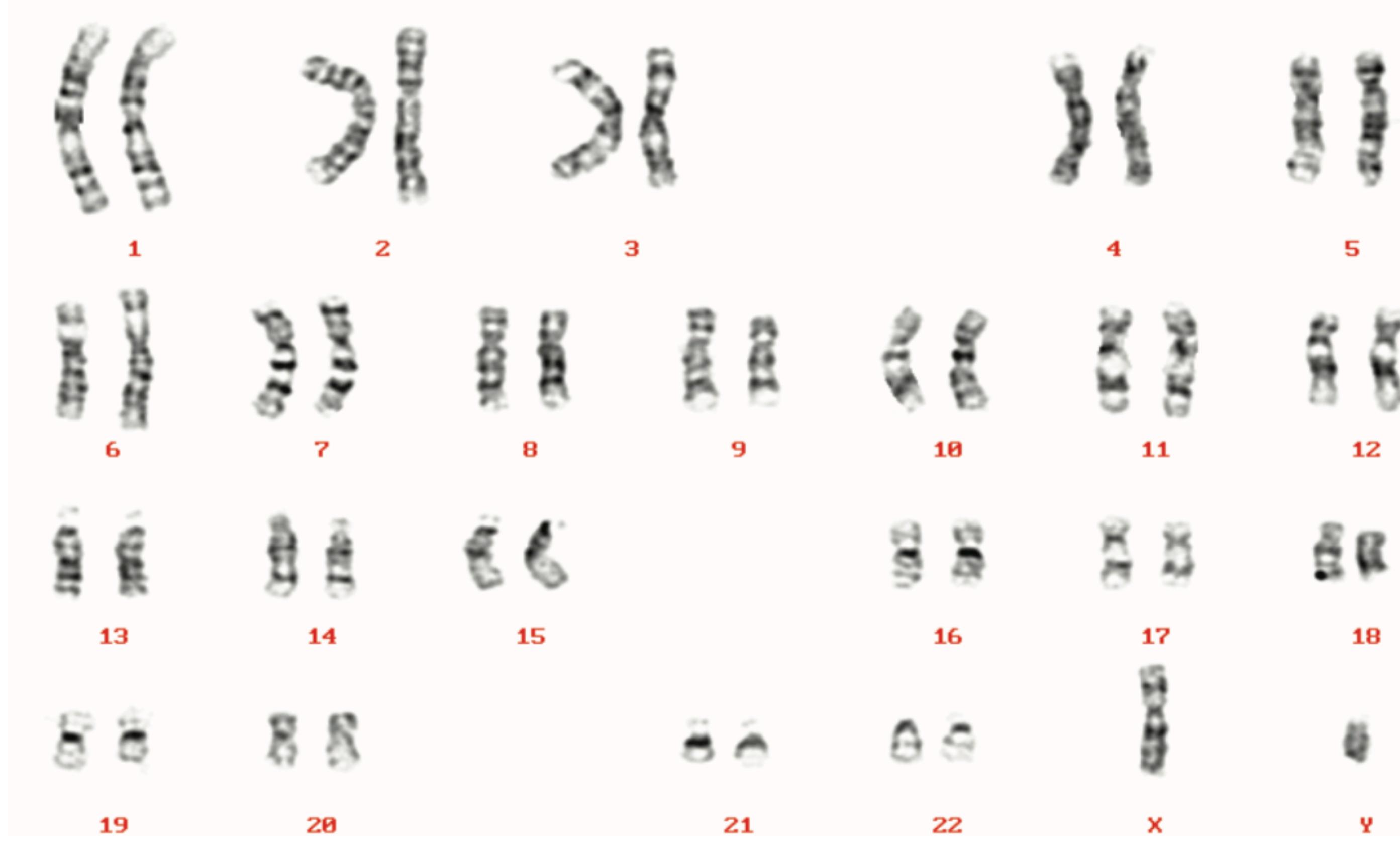
Nuclear vs mitochondrial DNA discrepancy

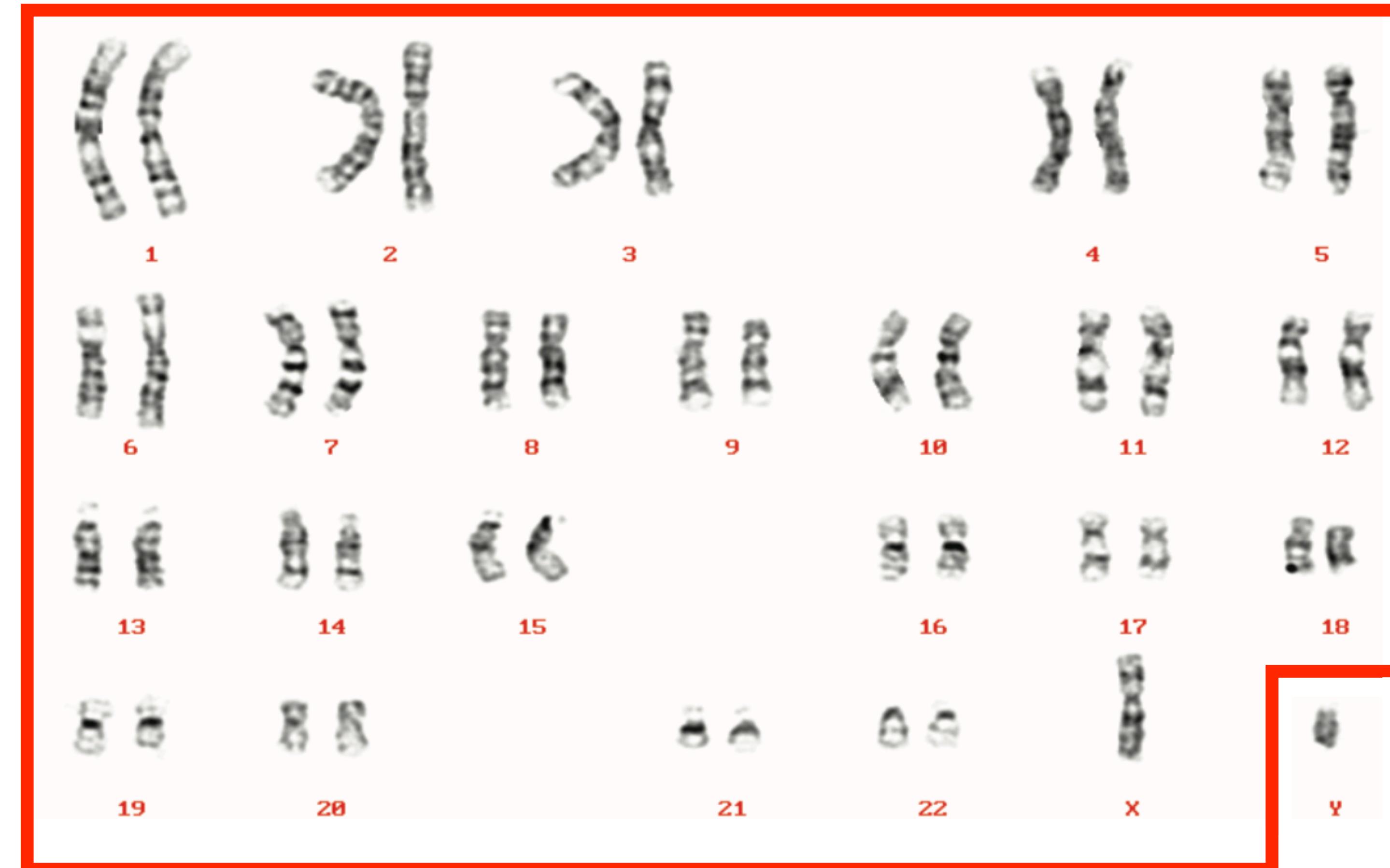


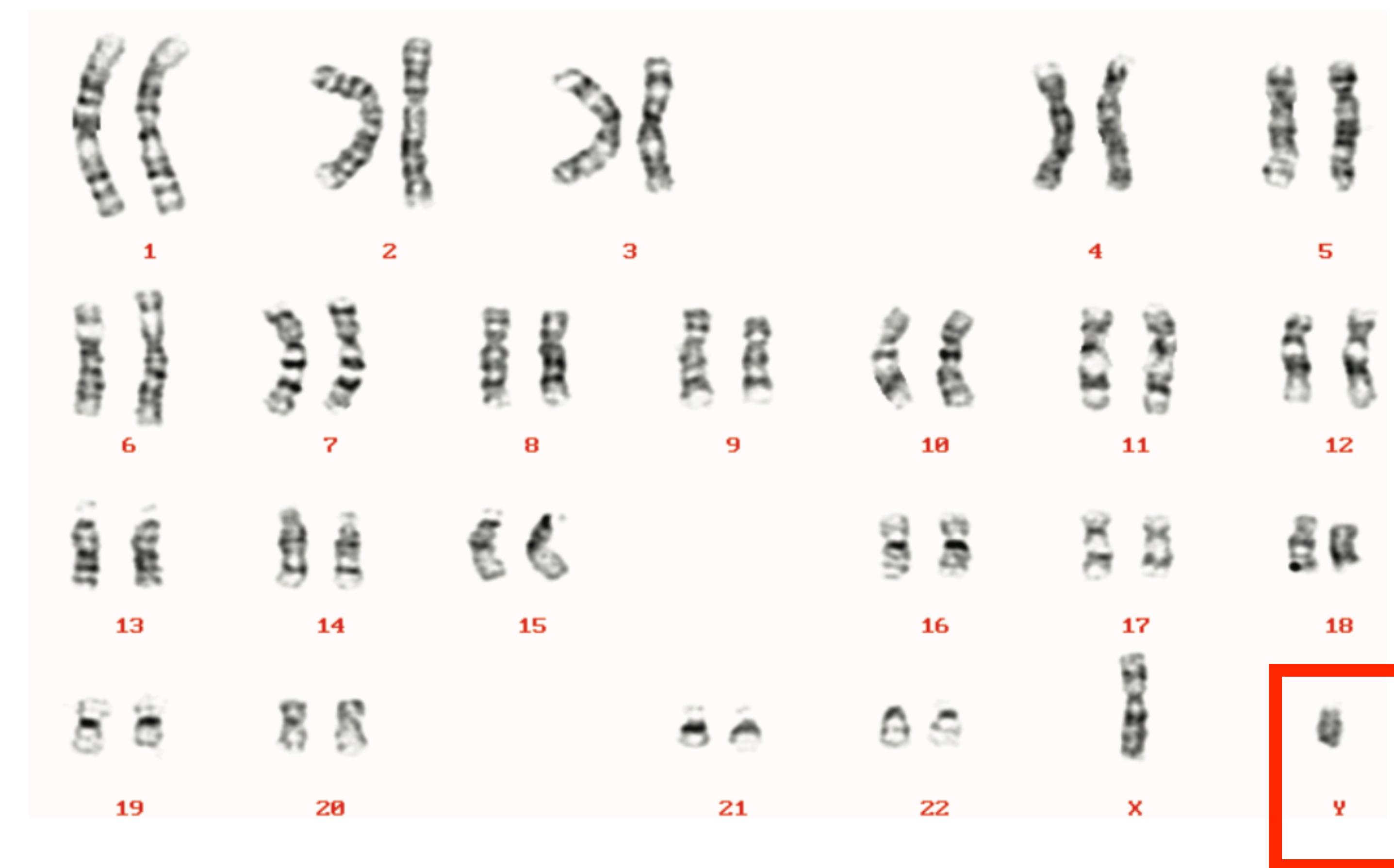
Meyer *et al.* (Nature, 2014)

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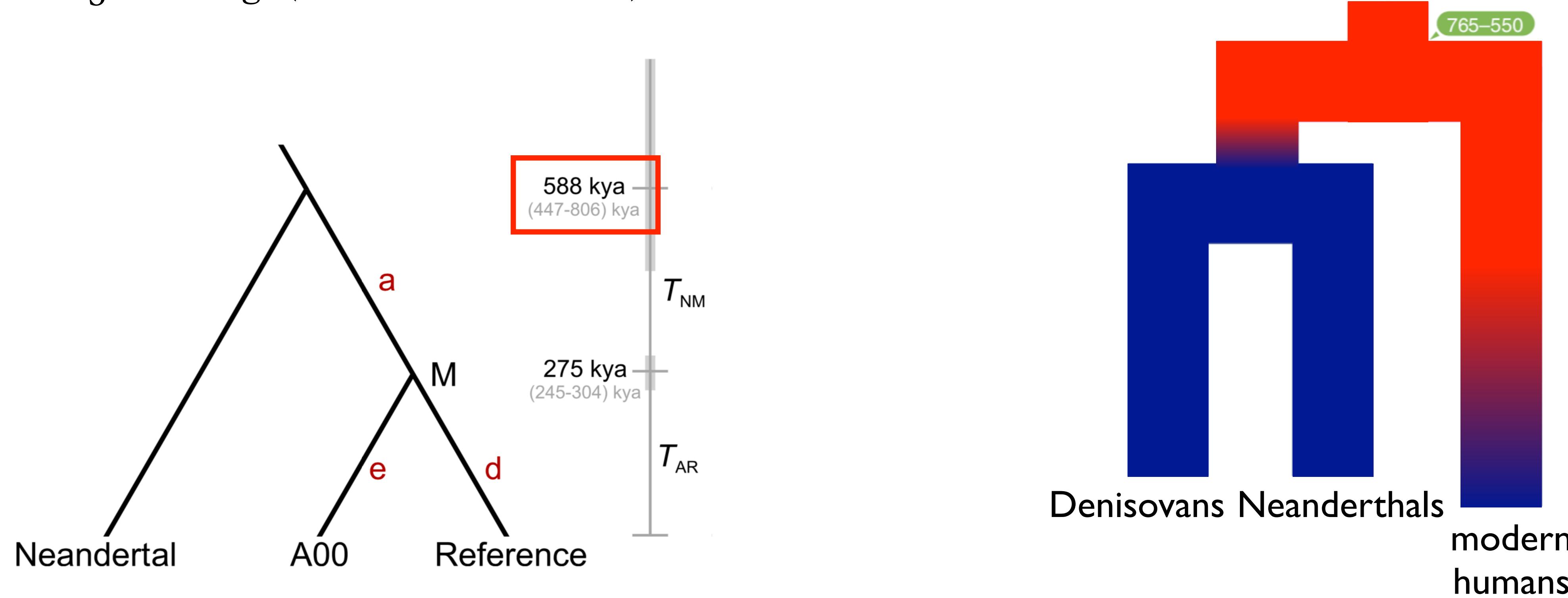




First Neanderthal Y chromosome study

118 kb of *El Sidrón* 1253 exome sequence

~3X coverage (even 1X sites included)



Male archaic humans sampled to date



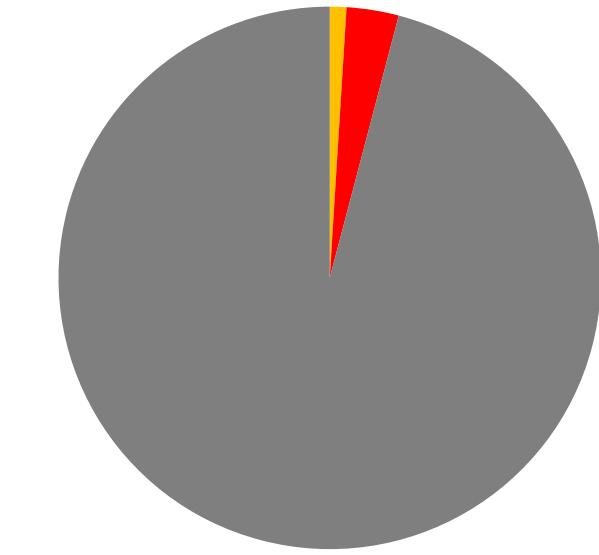
El Sidrón 1253: Castellano *et al.* (PNAS, 2014)

Denisova 4, Denisova 8: Sawyer and Renaud *et al.* PNAS (2015)

Spy 94a, Mezmaiskaya 2: Hajdinjak *et al.* (Nature, 2018)

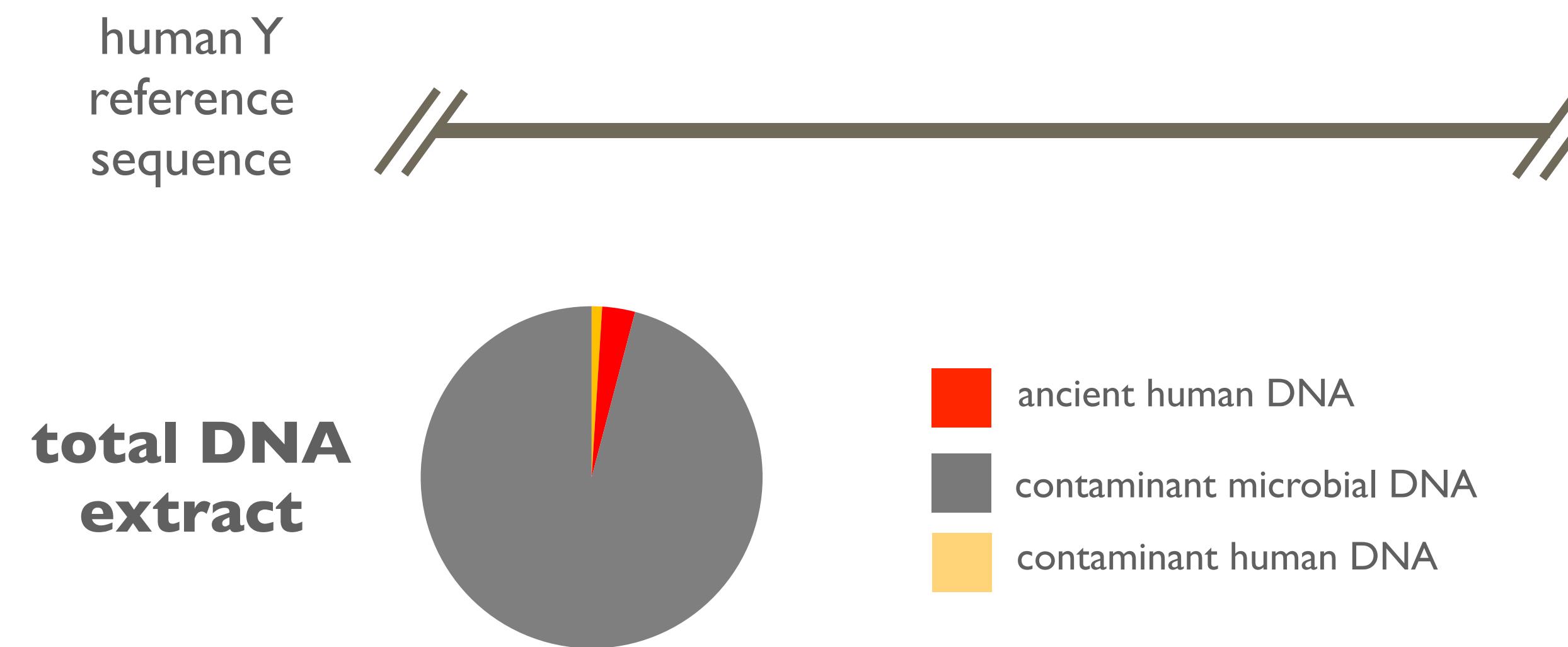
Fig. 1A

**total DNA
extract**

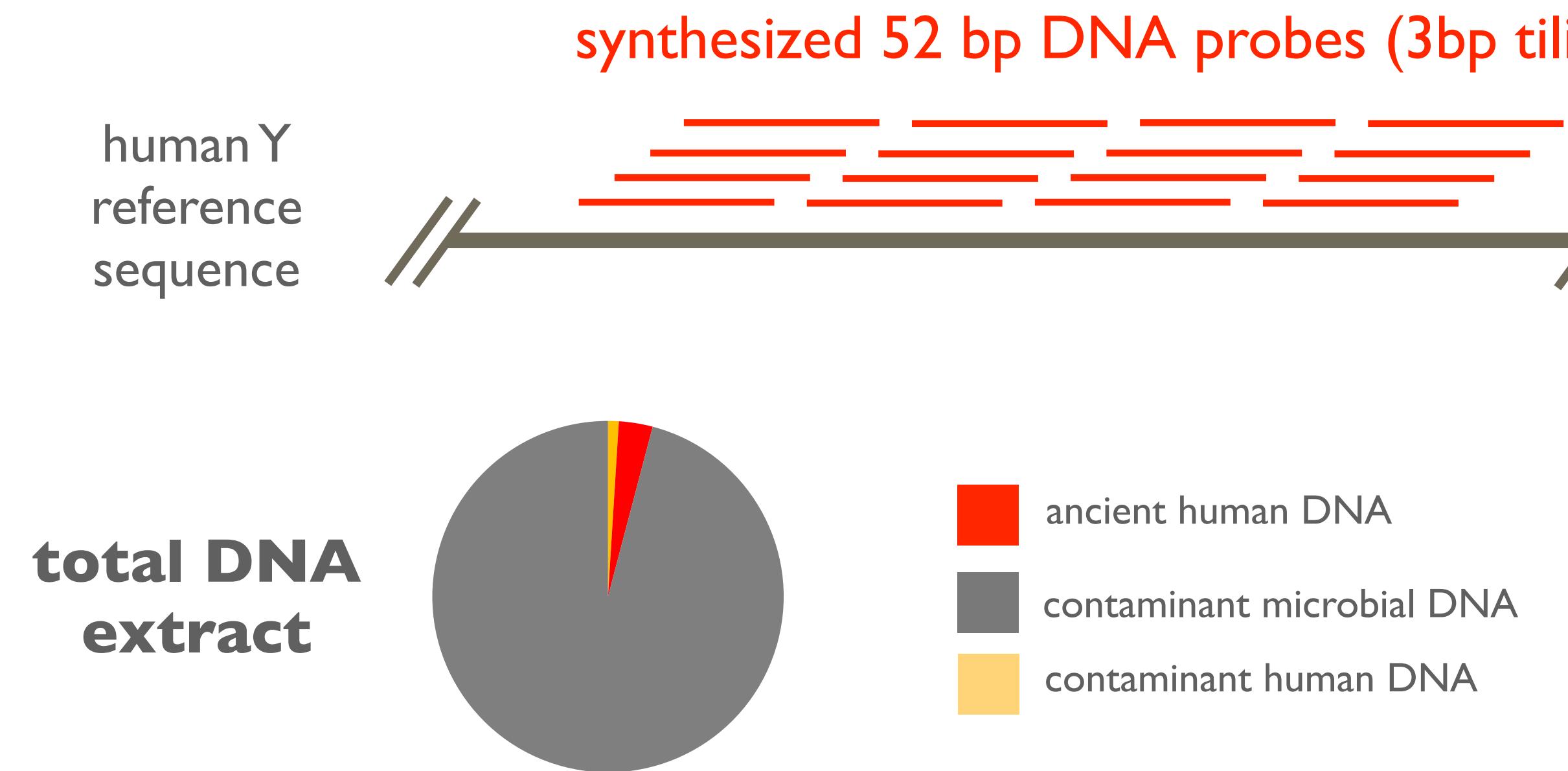


- ancient human DNA
- contaminant microbial DNA
- contaminant human DNA

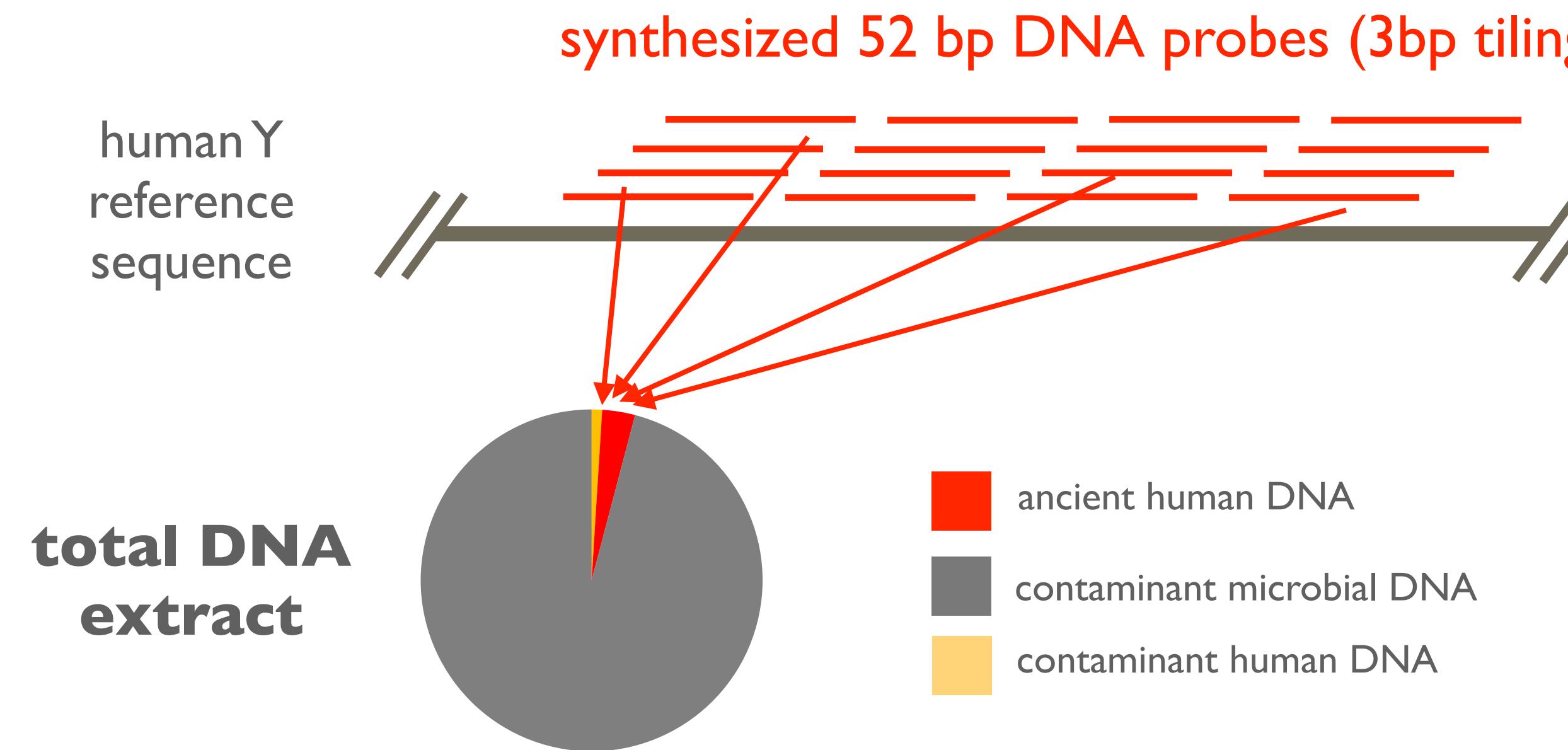
Whole chromosome capture



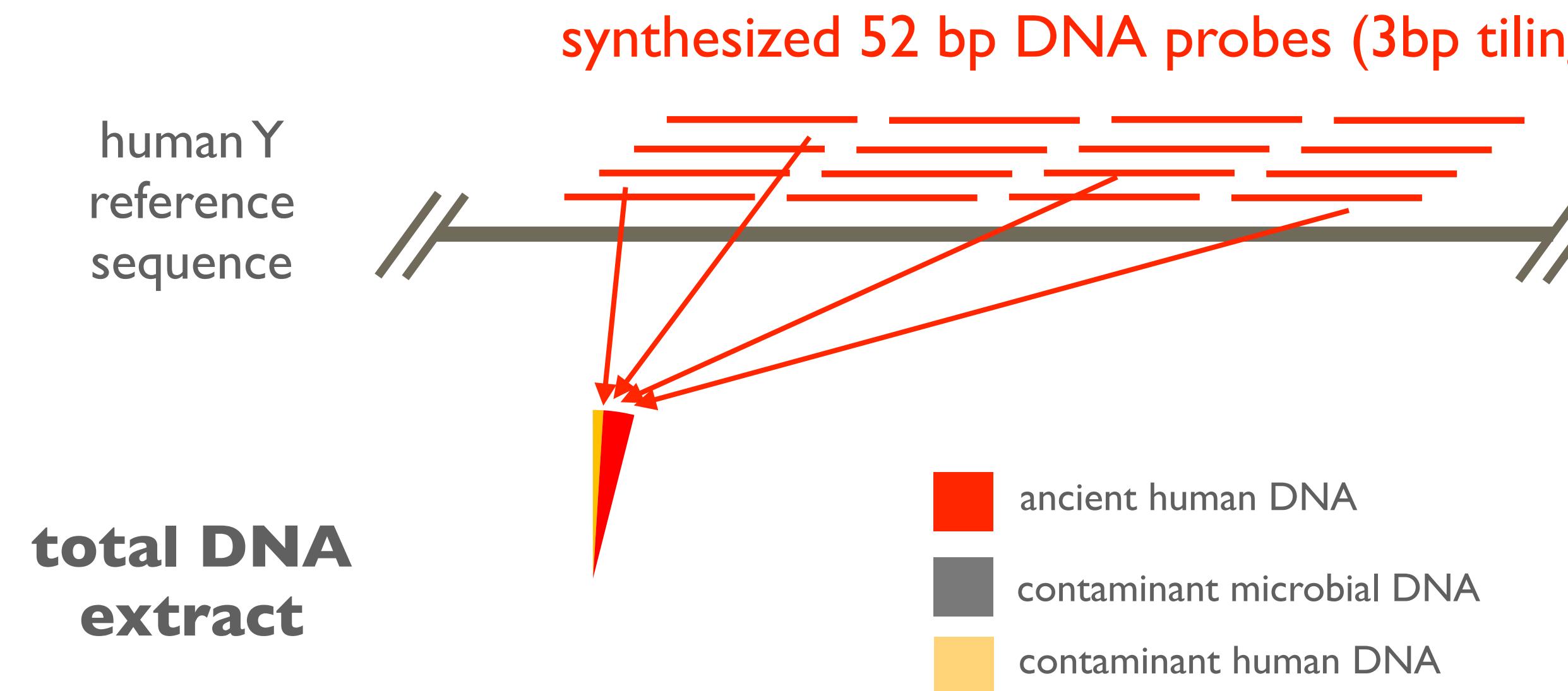
Whole chromosome capture



Whole chromosome capture

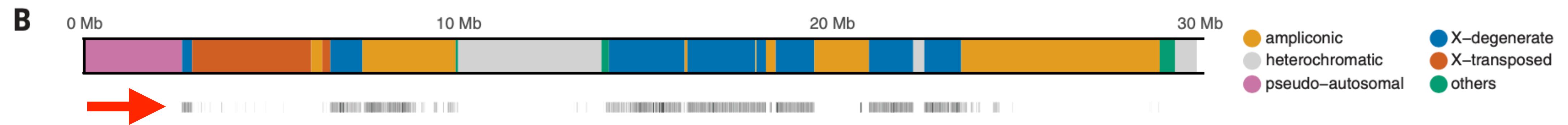


Whole chromosome capture



Sequencing coverage

~6.9 Mb capture target (usable for mapping short ancient DNA molecules)



Sequencing coverage

~6.9 Mb capture target (usable for mapping short ancient DNA molecules)

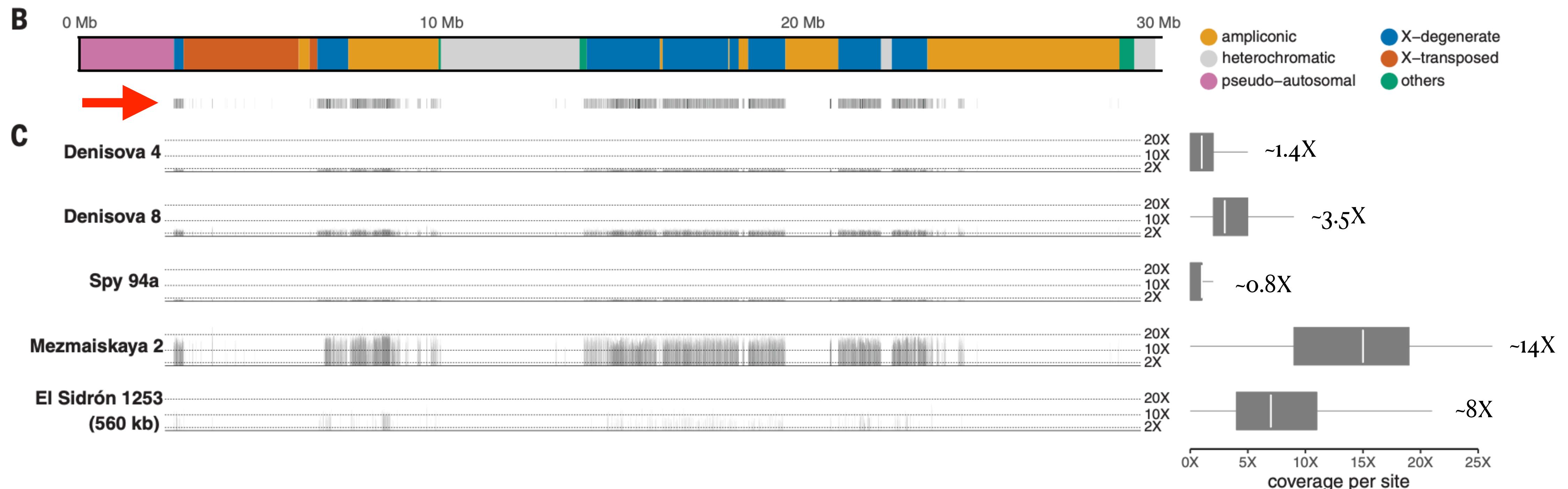


Fig. 1B, C

Quality control

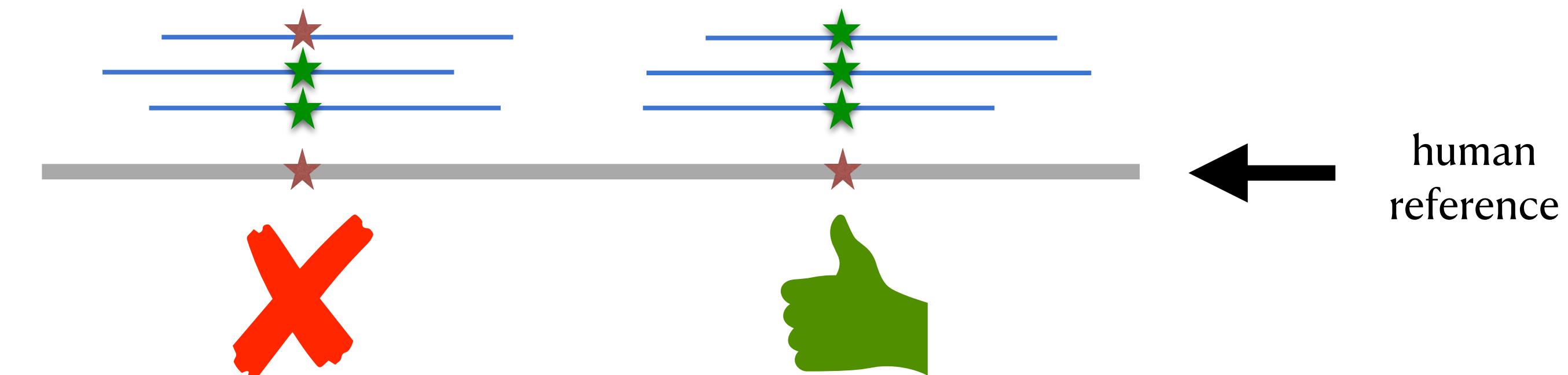
- ancient DNA damage profiles
- capture bias & mapping bias
- genotype calling and filtering
- modern human contamination

Genotype calling

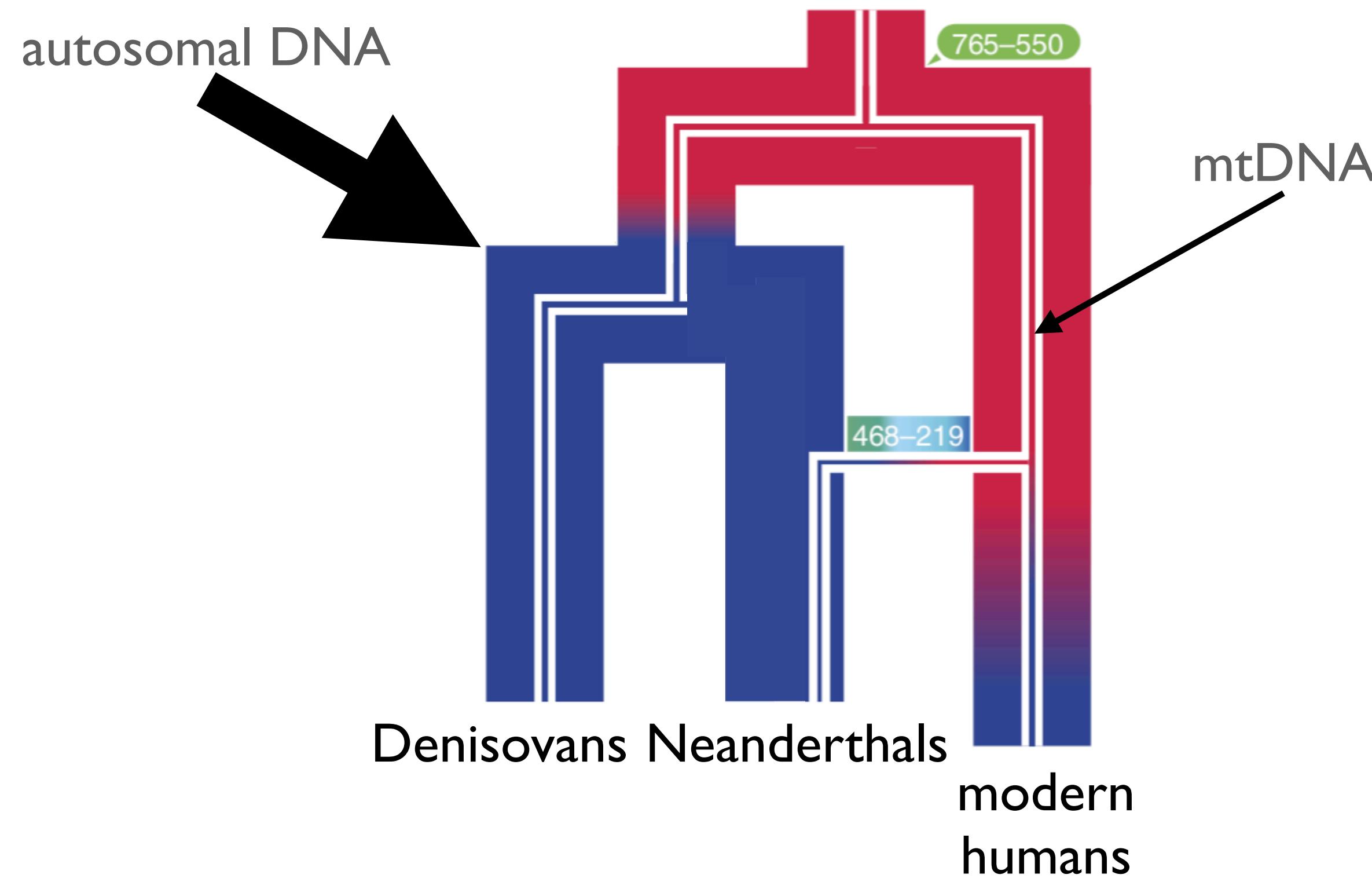
- no need to worry about false heterozygote sites
 - consider sites with ≥ 3 reads
 - genotypes called assuming $\geq 90\%$ pileup consensus

Genotype calling

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Autosomes vs mtDNA

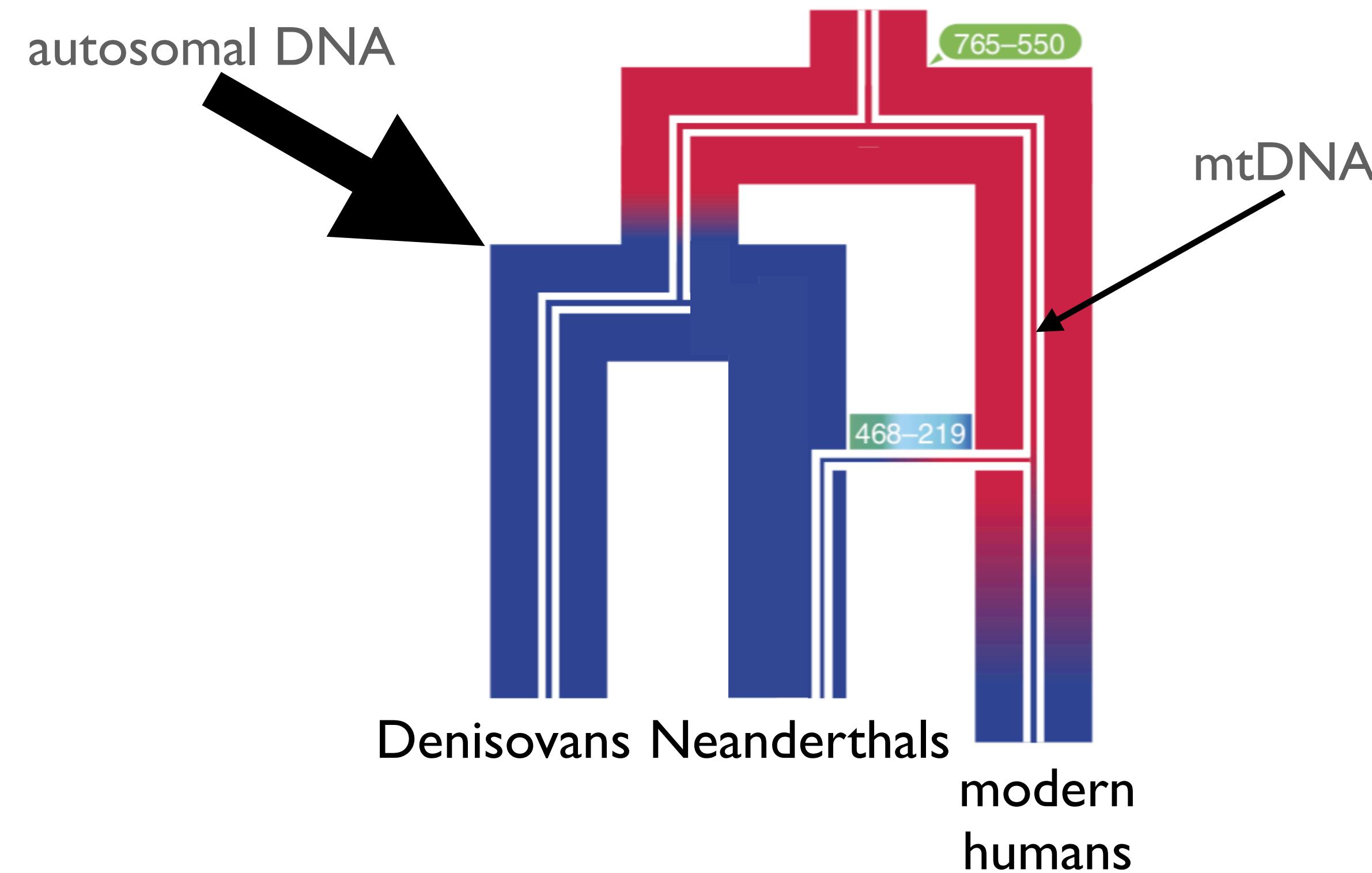


Meyer *et al.* (Nature, 2014)

Meyer *et al.* (Nature, 2016)

Posth *et al.* (Nat Comm, 2017)

Autosomes vs mtDNA vs Ychromosomes?



Meyer *et al.* (Nature, 2014)

Meyer *et al.* (Nature, 2016)

Posth *et al.* (Nat Comm, 2017)

Phylogenetic relationships

(NJ-tree - without C-T/G-A polymorphisms!)

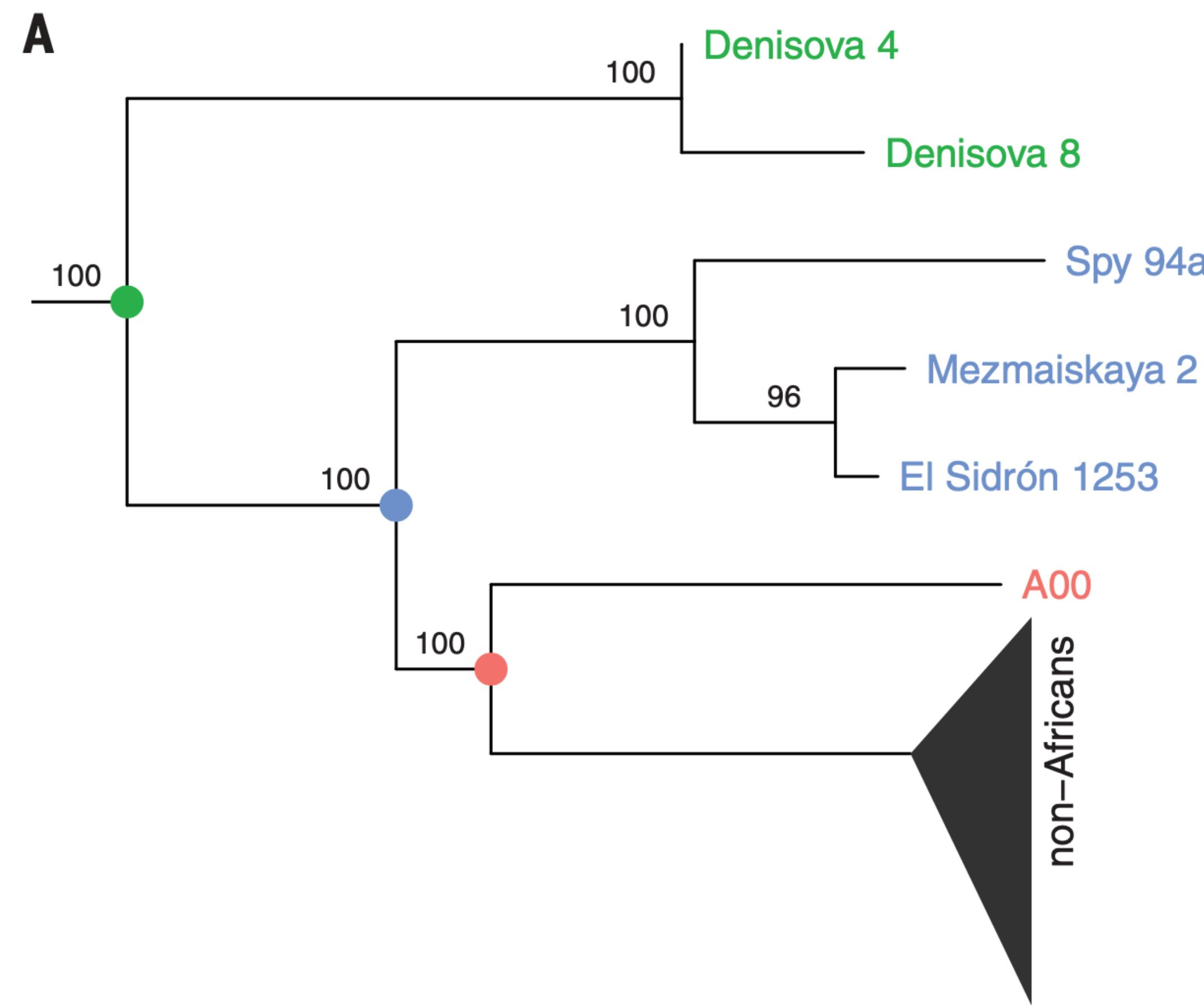


Fig. 2A

Phylogenetic relationships

(NJ-tree - without C-T/G-A polymorphisms!)

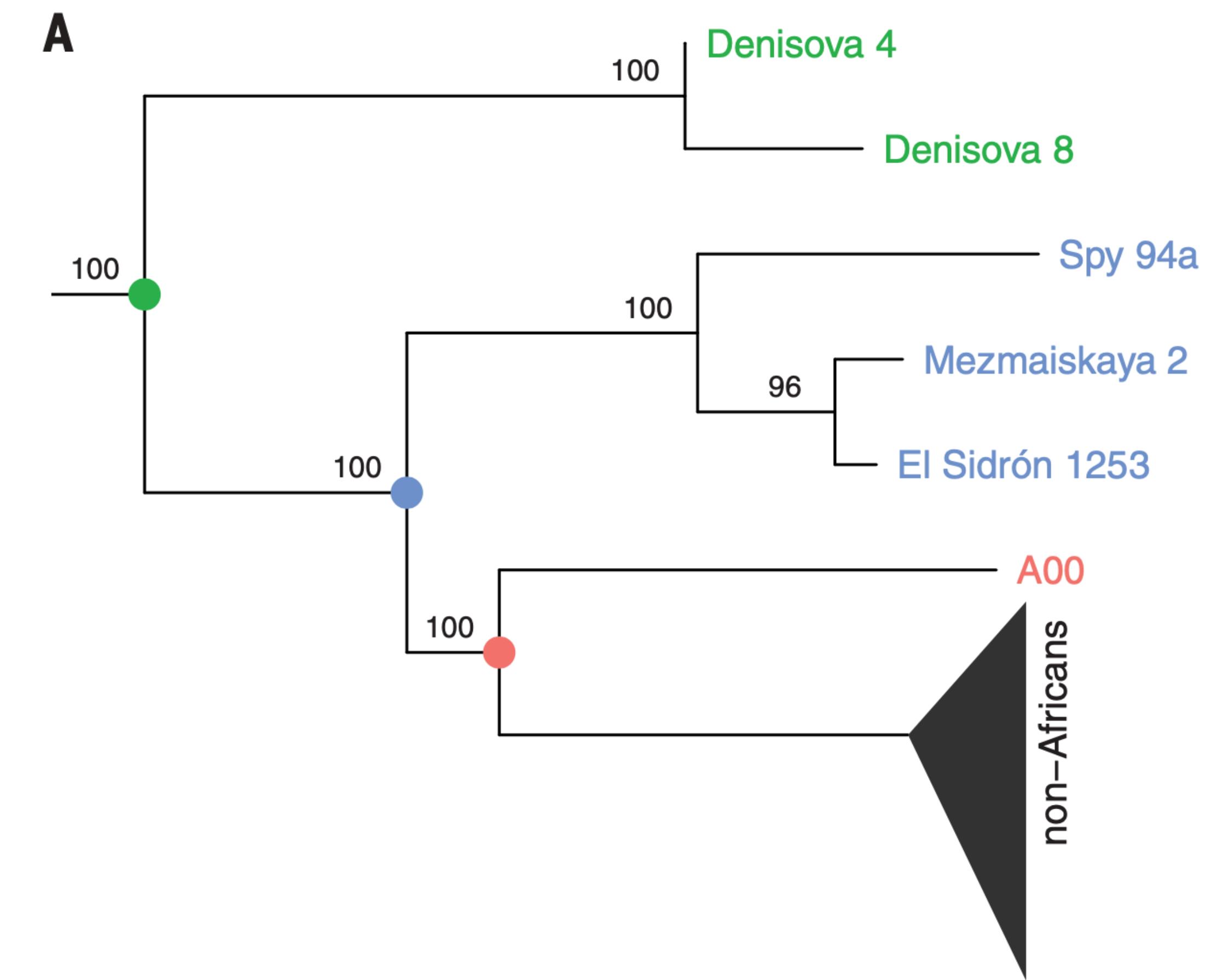
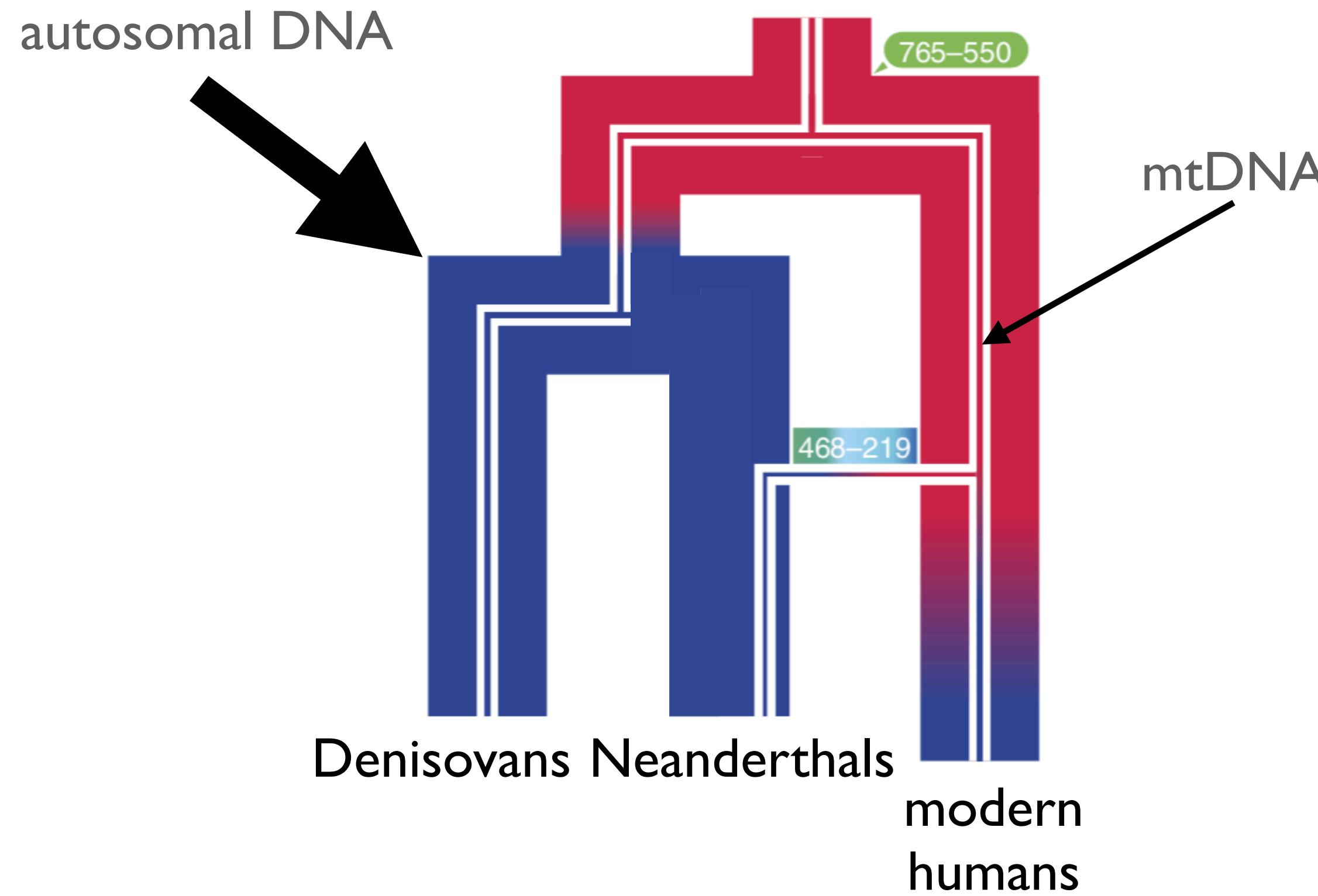
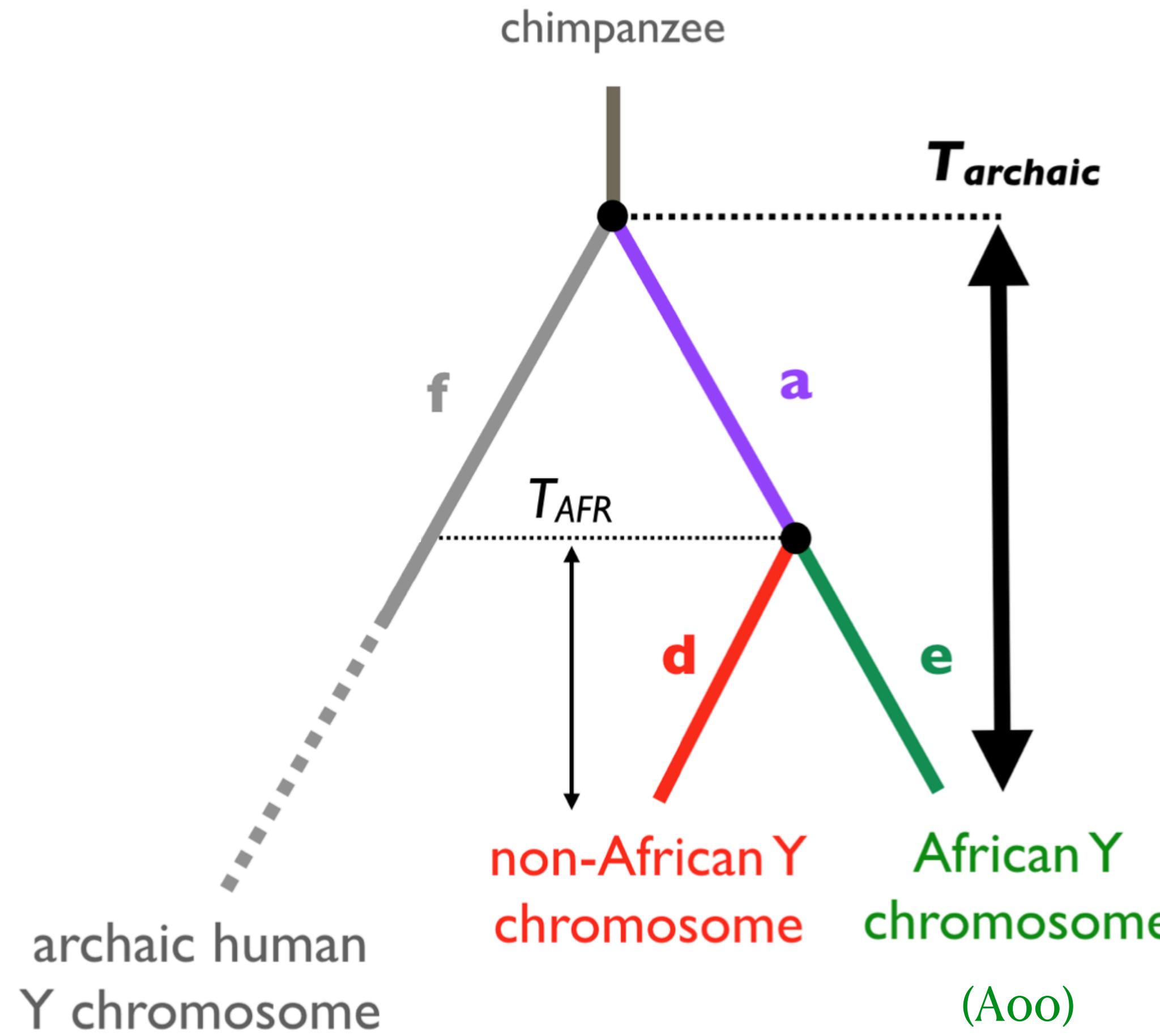


Fig. 2A

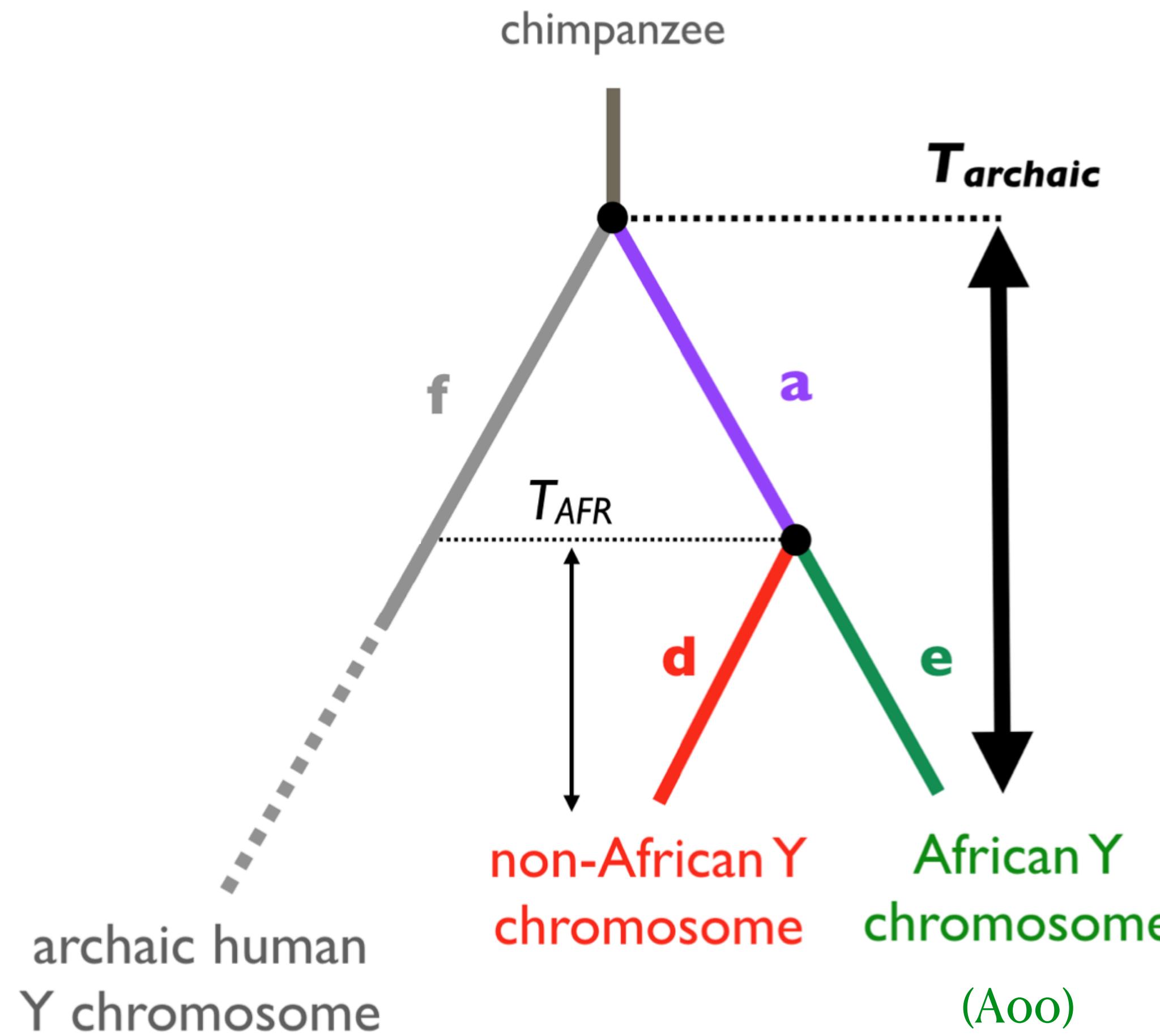
Y chromosome TMRCA estimates



method adapted from Mendez *et al.* (AJHG 2016)

Fig. S14

Y chromosome TMRCA estimates



$$TMRCA_{archaic} = \alpha \times TMRCA_{AFR}$$

method adapted from Mendez *et al.* (AJHG 2016)

Fig. S14

Y chromosome TMRCA estimates

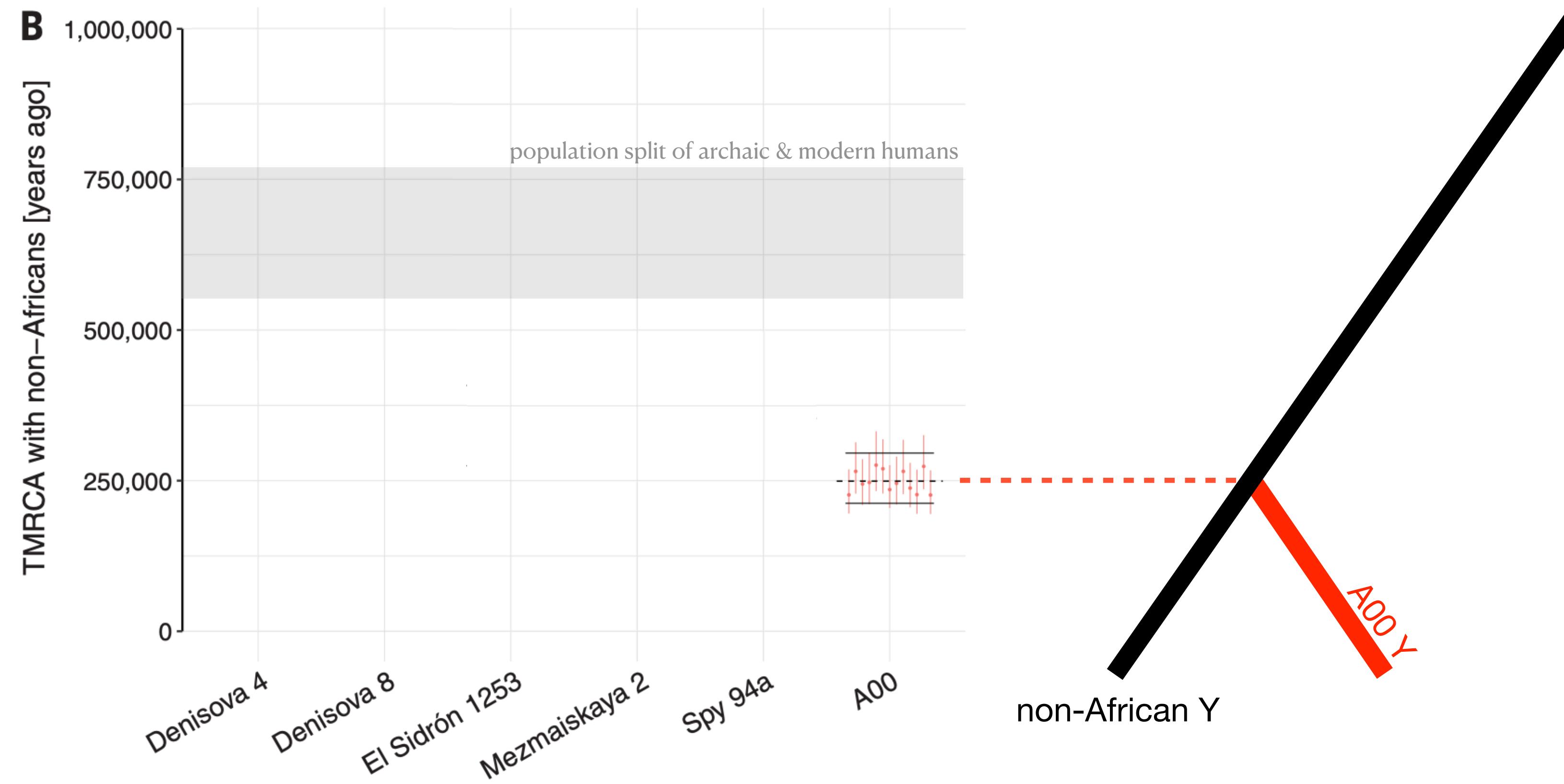


Fig. 2B

Y chromosome TMRCA estimates

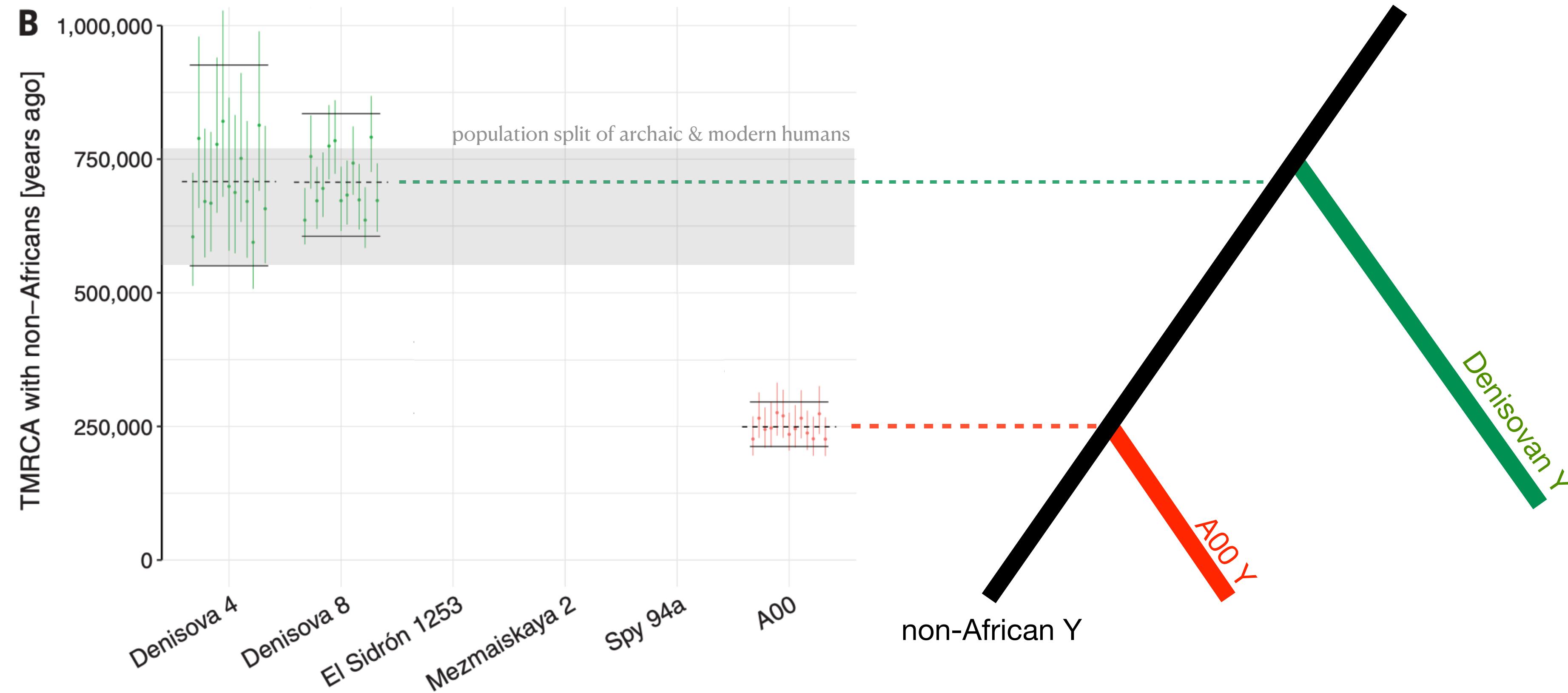


Fig. 2B

Y chromosome TMRCA estimates

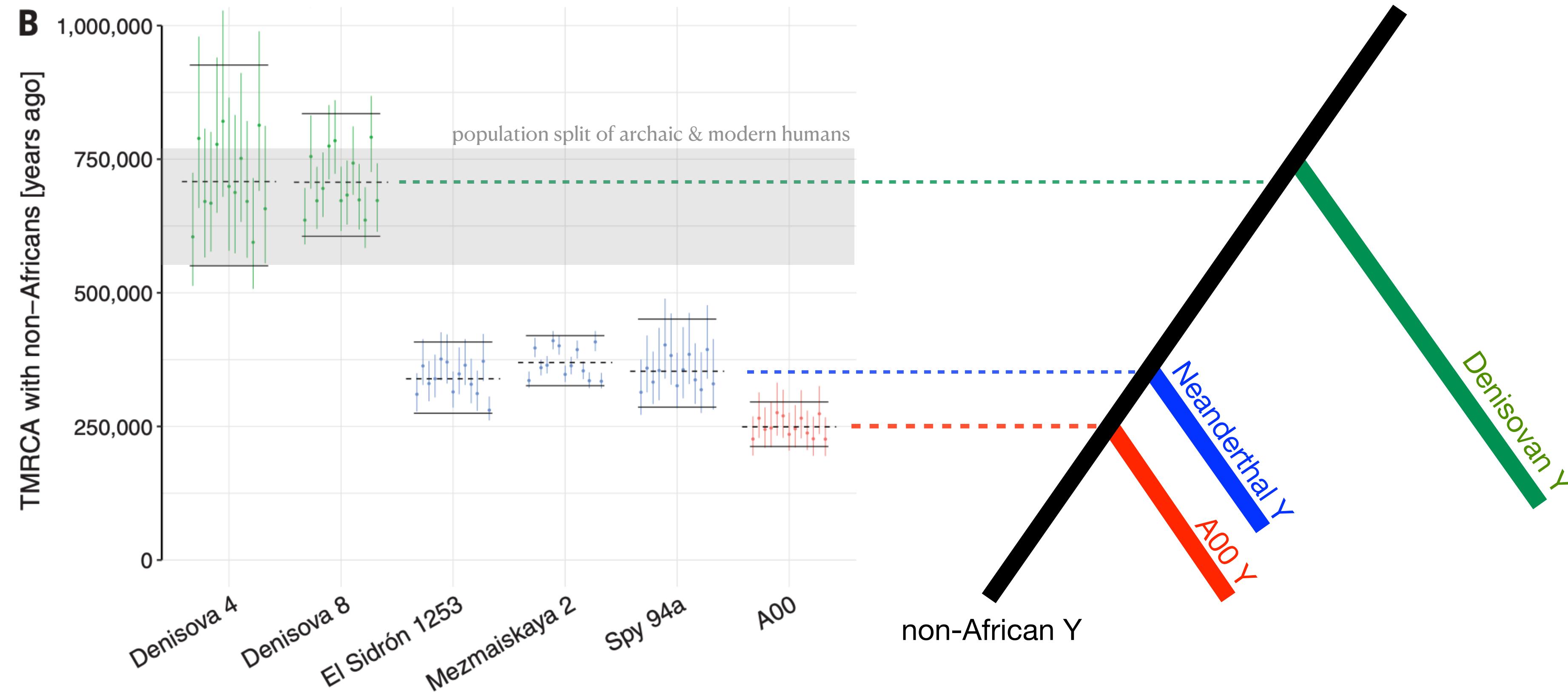
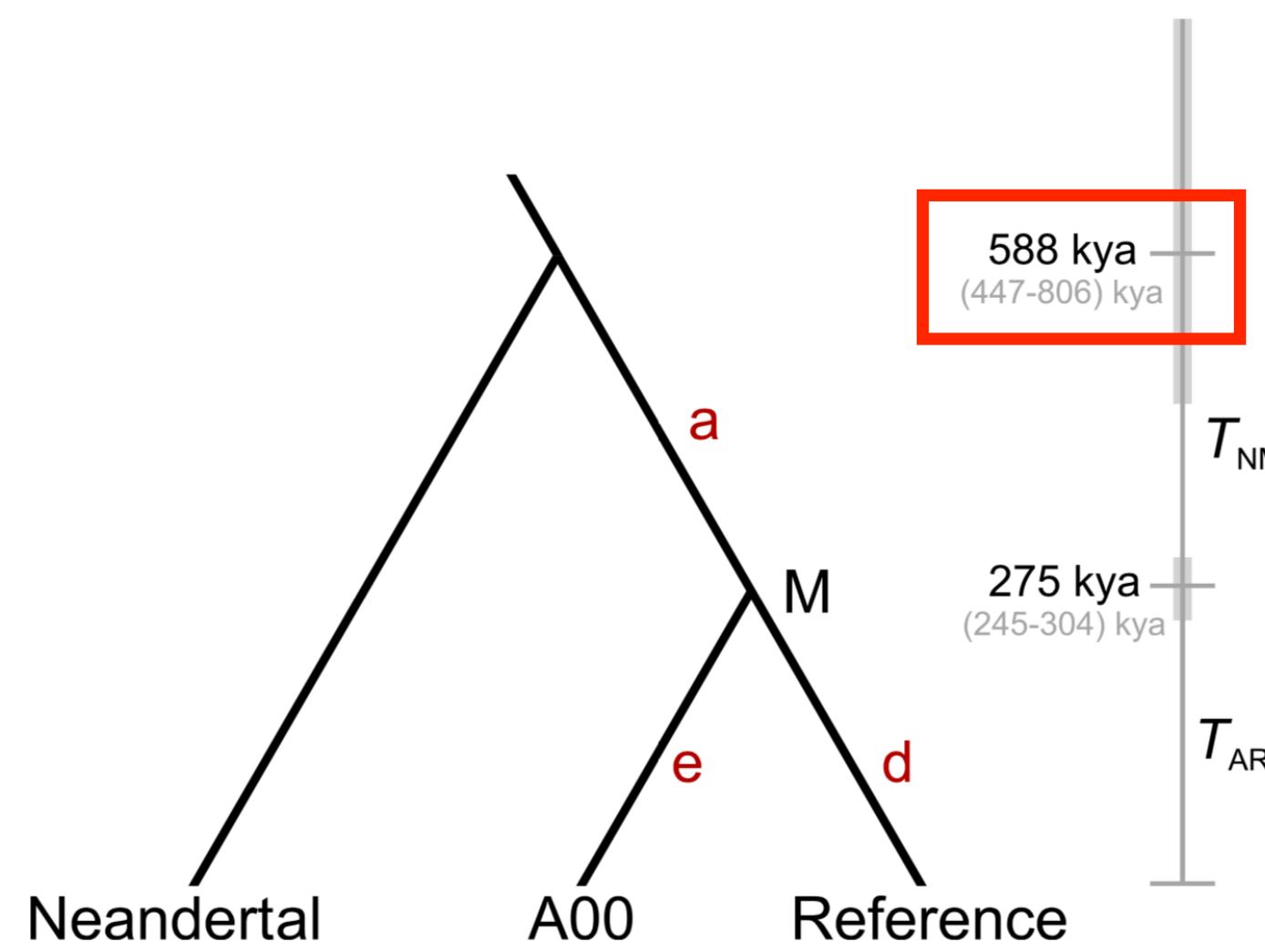
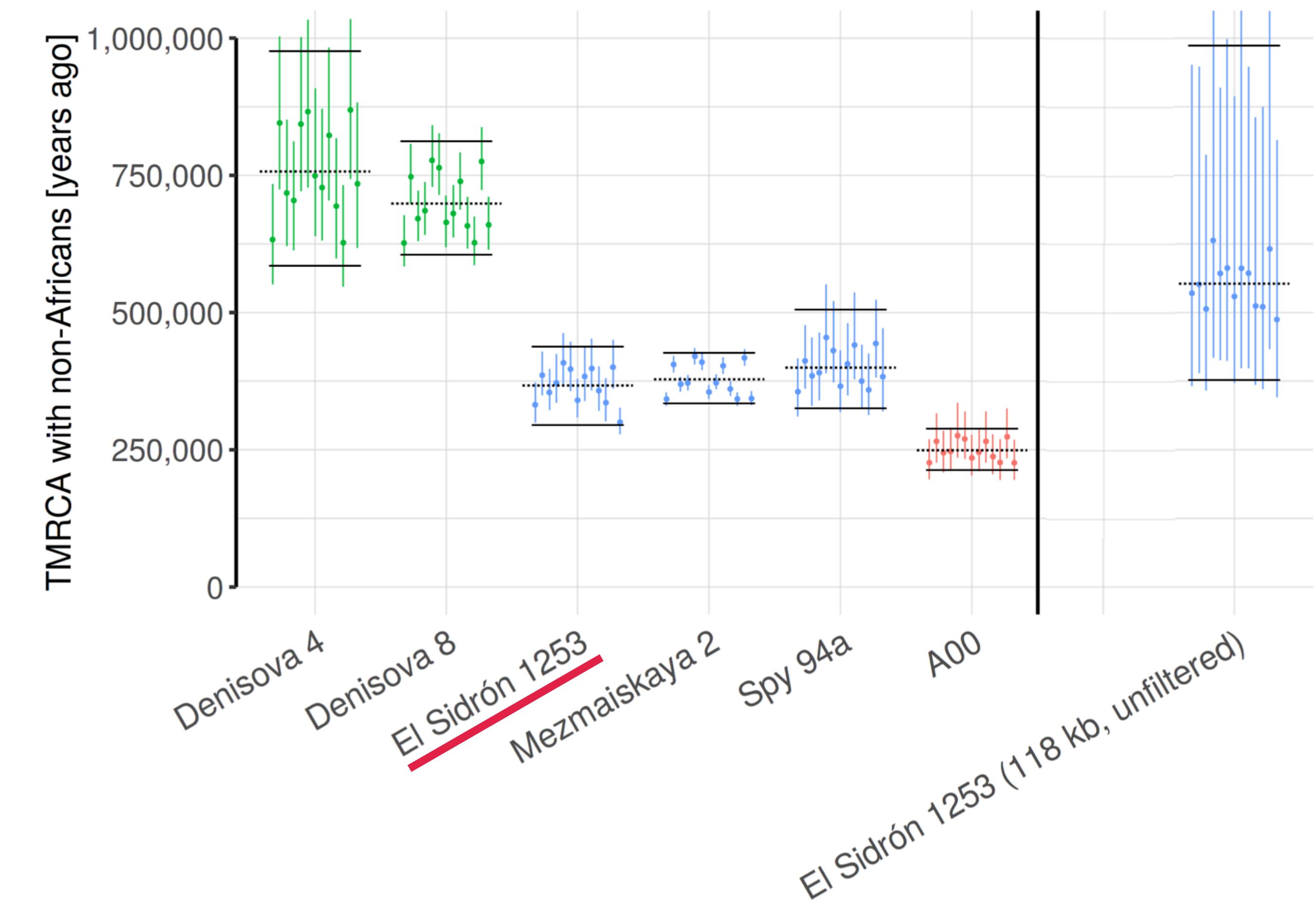
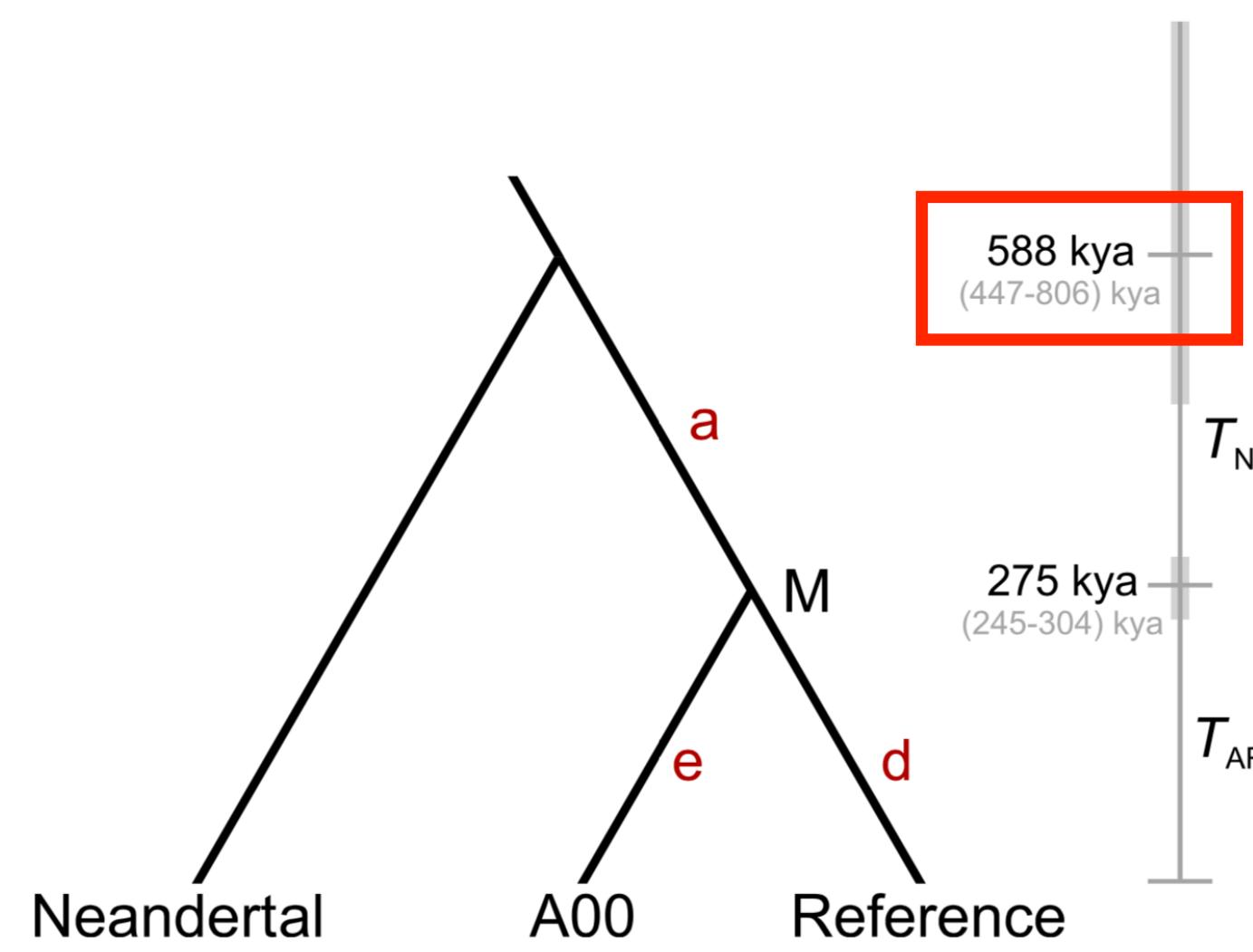


Fig. 2B

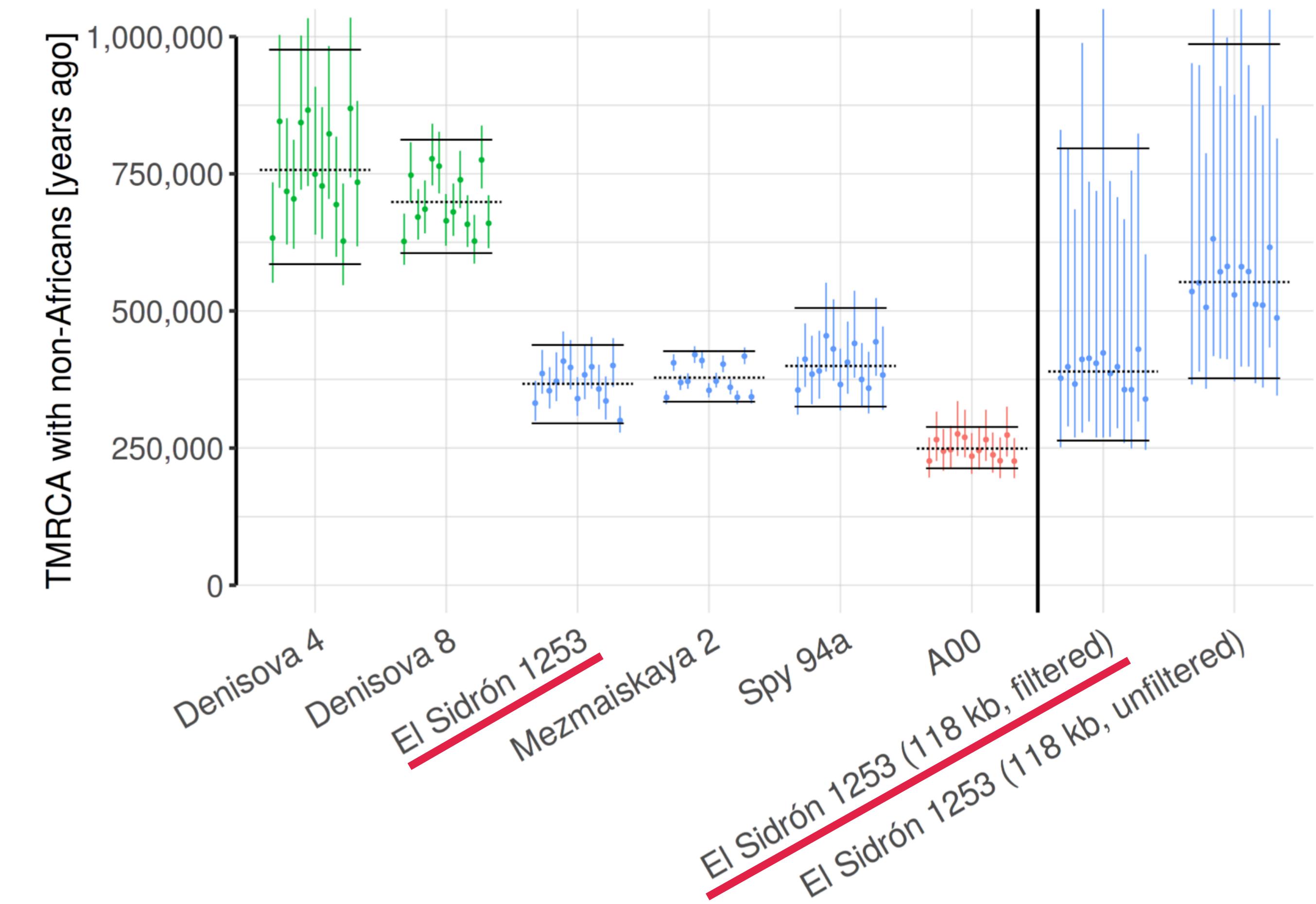
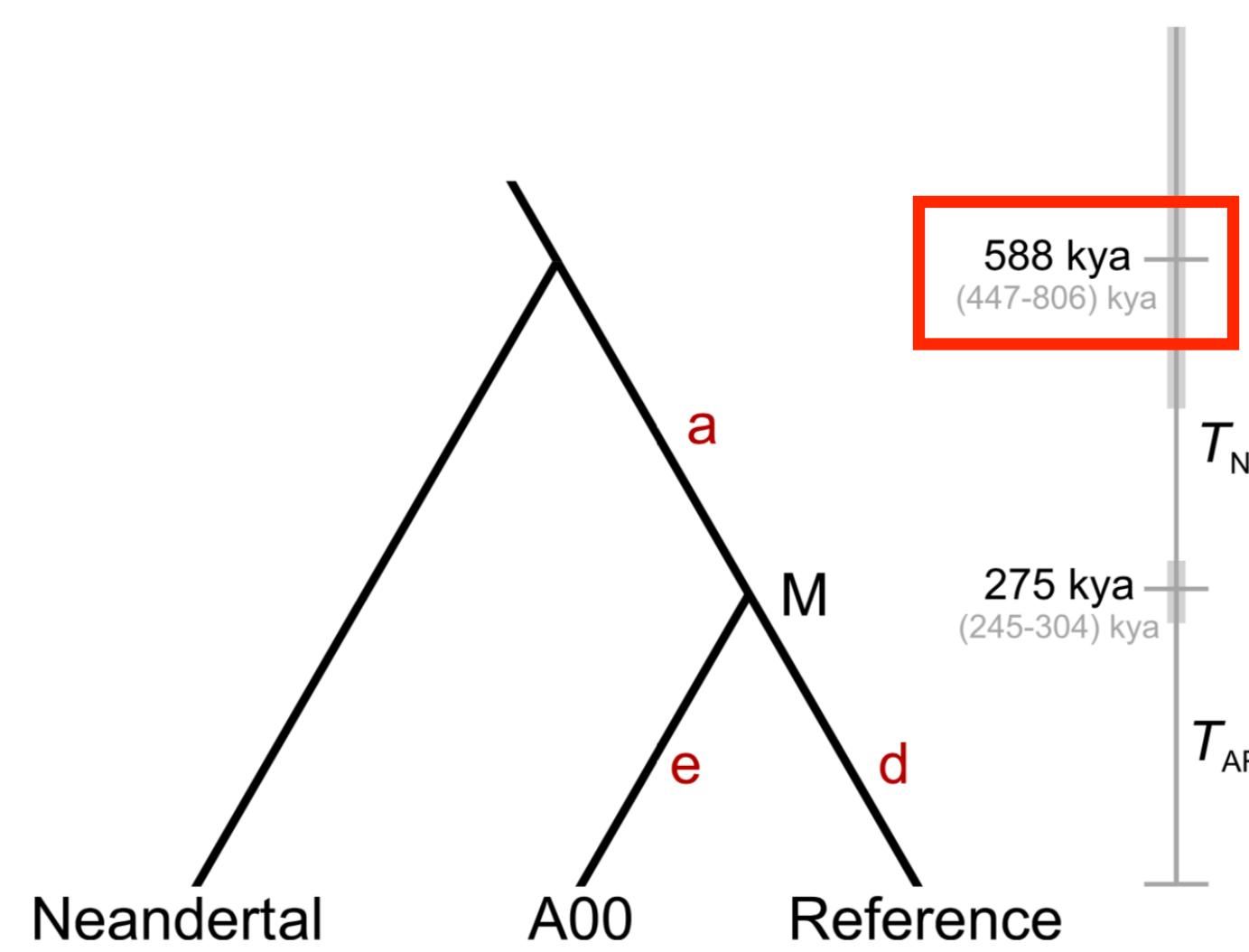
El Sidrón TMRCA discrepancy



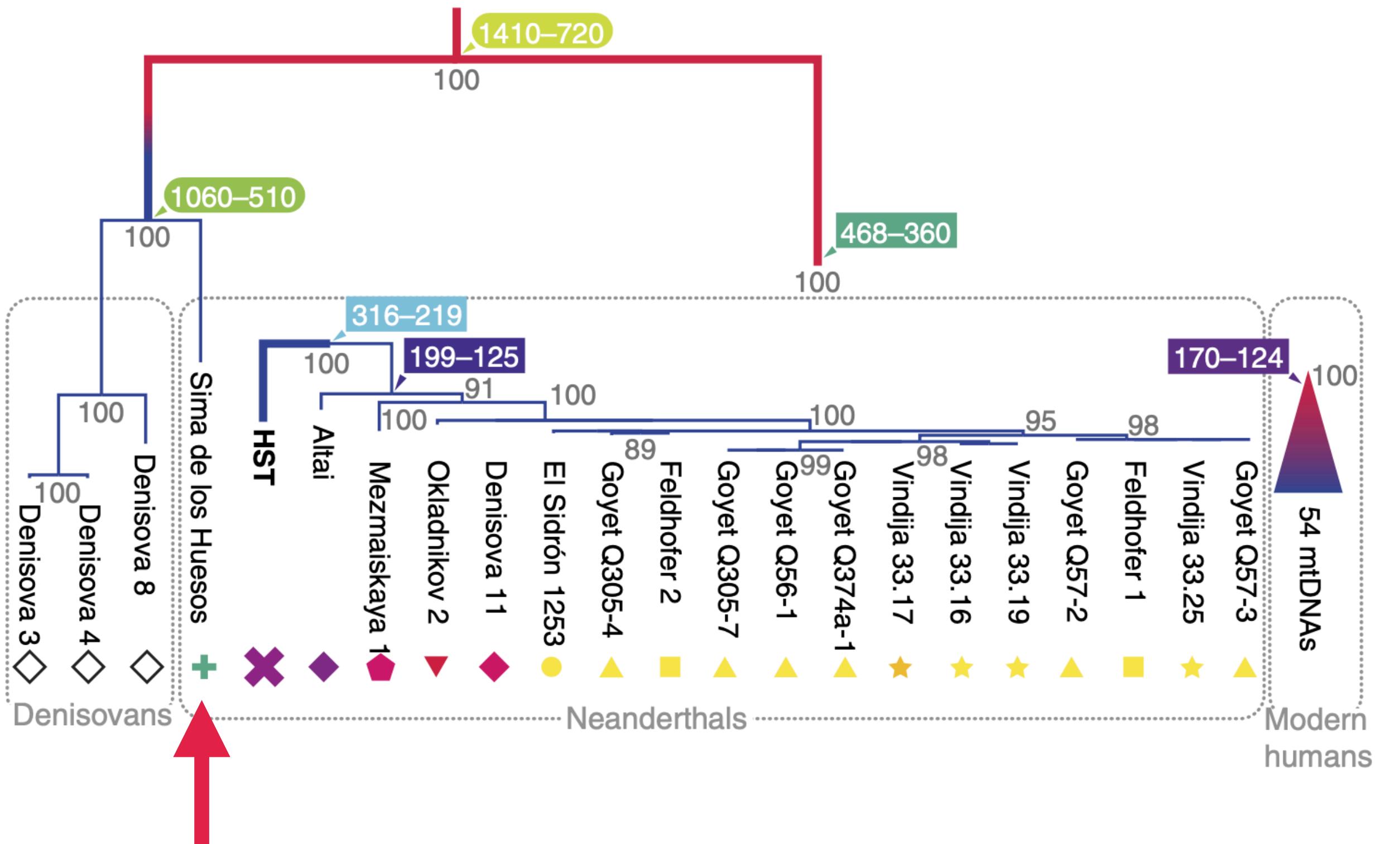
El Sidrón TMRCA discrepancy



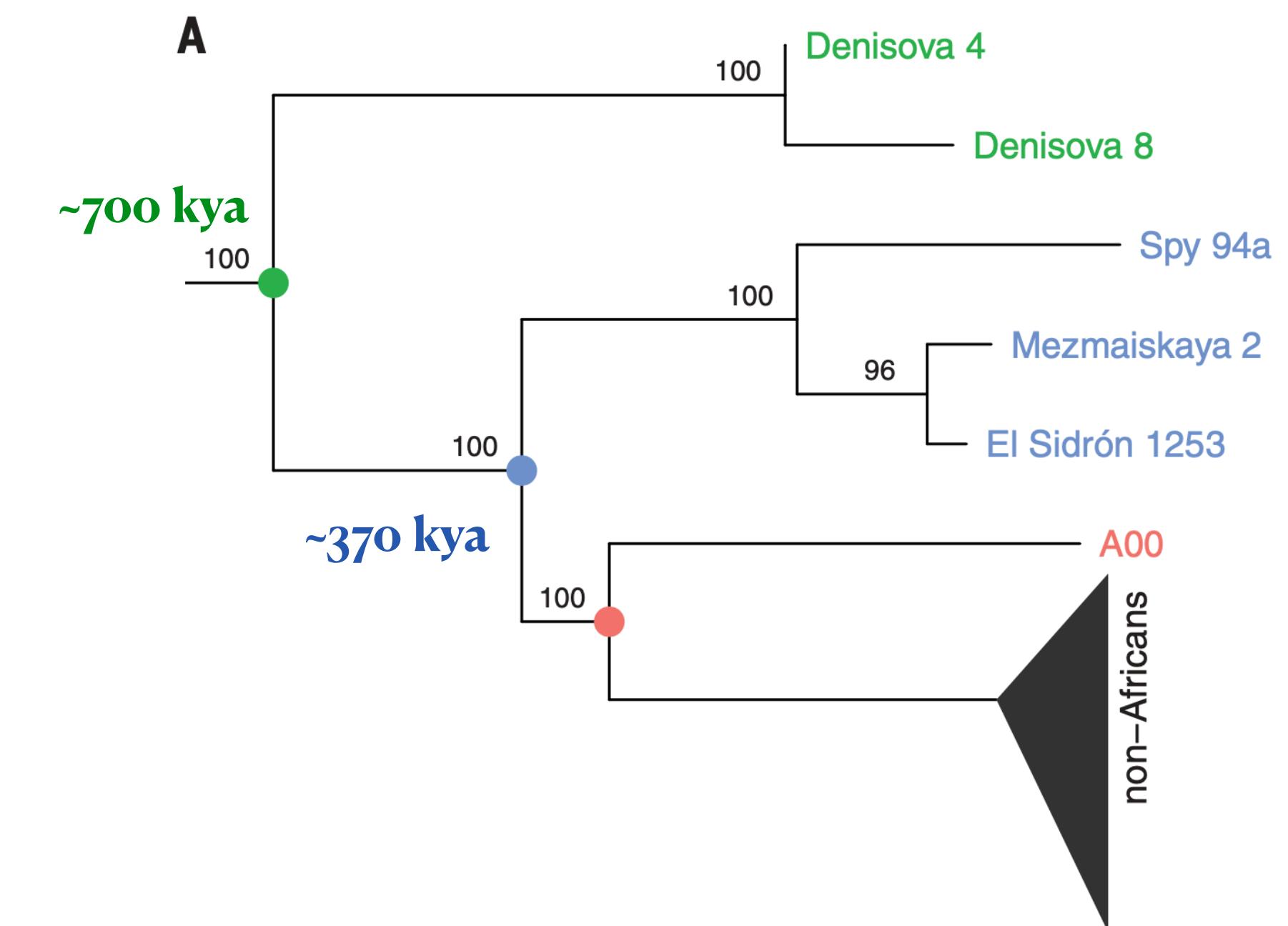
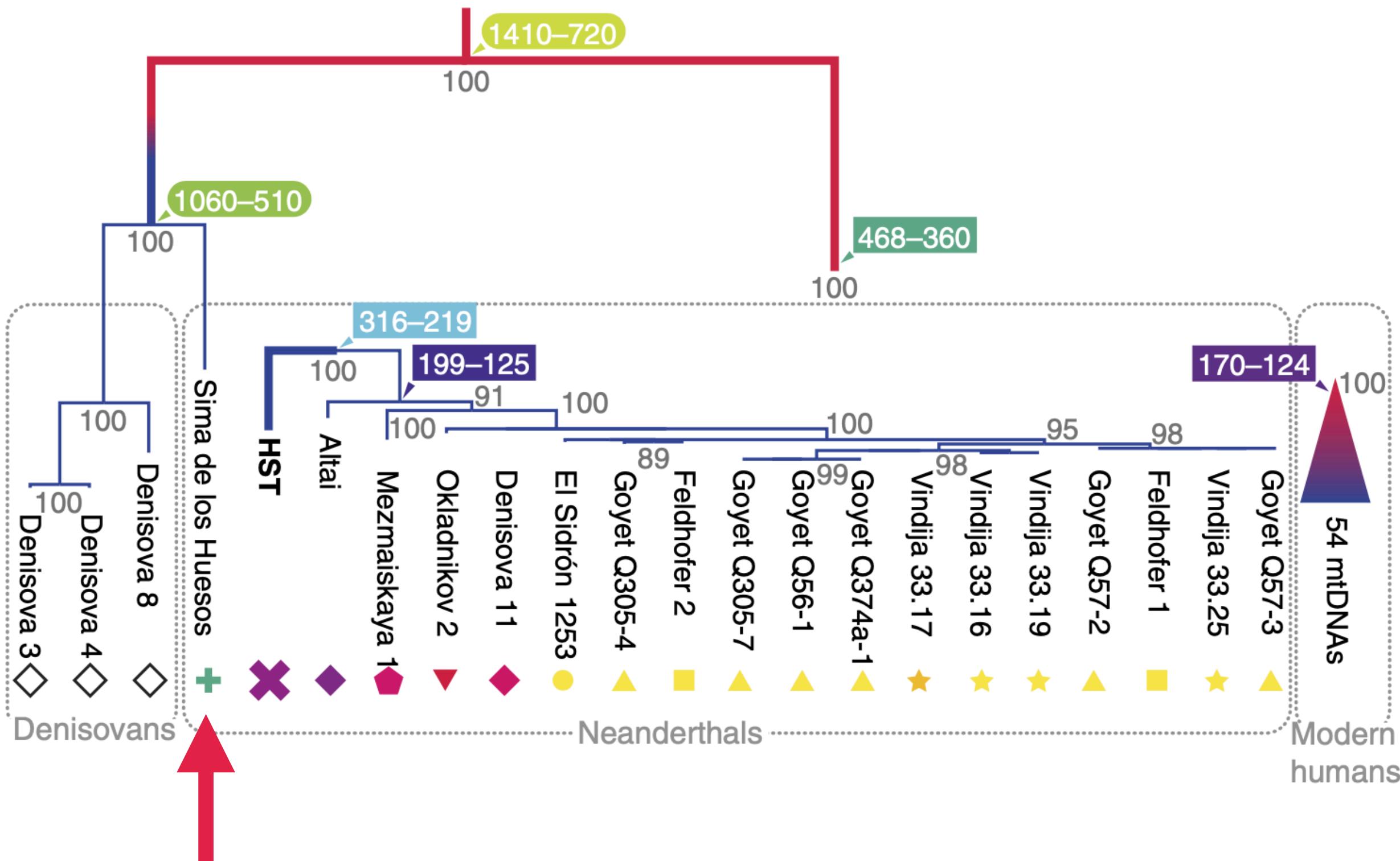
El Sidrón TMRCA discrepancy



mtDNA replacement



mtDNA replacement & Y replacement?



Problem: replacement rather unlikely

(under neutrality)

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(under neutrality)

Population genetics theory:

introgression at $X\%$ → probability of fixation (i.e. replacement) = $X\%$

Problem: replacement rather unlikely

(under neutrality)

Population genetics theory:

introgression at $X\%$ → probability of fixation (i.e. replacement) = $X\%$

Basic probability theory:

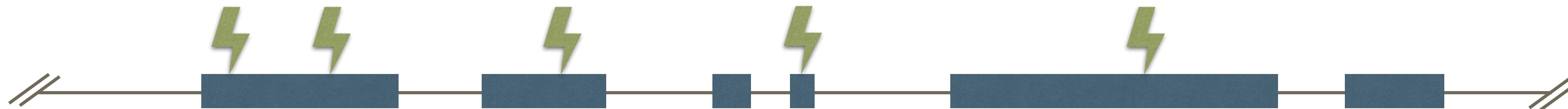
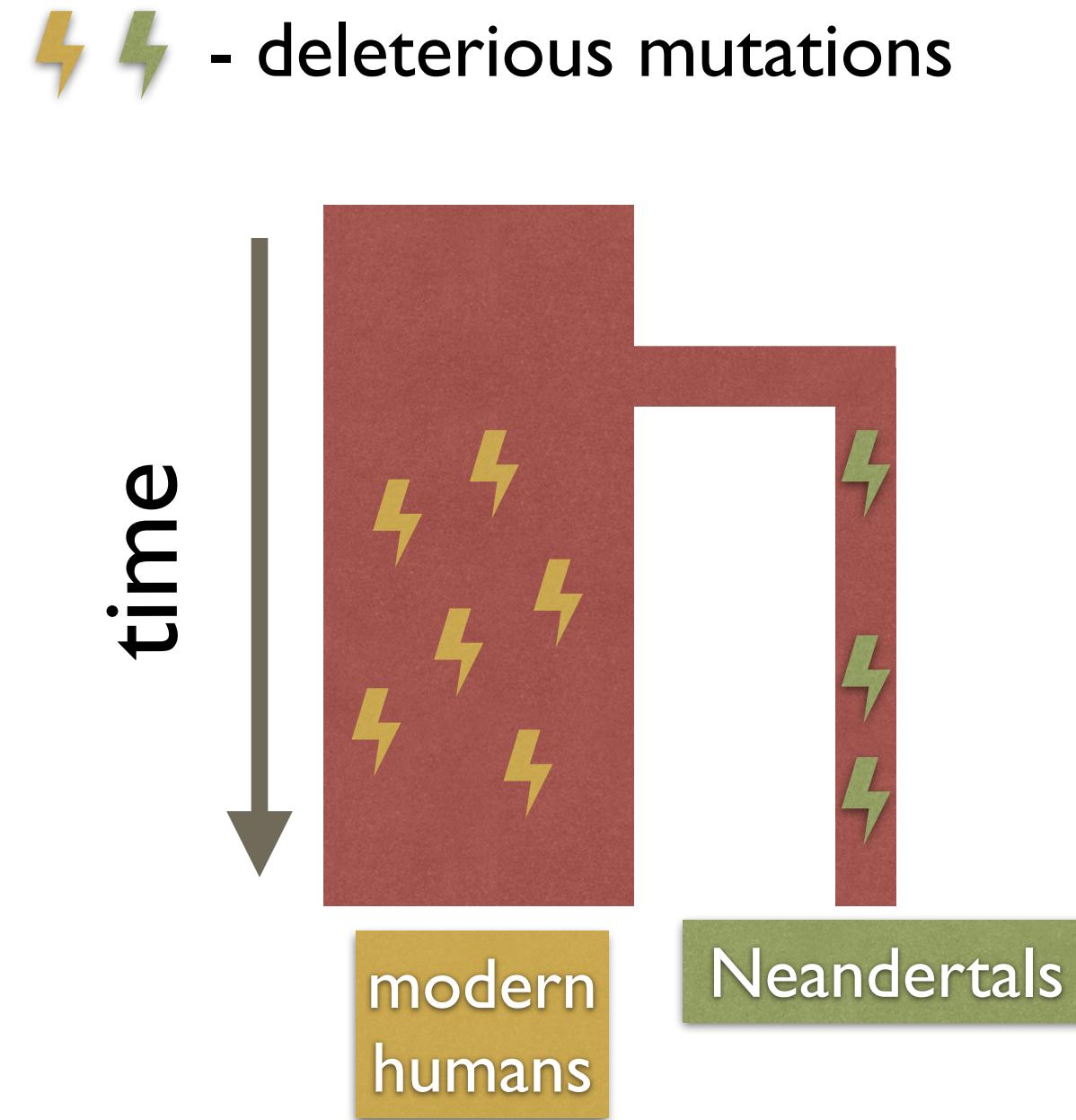
$$P[\text{mtDNA replacement}] = 3\%$$

$$P[\text{Y replacement}] = 3\%$$

$$P[\text{mtDNA and Y replacement}] = 3\% \times 3\% \rightarrow 0.09\%$$

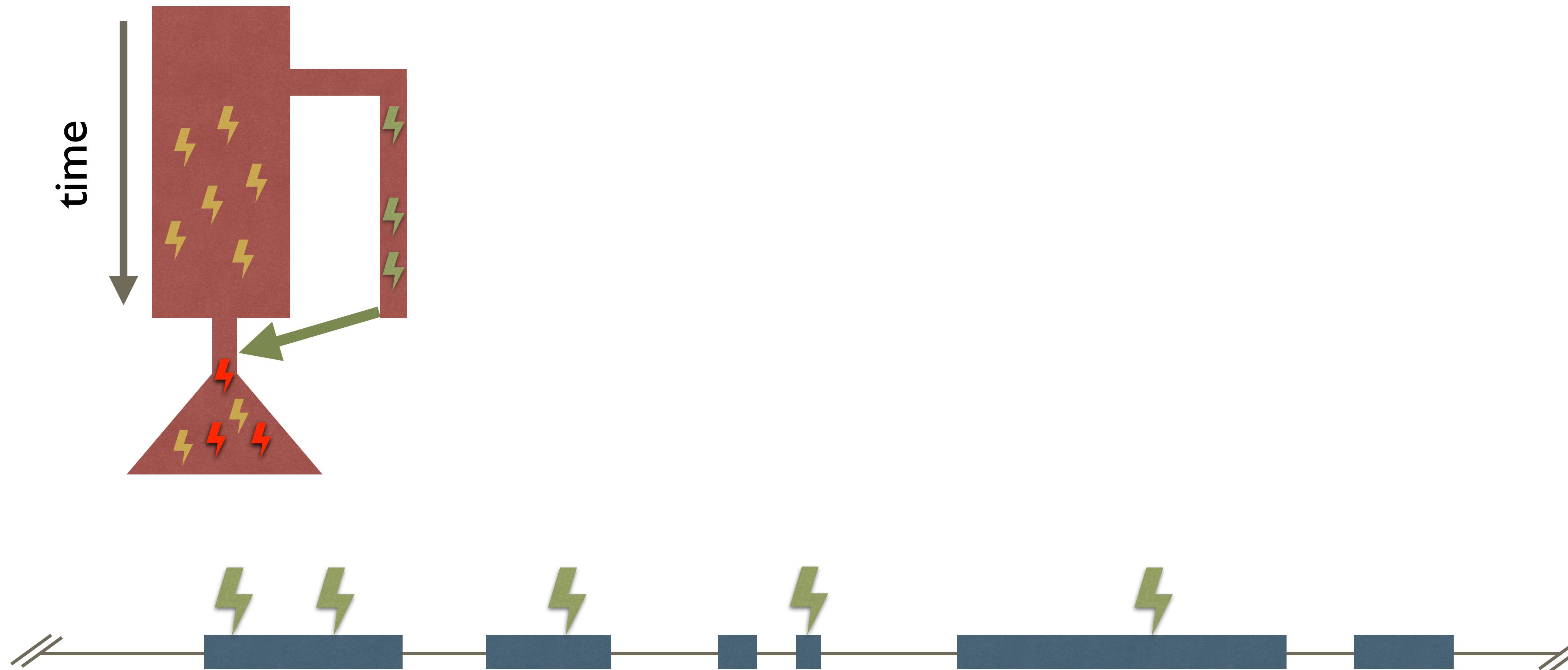
Introgression was not neutral

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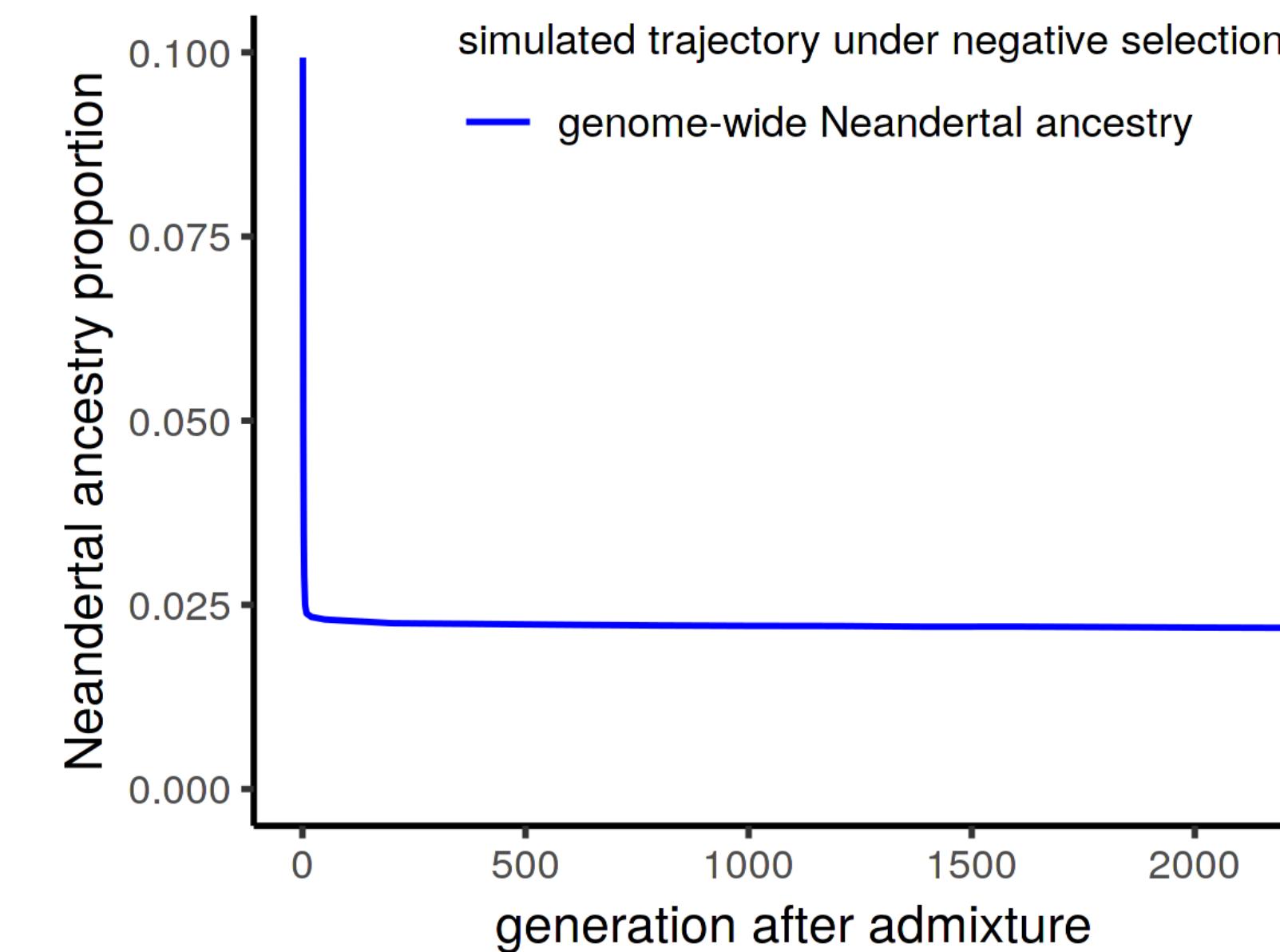
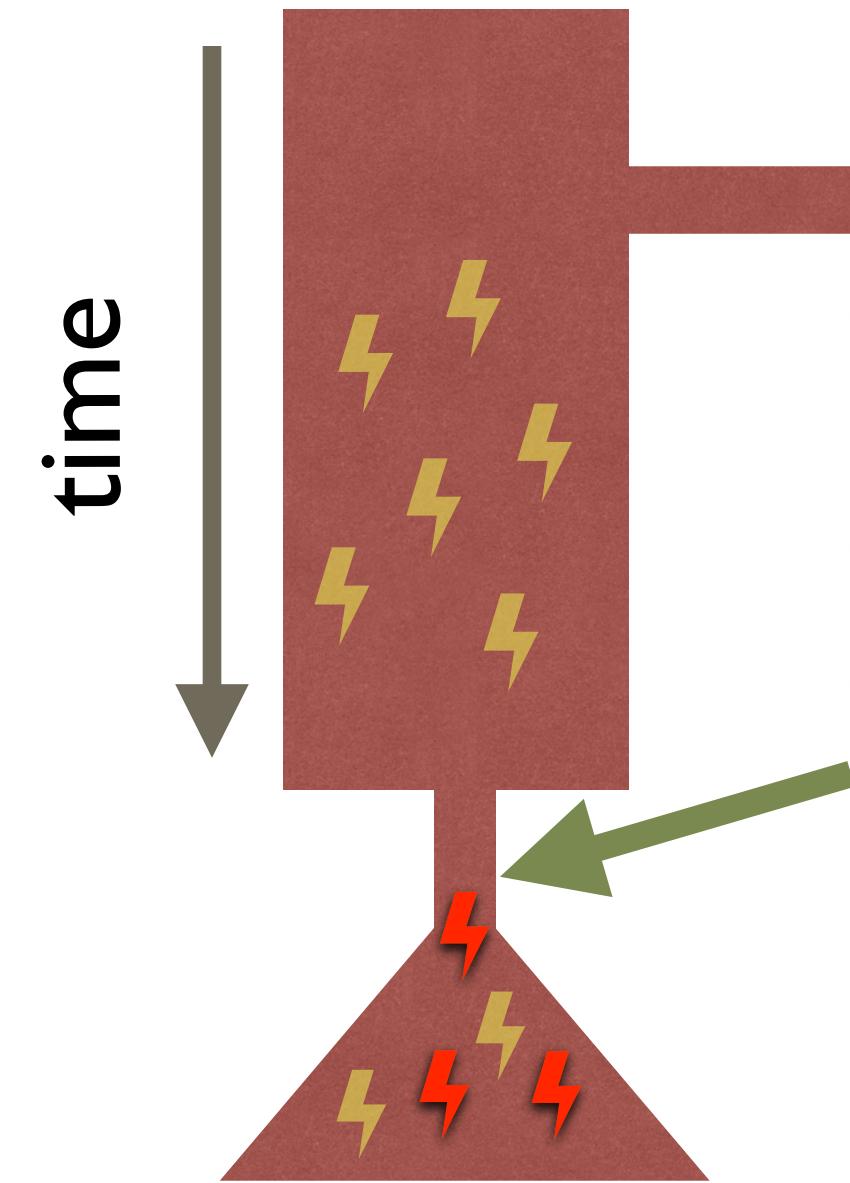
Introgression was not neutral

⚡ ⚡ - deleterious mutations

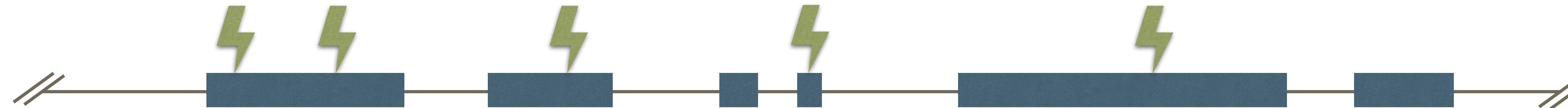


Introgression was not neutral

⚡ ⚡ - deleterious mutations

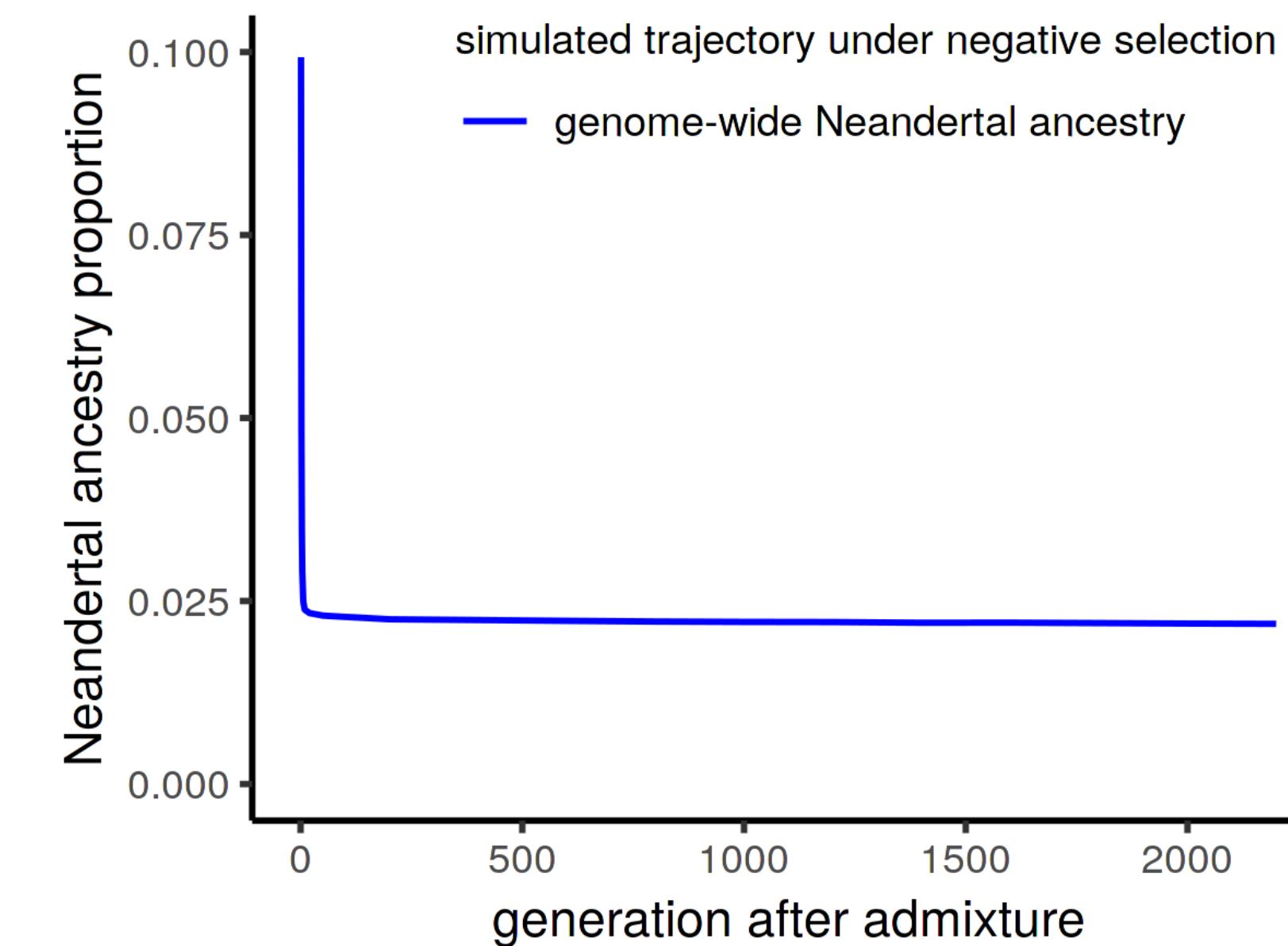
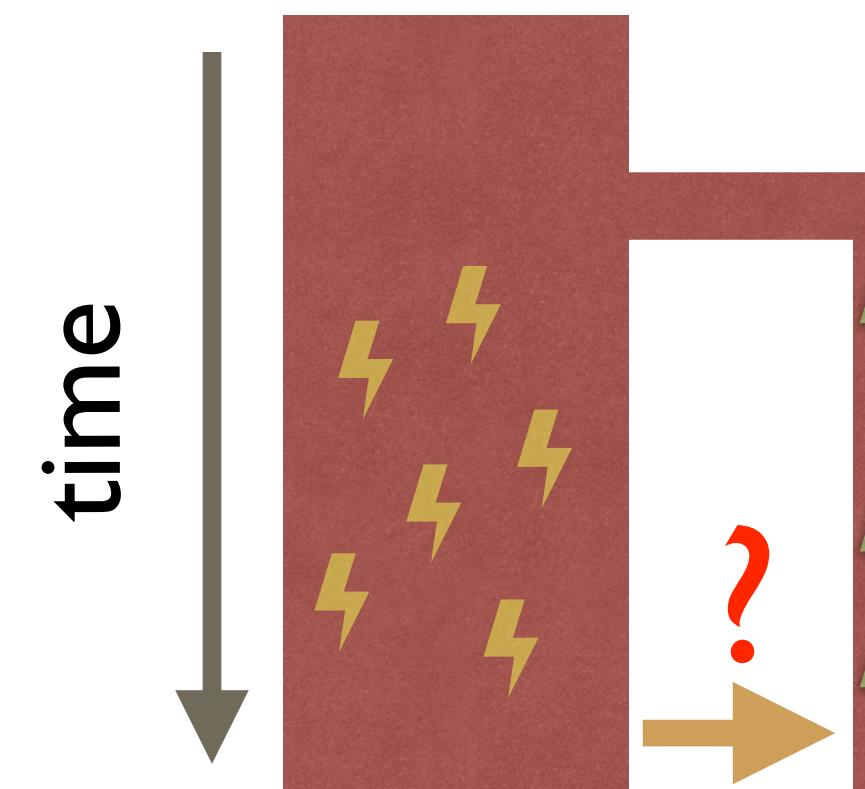


- Harris and Nielsen (Genetics, 2016)
Juric *et al.* (PLOS Genetics, 2016)
Petr *et al.* (PNAS, 2019)

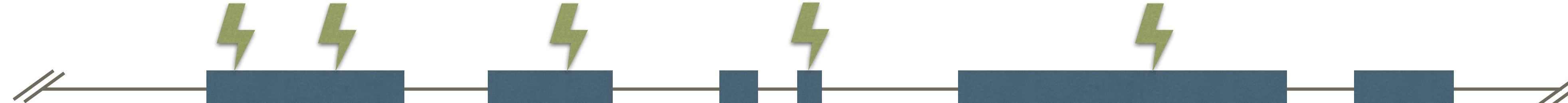


Introgression was not neutral

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- Harris and Nielsen (Genetics, 2016)
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Selection favors introgressed modern human Y

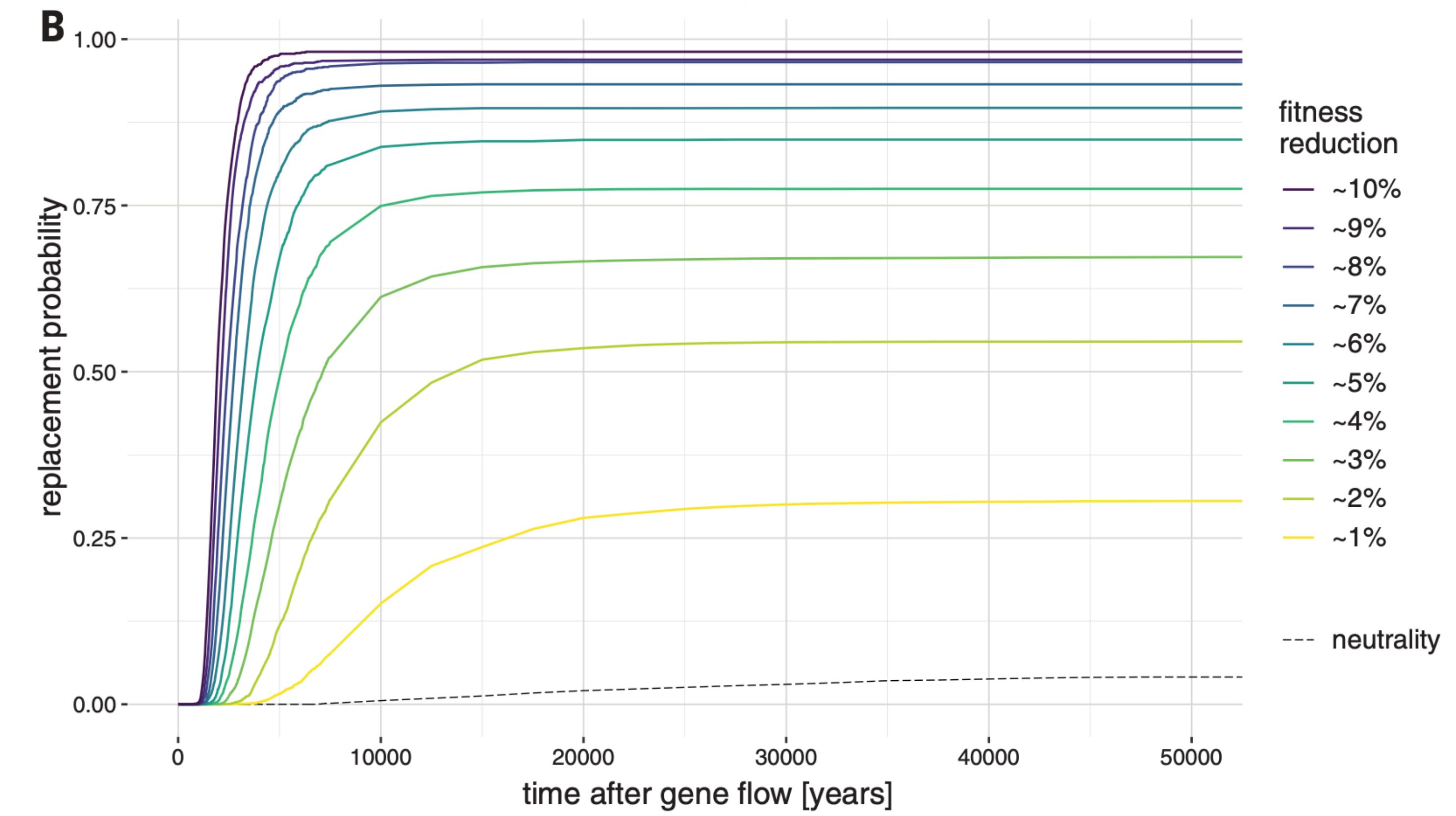
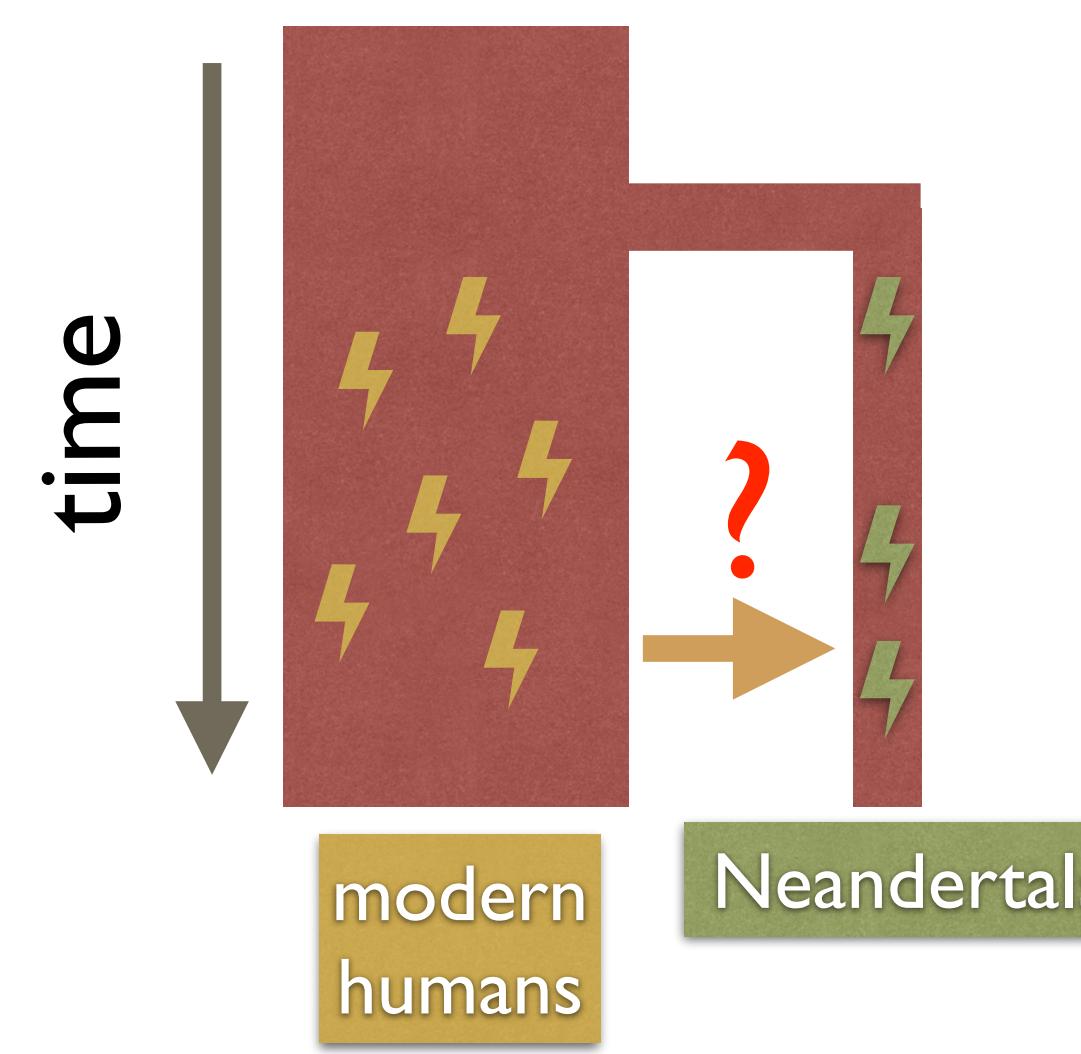


Fig. 3B

mtDNA & Y chromosomes & autosomal DNA

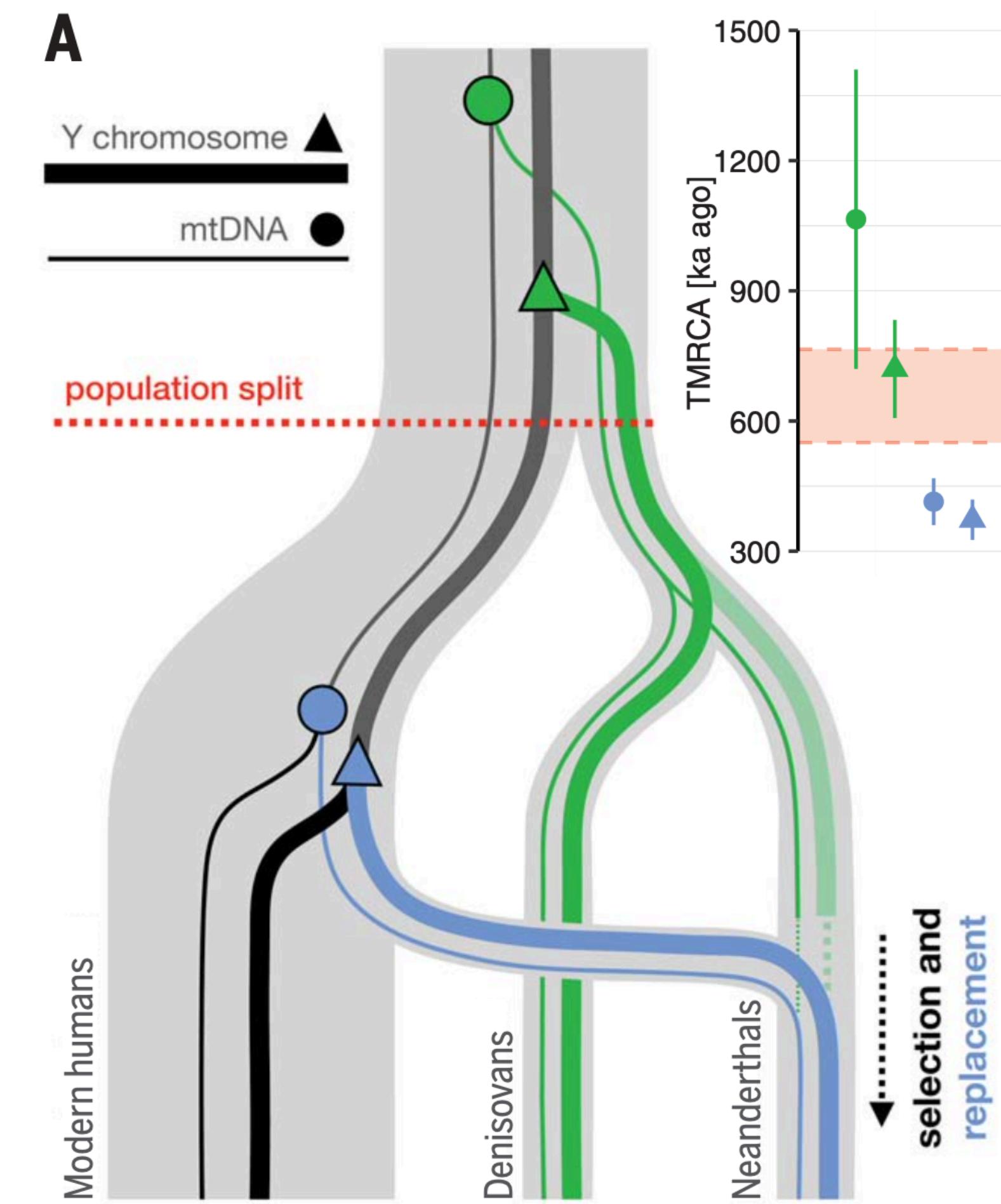


Fig. 3A

mtDNA & Y chromosomes & autosomal DNA

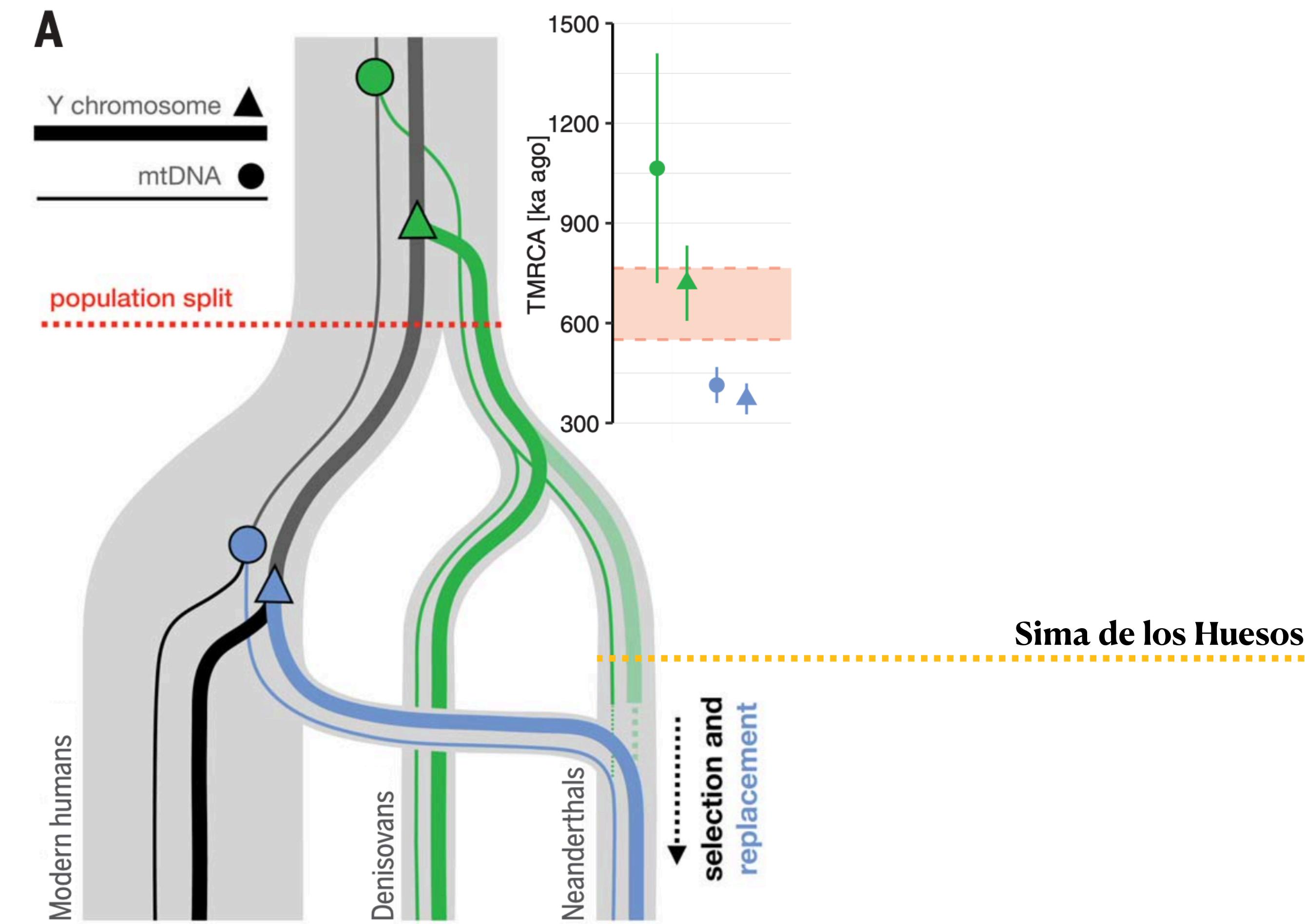
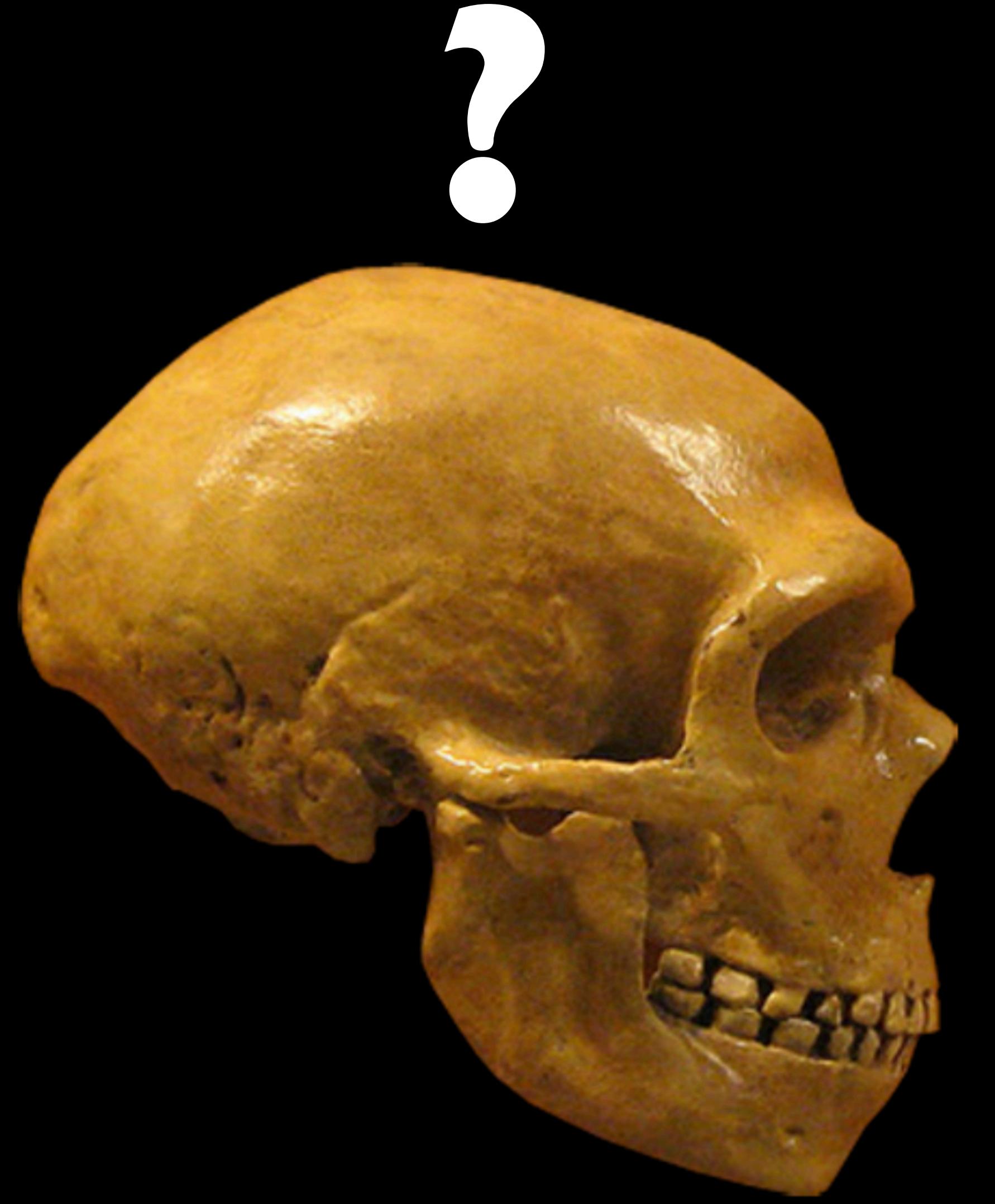


Fig. 3A

Thank you!

The evolutionary history of Neanderthal and Denisovan Y chromosomes

Martin Petr^{1*}, Mateja Hajdinjak^{1,2}, Qiaomei Fu^{3,4,5}, Elena Essel¹, Hélène Rougier⁶, Isabelle Crevecoeur⁷,
Patrick Semal⁸, Liubov V. Golovanova⁹, Vladimir B. Doronichev⁹, Carles Lalueza-Fox¹⁰,
Marco de la Rasilla¹¹, Antonio Rosas¹², Michael V. Shunkov¹³, Maxim B. Kozlikin¹³,
Anatoli P. Derevianko¹³, Benjamin Vernot¹, Matthias Meyer¹, Janet Kelso^{1*}



mp@bodkan.net
kelso@eva.mpg.de

Capture bias & mapping bias

Capture bias & mapping bias



Capture bias & mapping bias

Given genomic coverage λ ...



Capture bias & mapping bias

Given genomic coverage λ ...

$$\lambda = 1X$$



Capture bias & mapping bias

Given genomic coverage λ ...

$$\lambda = 1X$$



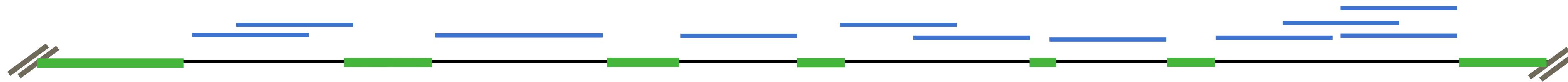
... we expect a proportion $Poisson(k=0, \lambda)$ of sites to have no coverage.

Capture bias & mapping bias

Given genomic coverage λ ...

$$\lambda = 1X$$

$$Poisson(k=0, \lambda=1) \sim 0.36 = 36\%$$



... we expect a proportion $Poisson(k=0, \lambda)$ of sites to have no coverage.

Capture bias & alignment bias

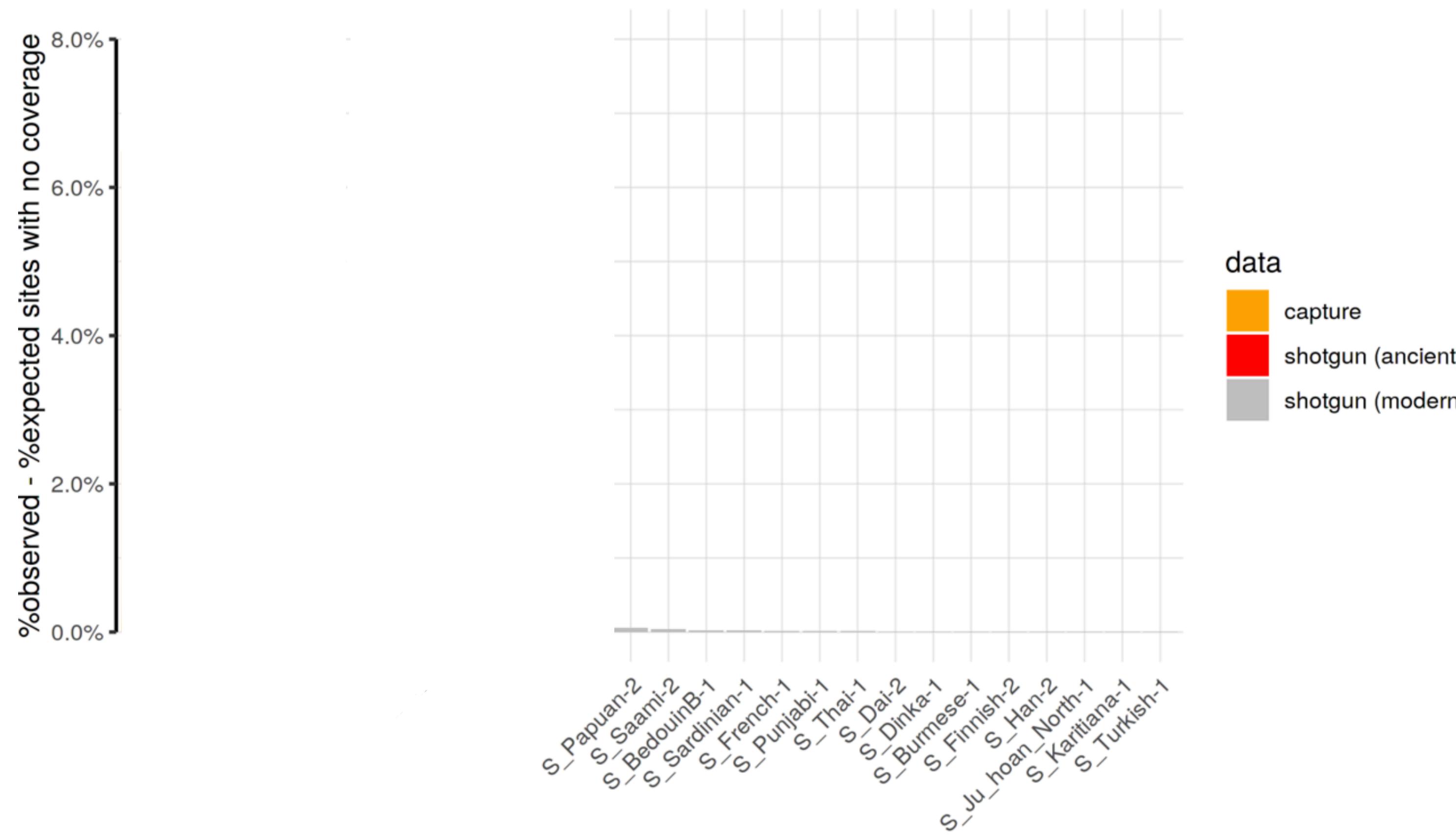


Fig. S7

Capture bias & alignment bias

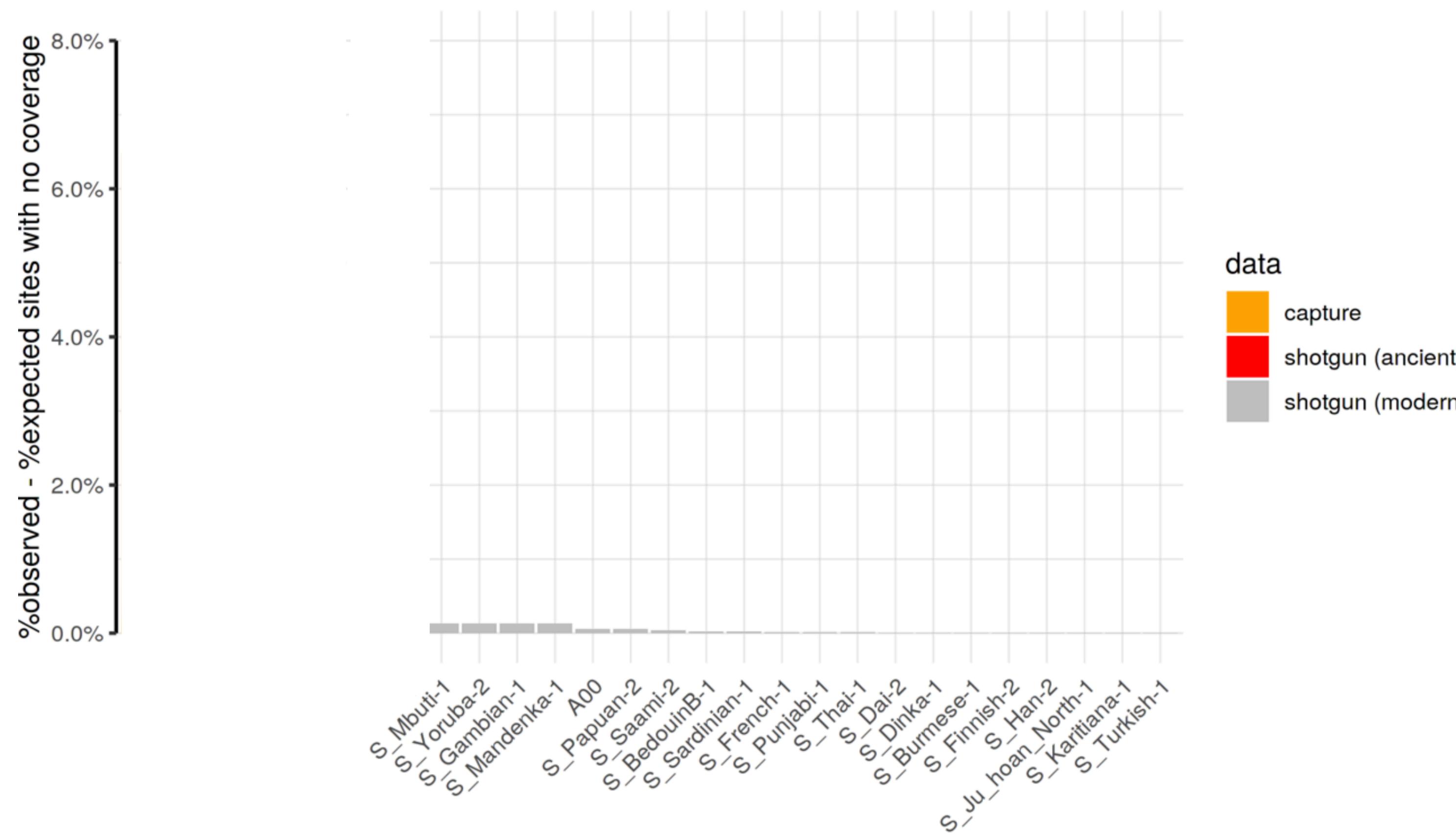


Fig. S7

Capture bias & alignment bias

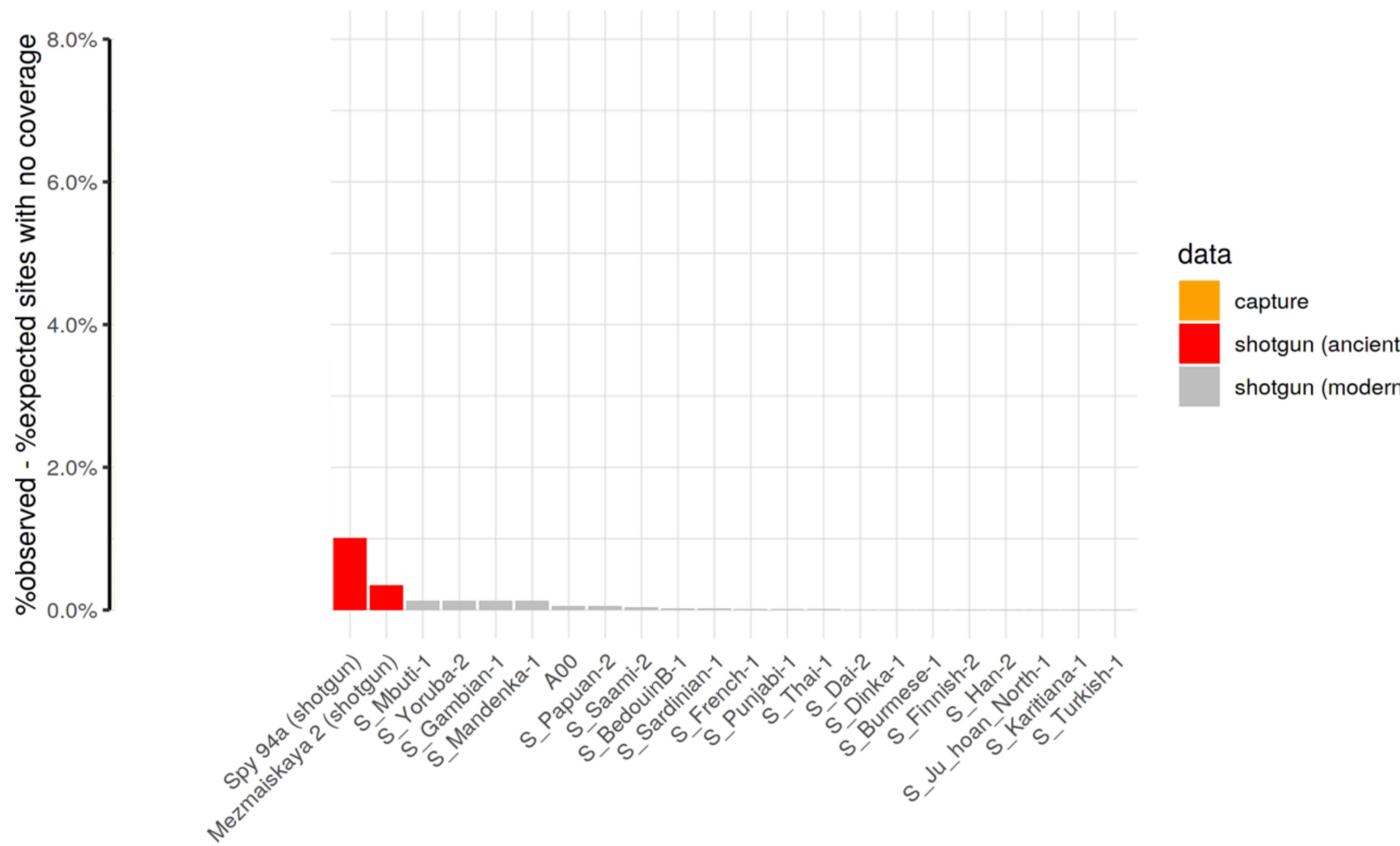


Fig. S7

Capture bias & alignment bias

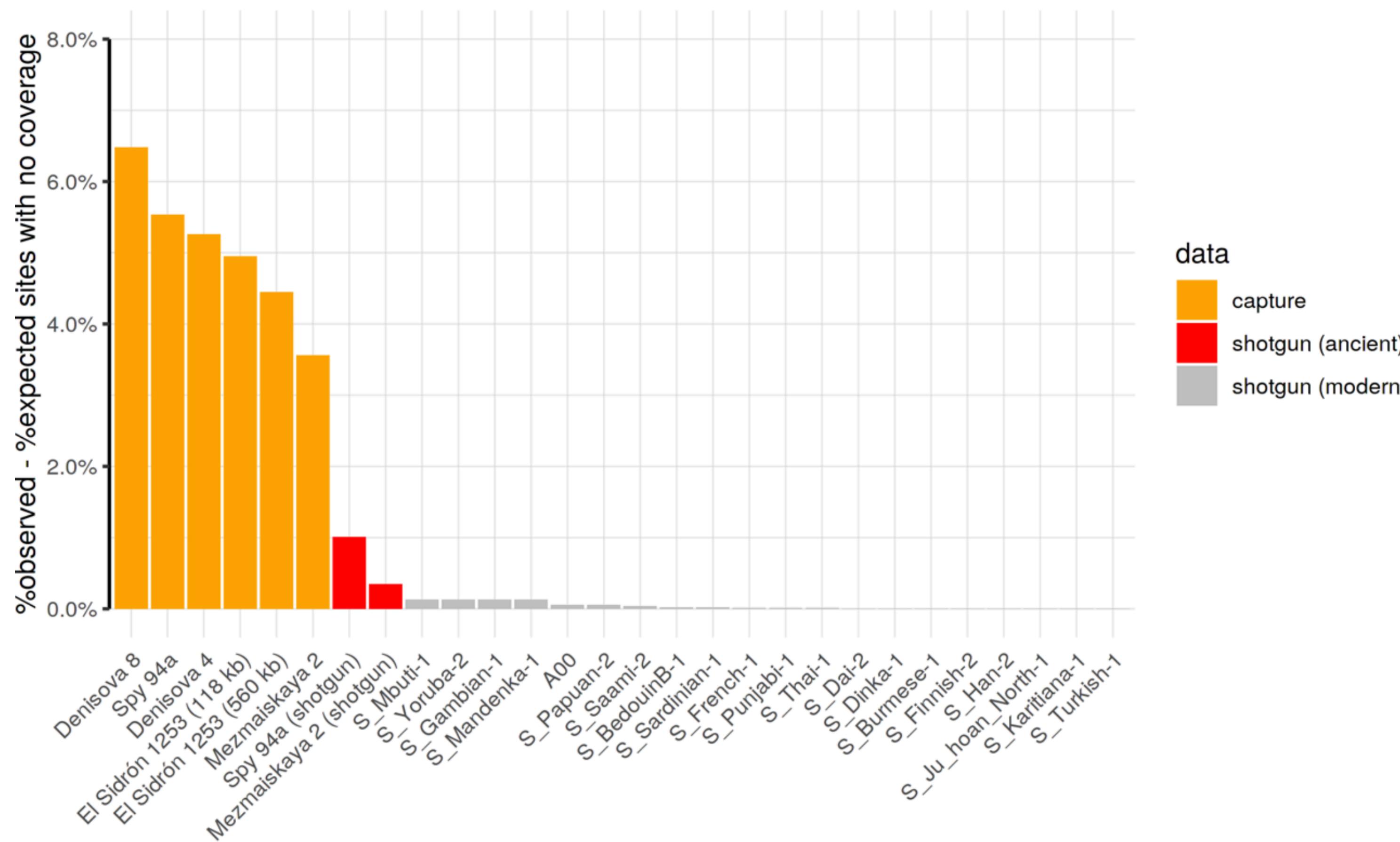


Fig. S7

Capture bias & alignment bias

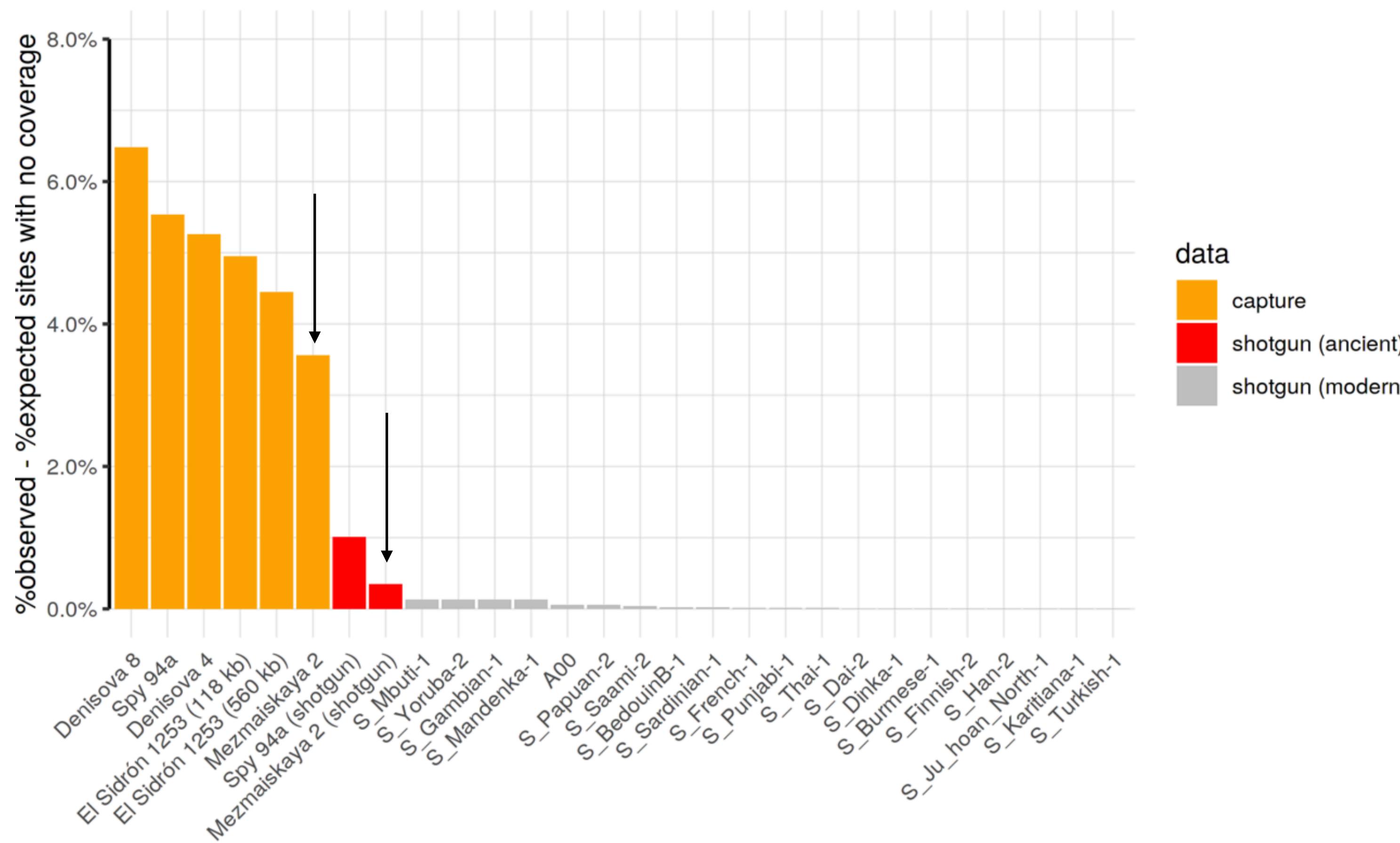


Fig. S7

Capture bias & alignment bias

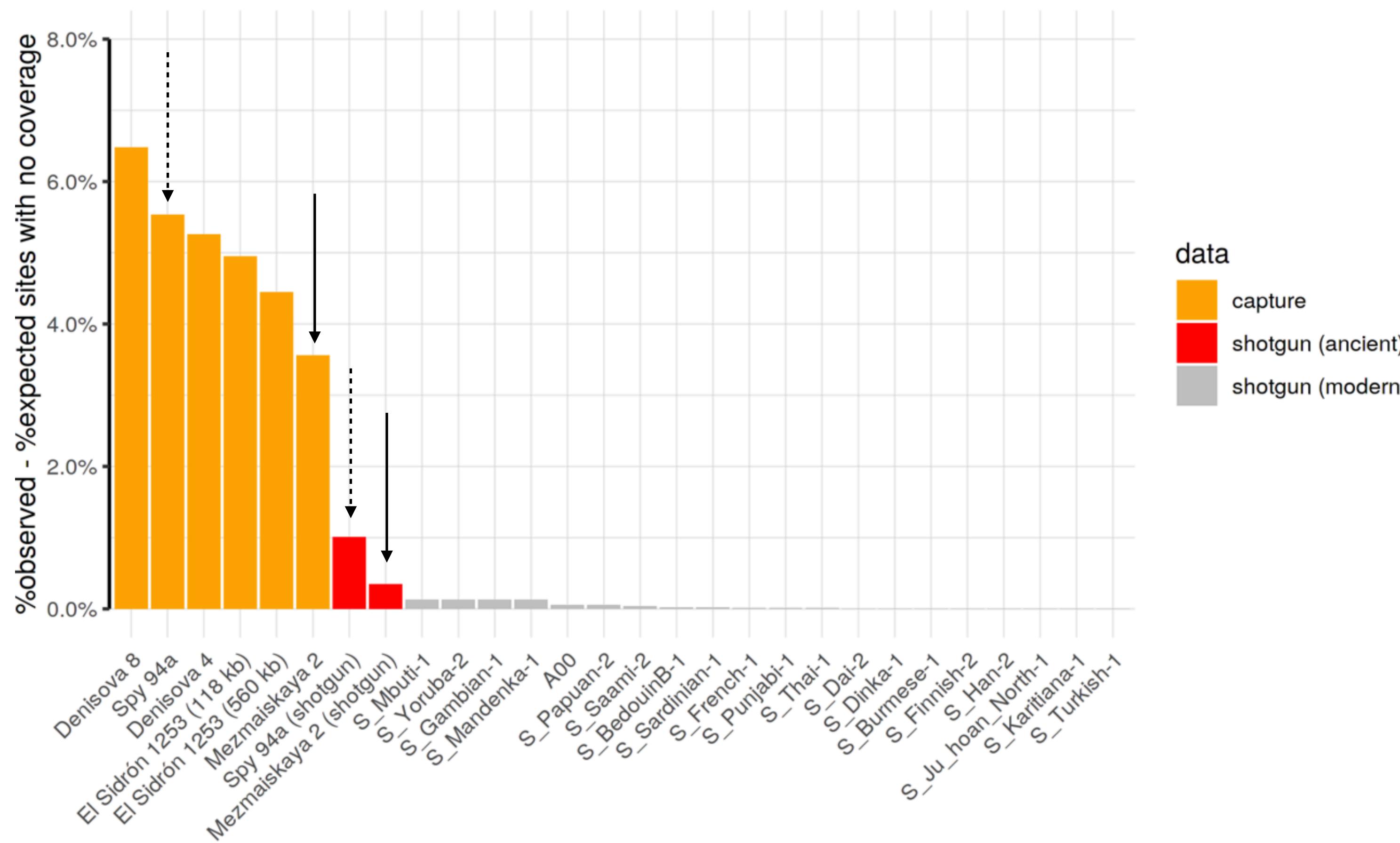
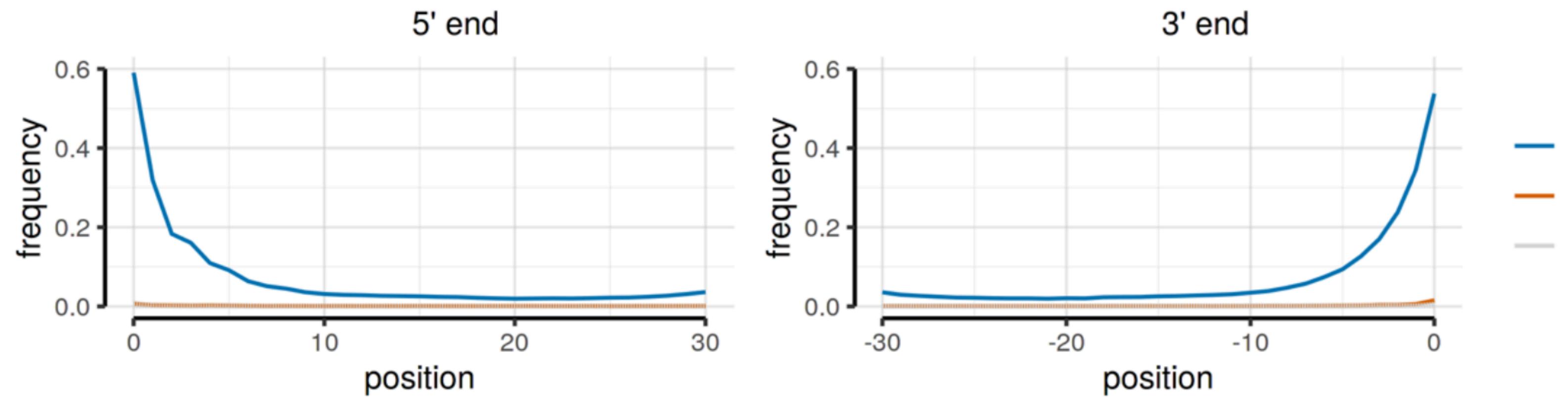


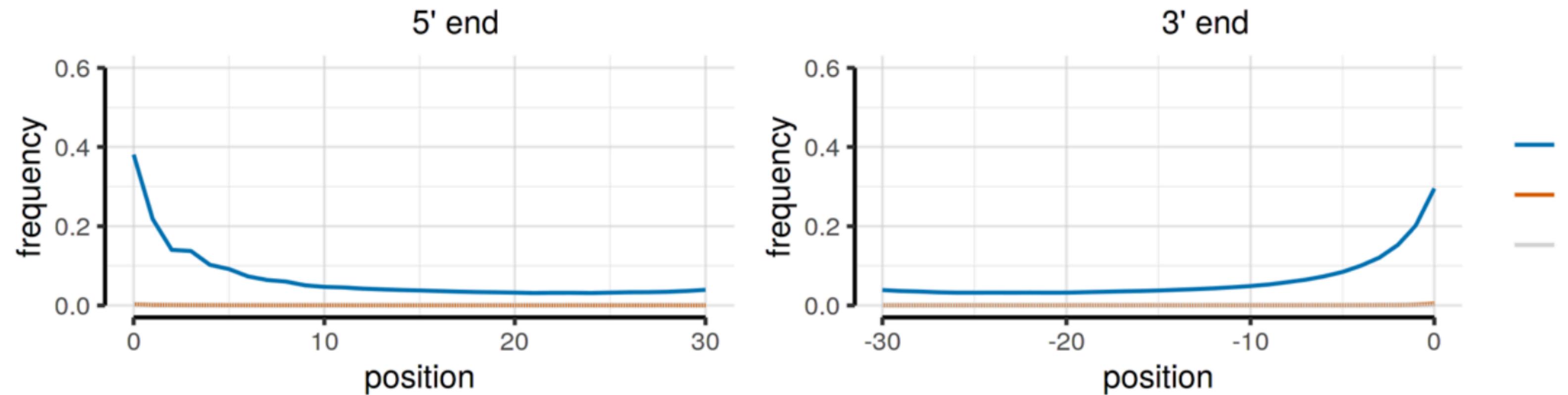
Fig. S7

Ancient DNA damage

Denisova 8



Mezmaiskaya 2



Ancient DNA damage (after genotype calling)

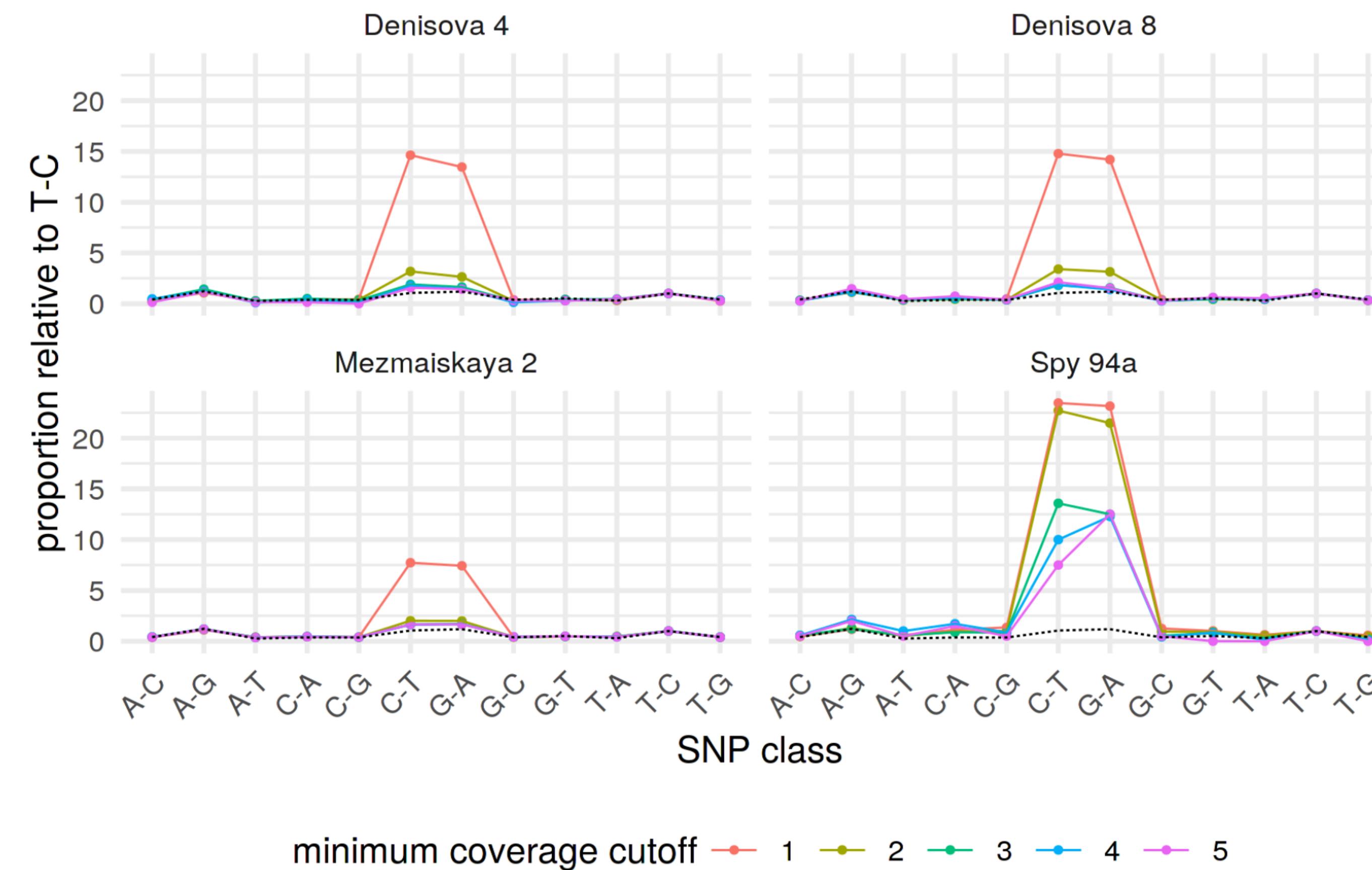


Fig. S8

Modern human contamination

Modern human contamination

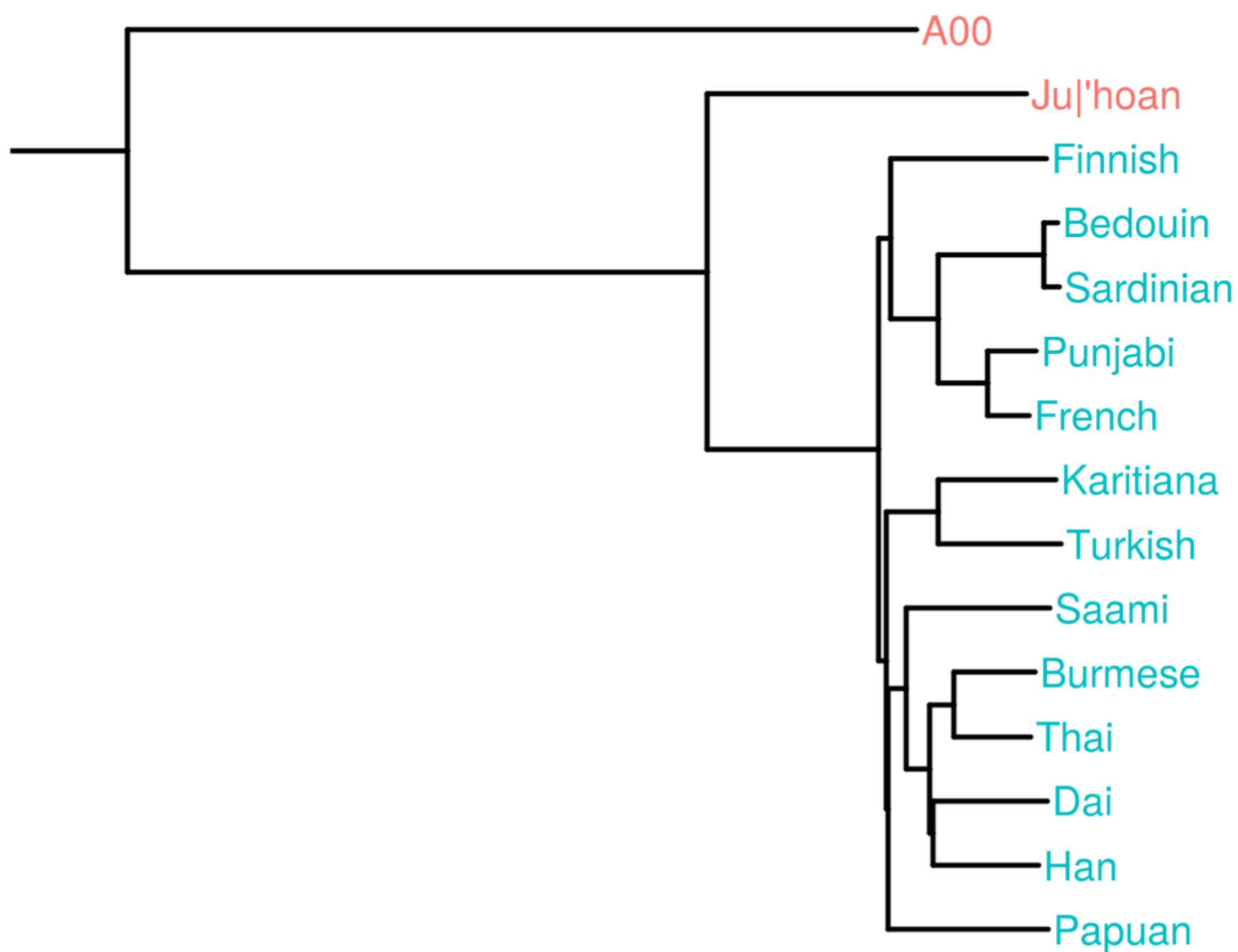


Fig. S6. Phylogenetic tree demonstrating the definition of positions informative about modern human contamination.

Modern human contamination

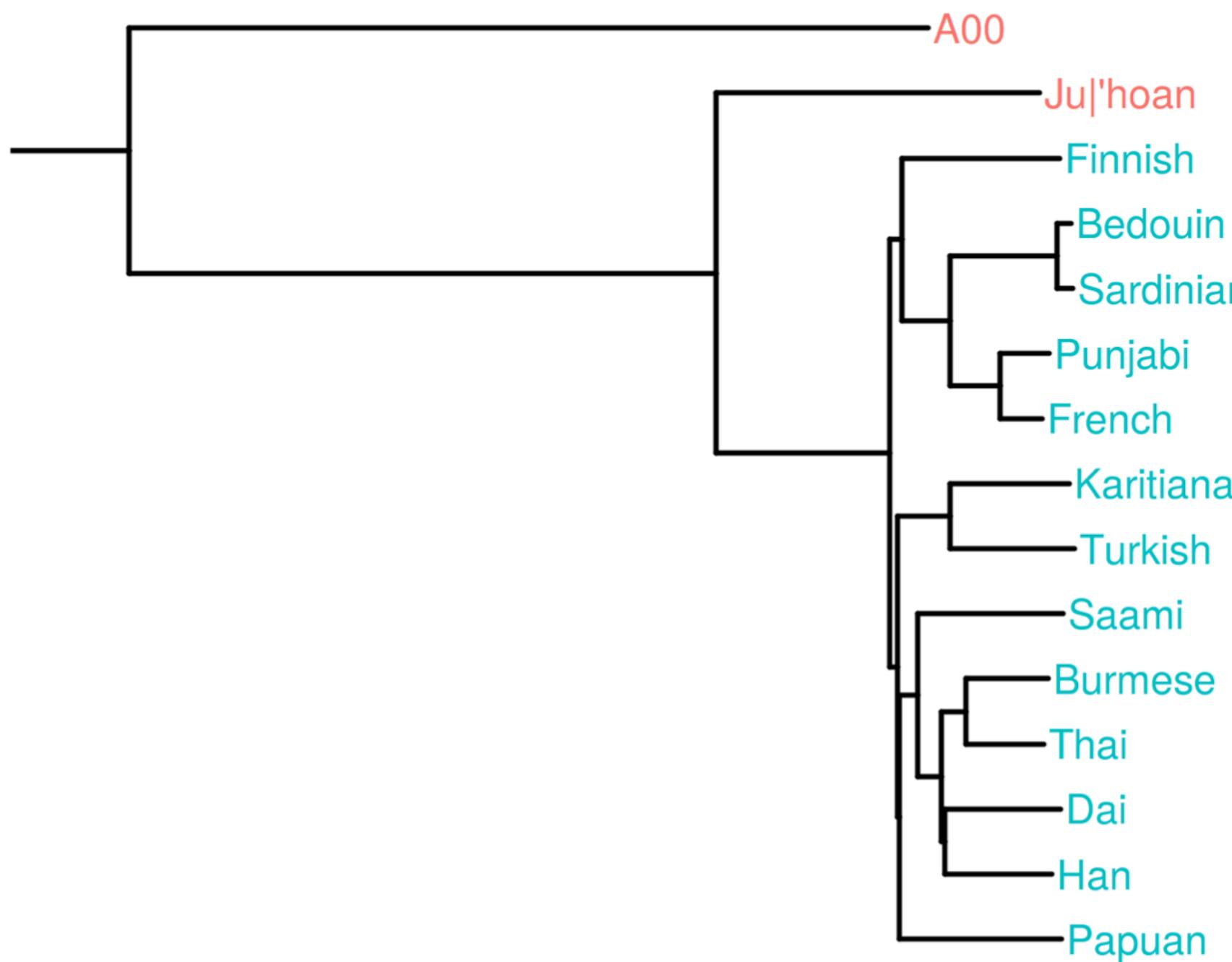
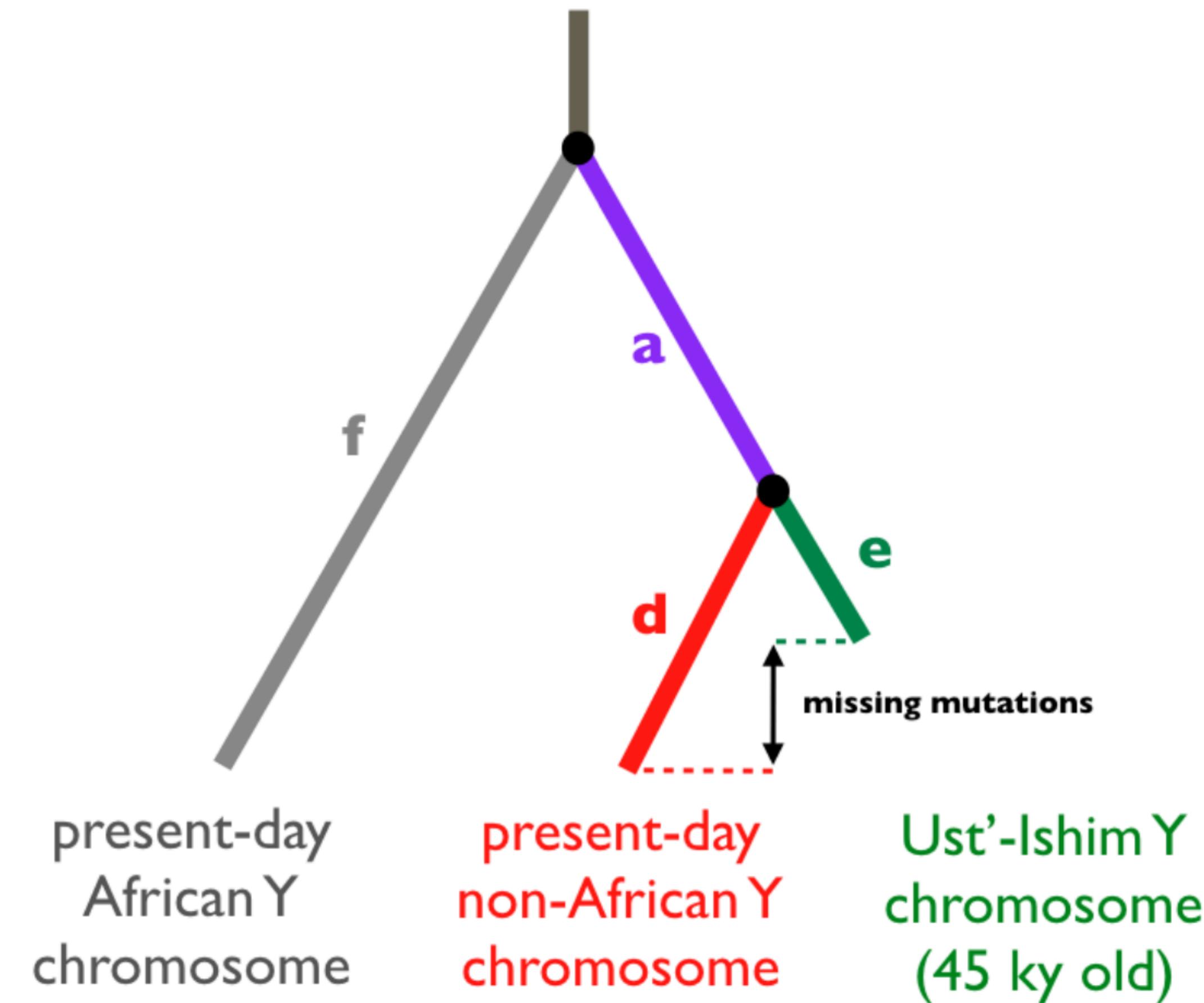


Fig. S6. Phylogenetic tree demonstrating the definition of positions informative about modern human contamination.

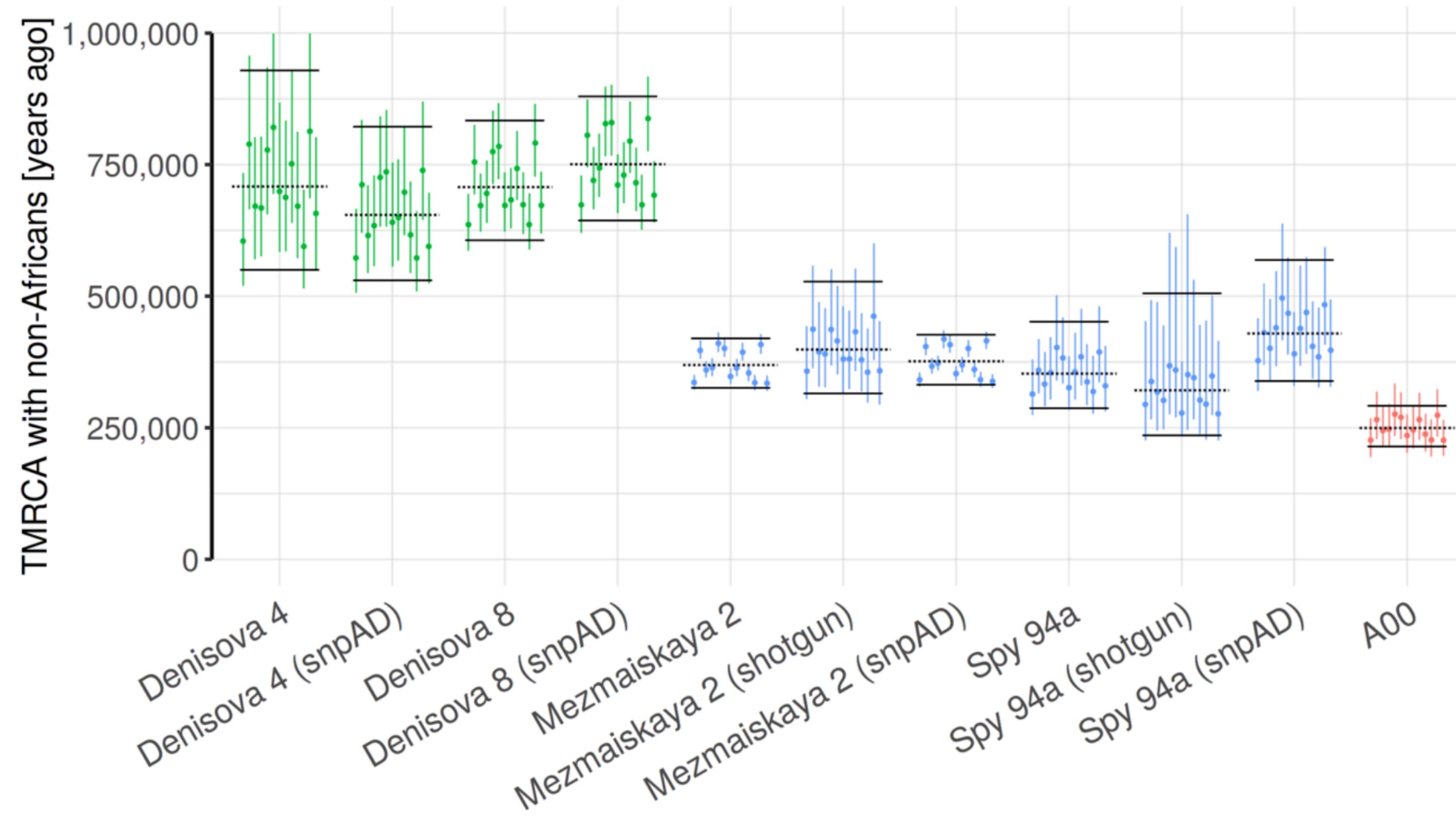
individual	ancestral count	derived count	total	derived/total
Spy 94a	15	1	16	0.0625
Mezmaiskaya 2	189	0	189	0.0000
Denisova 4	14	0	14	0.0000
Denisova 8	90	0	90	0.0000
El Sidrón 1253 (560 kb)	29	0	29	0.0000

Table S6. Counts and proportions of potential ‘contaminant-derived’ non-African alleles in all archaic human Y chromosomes.

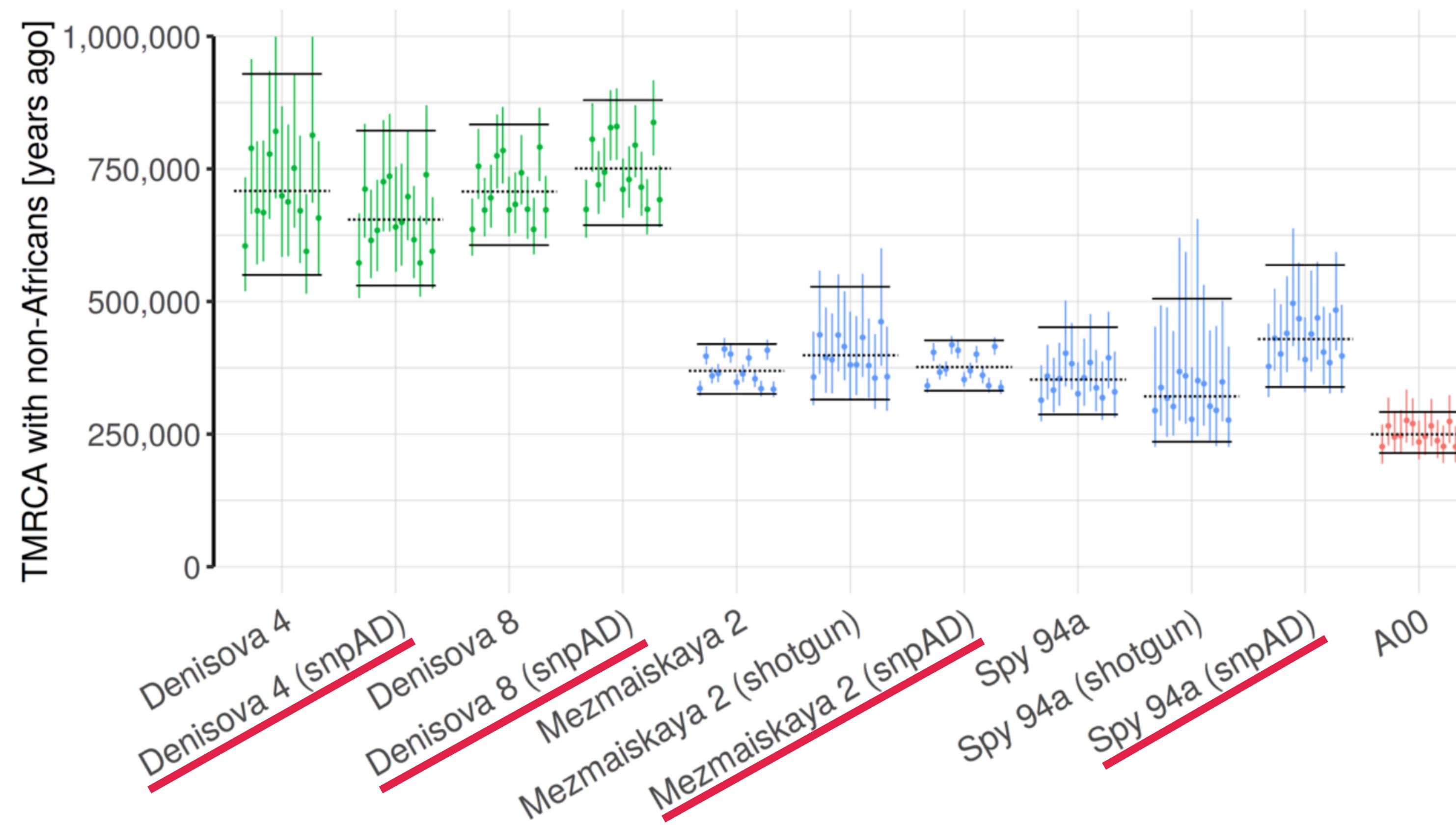
Estimating mutation rate & T_{AFR}



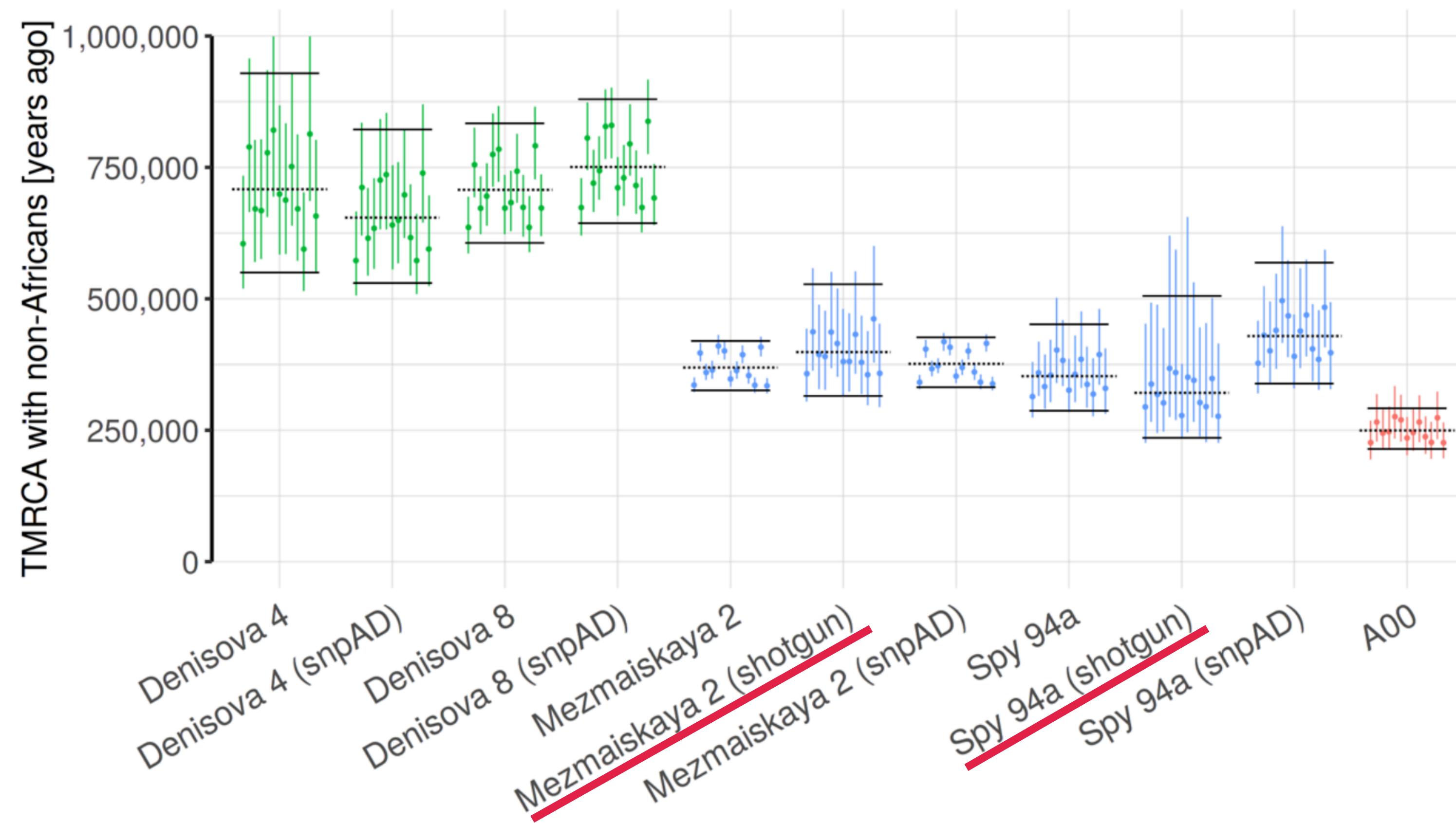
Y chromosome TMRCA estimates



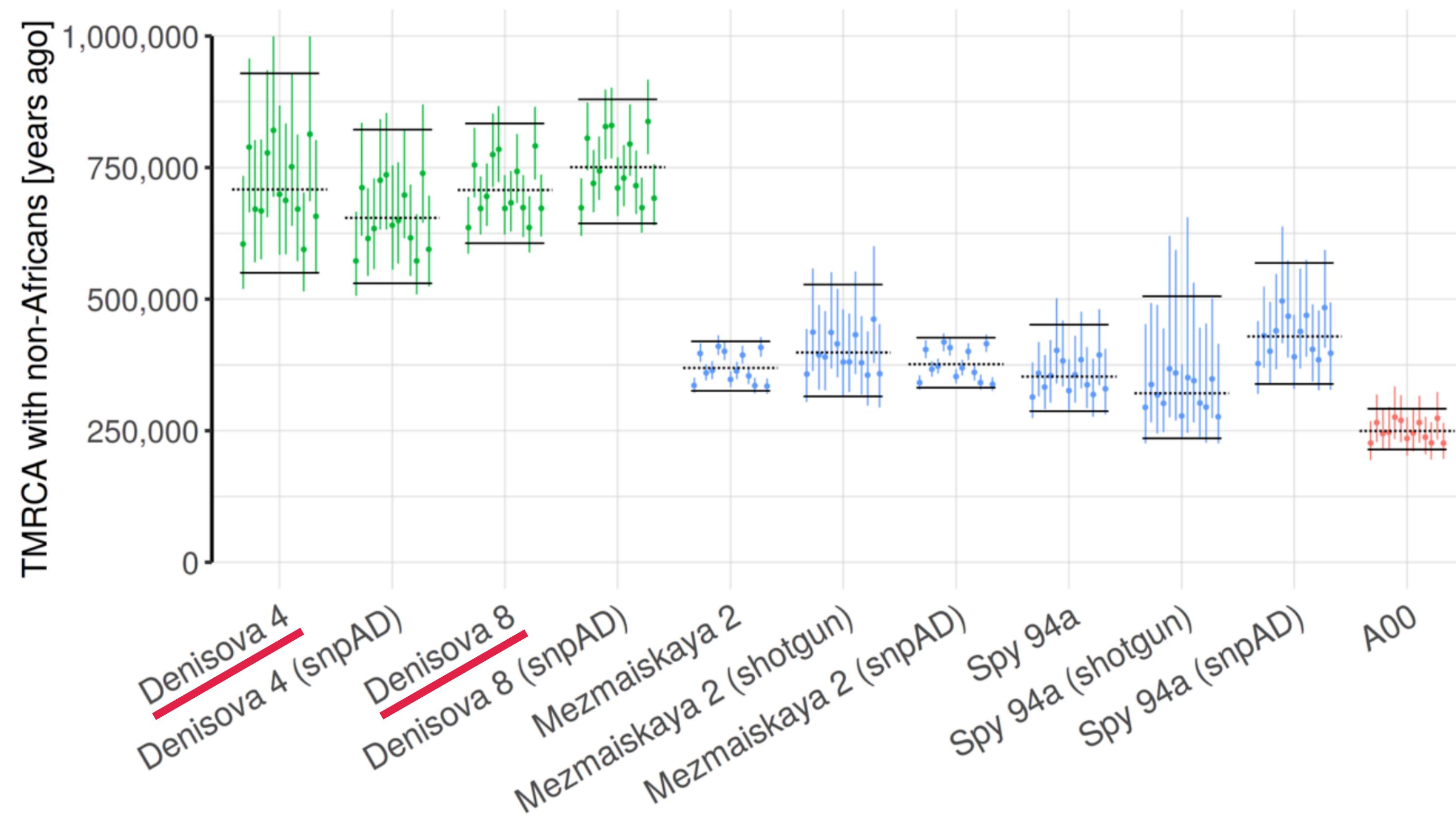
Y chromosome TMRCA estimates



Y chromosome TMRCA estimates



Y chromosome TMRCA estimates



Y chromosome capture design

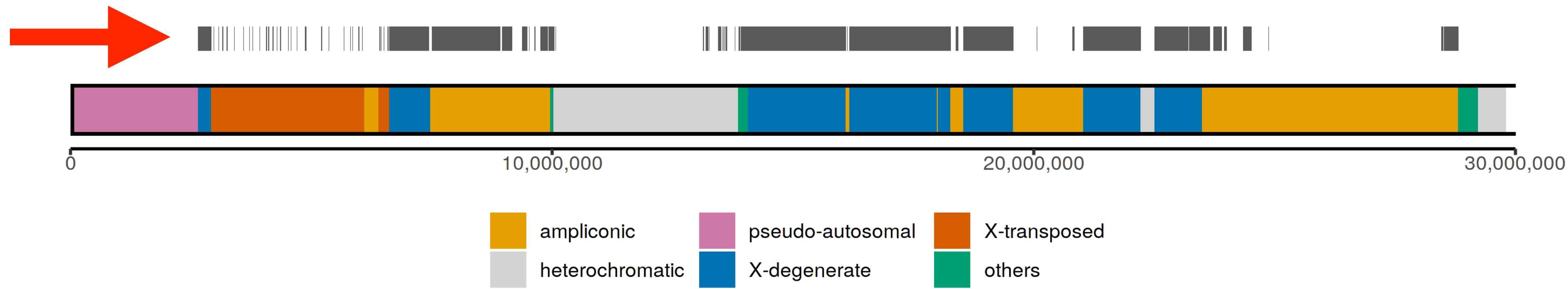


Fig. 1B