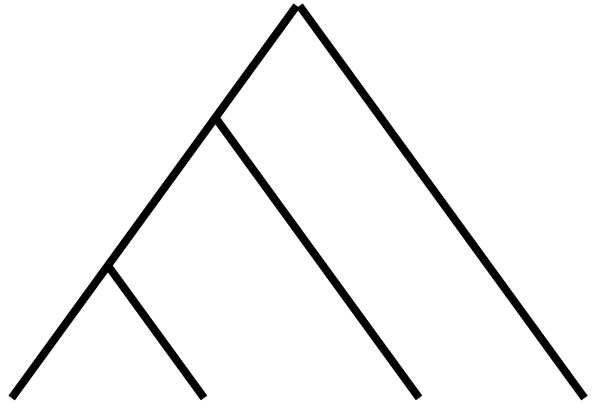
Detecting hybridization with ADMIXTOOLS

Patterson’s D statistics to identify hybridization

- Also called ABBA-BABA test: D=(ABBA-BABA)/(BABA+ABBA)



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

P1	P2	P3	P4	
T	**T**	A	A	
G	**G**	**G**	T	Concordant SNPs
C	T	T	T	
C	A	**C**	A	Discordant SNPs
A	**T**	**T**	A	

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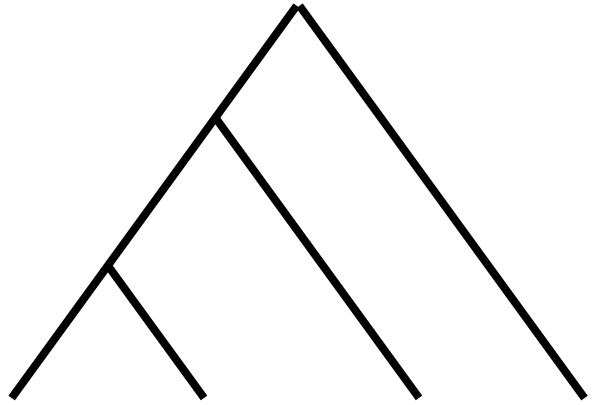


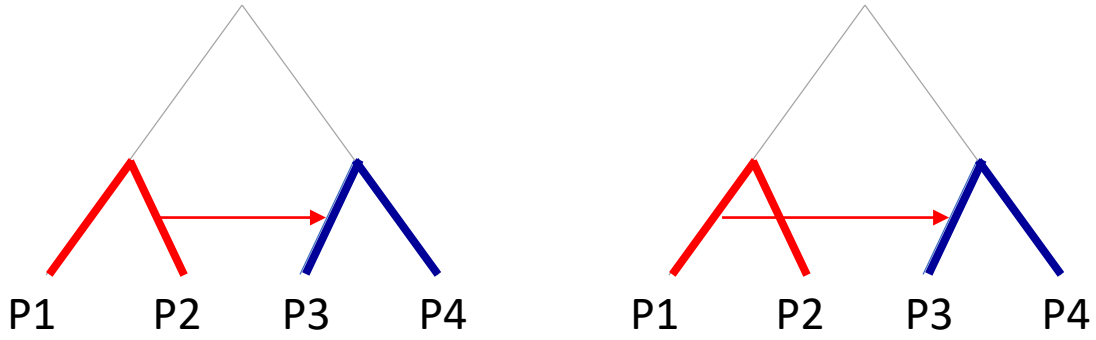
$$D = \frac{ABBA - BABA}{ABBA + BABA}$$

P1	P2	P3	P4	
T	**T**	A	A	
G	**G**	**G**	T	Concordant SNPs
C	T	T	T	
C	A	**C**	A	← BABA
A	**T**	**T**	A	← ABBA
C	**G**	**G**	C	← ABBA

$$D = \frac{2-1}{2+1} = 1/3$$

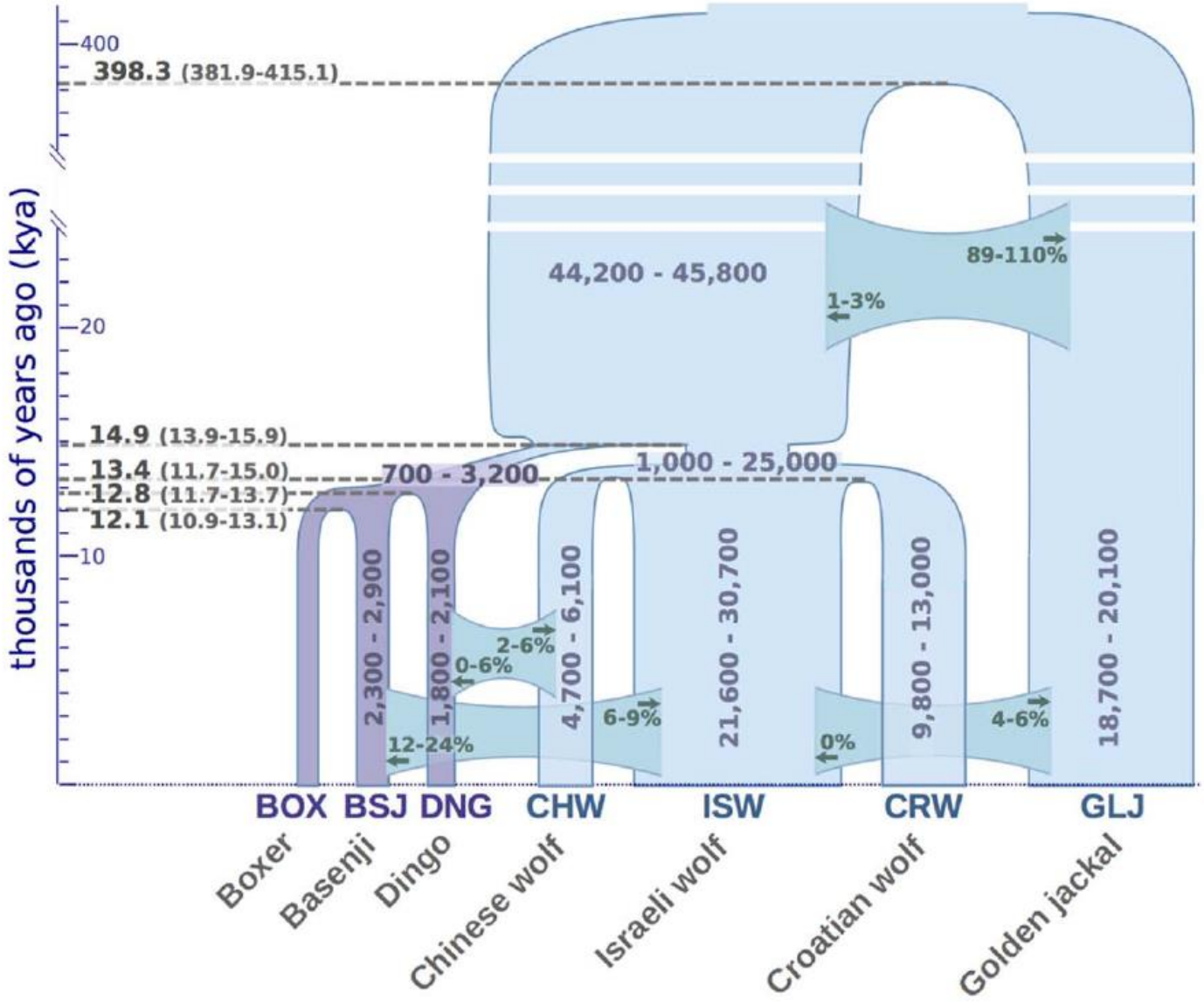
f4 tests to identify hybridization

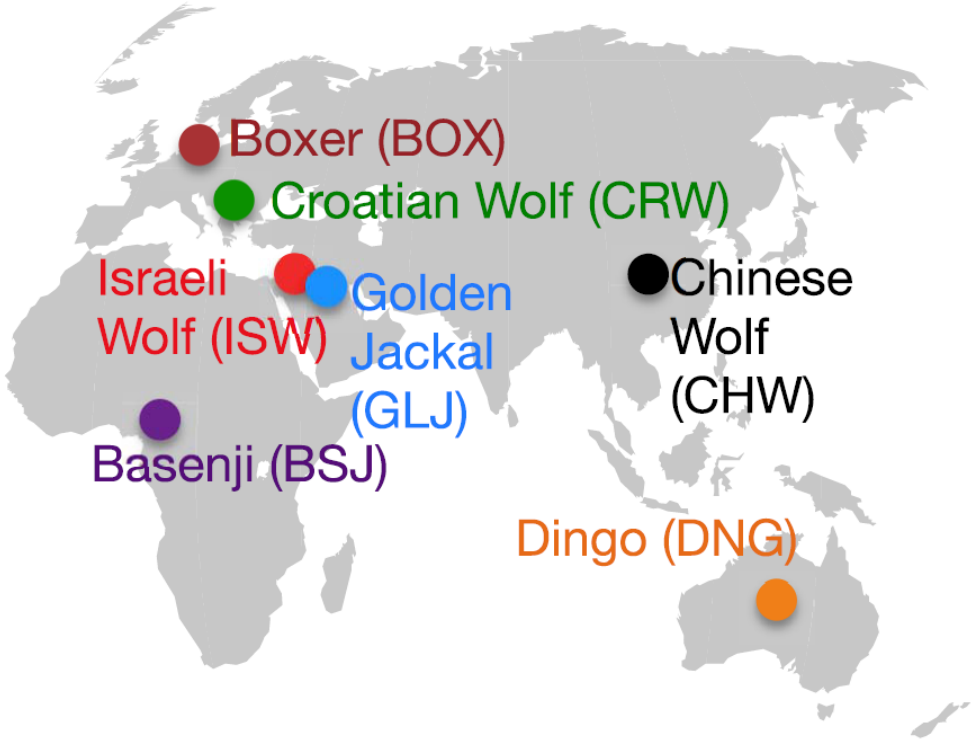
- F statistics are based on drift indices or variance in allele frequencies between 4 populations
- F4(P1,P2:P3,P4) should be zero as no shared drift path without hybridization
- If ((P1,P2),(P3,P4)) is correct, the allele frequency differences between P1 and P2 should be uncorrelated with those between P3 and P4, which we can assess by averaging the quantity (p1-p2)(p3-p4) across SNPs.
- D statistic: Normalized f4 statistic with polarized alleles (conditions on derived allele frequency using an outgroup)



Freedman et al., 2014, PLoS Genetics: GPhoCS

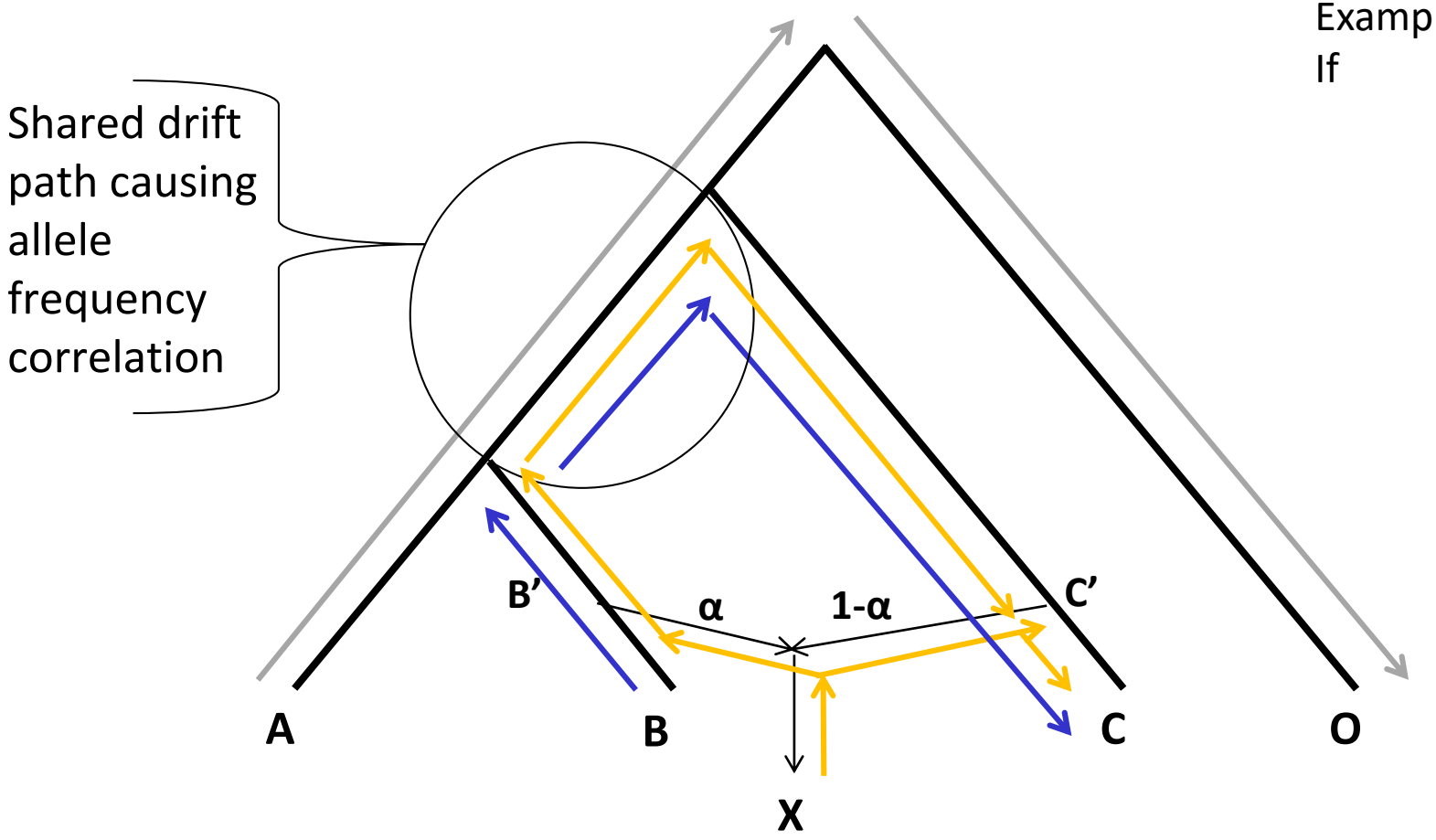
None of the tested wolves is closer to the dogs but some hybridized



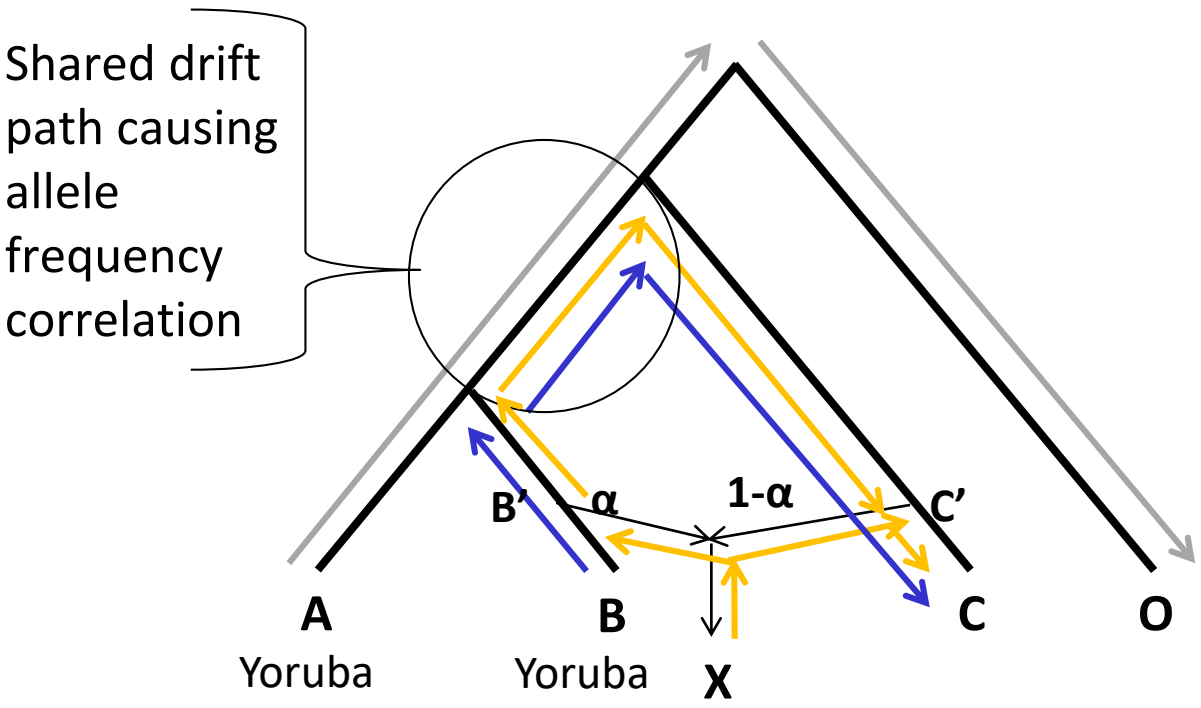


f4 ratio test to infer the amount of admixture

Example correlation:
If



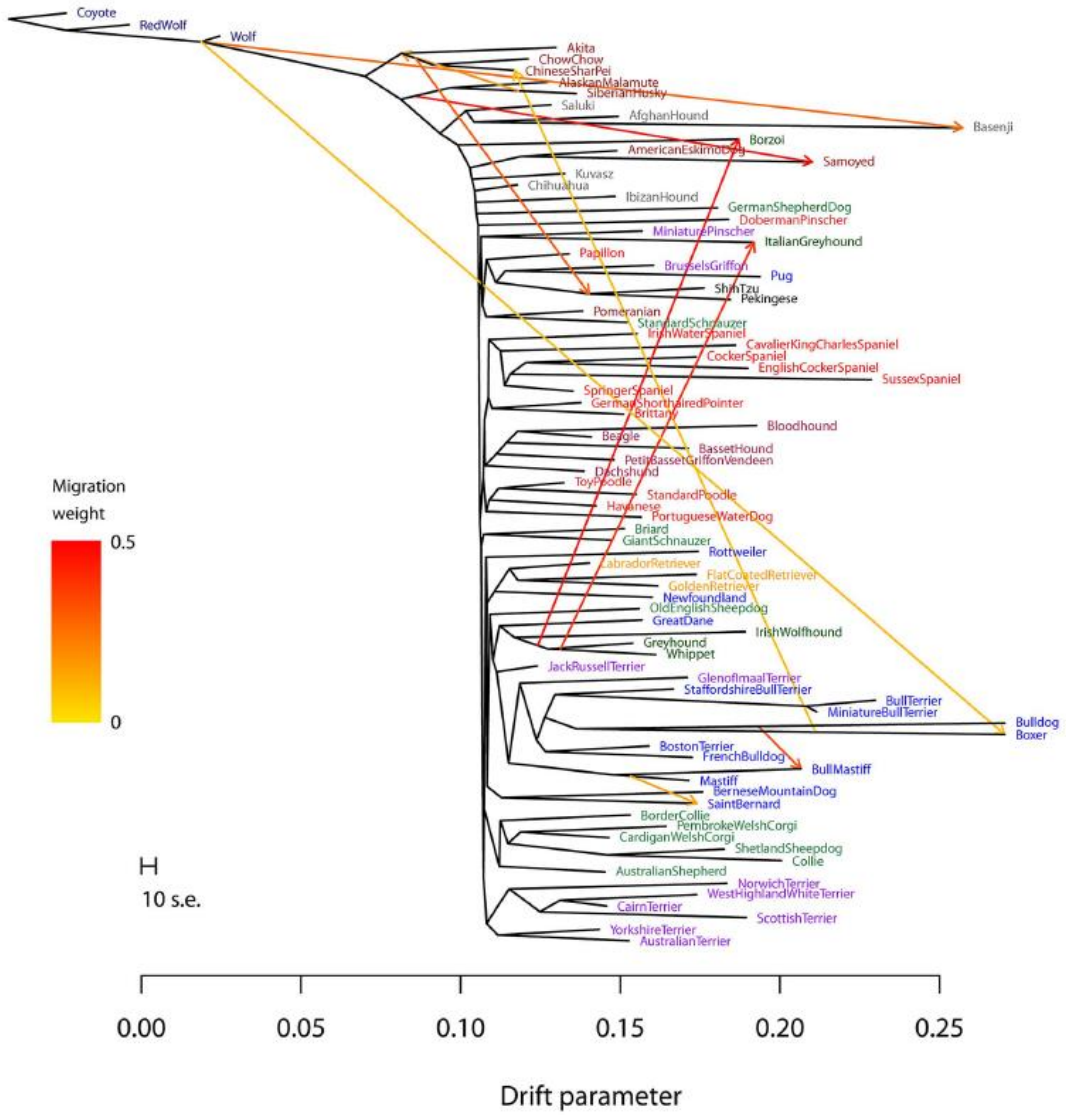
f4 ratio test to infer the amount of admixture



The shared drift path generates correlation between A-O and B-C. X-C share the same drift path by the proportion α.

$$\alpha = \frac{F_4(A,O;X,C)}{F_4(A,O;B,C)} = \frac{E[(a-o)(x-c)]}{E[(a-o)(b-c)]} = \frac{\text{Correlation of allele frequency difference between a-o and x-c}}{\text{Correlation of allele frequency difference between a-o and b-c}}$$

Treemix (Pickrell & Pritchard, 2012, Plos Genetics)



- Treemix uses covariances of allele frequencies to infer a maximum likely tree with a user-specified number of migration edges
- Gene flow edges are added sequentially to account for the greatest errors in the fit. This format makes TreeMix well-suited to handling very large trees: the entire fitting process is automated and can include arbitrarily many admixture events simultaneously.
- Treemix has most problems with inferring the direction of gene flow and sometimes places migration edges to taxa that are closely related but not involved in the hybridization event
- Treemix should not be used as only source of information and may sometimes not work at all…

Alternatives to treemix

- MixMapper (Lipson et al., 2013, MBE): partially supervised, first scaffold tree building without the putatively admixed taxon/taxa, then fitting the user can specify to fit a likely admixed taxon as combinations of two taxa in the tree (runs in Matlab)
- Admixturegraph R package: Full flexibility (and most work). Admixturegraph uses a set of f4 statistics (e.g. from ADMIXTOOLS) to infer the likelihood for a user-specified admixture graph
- G-PhoCS (Generalized Phylogenetic Coalescent Sampler, Gronau et al., 2011, Nature Genetics): Demographic modeling software designed for modeling population splits and gene flow «bands»

Which grey wolf is most similar to the ancestor of dogs?

Chinese Wolf

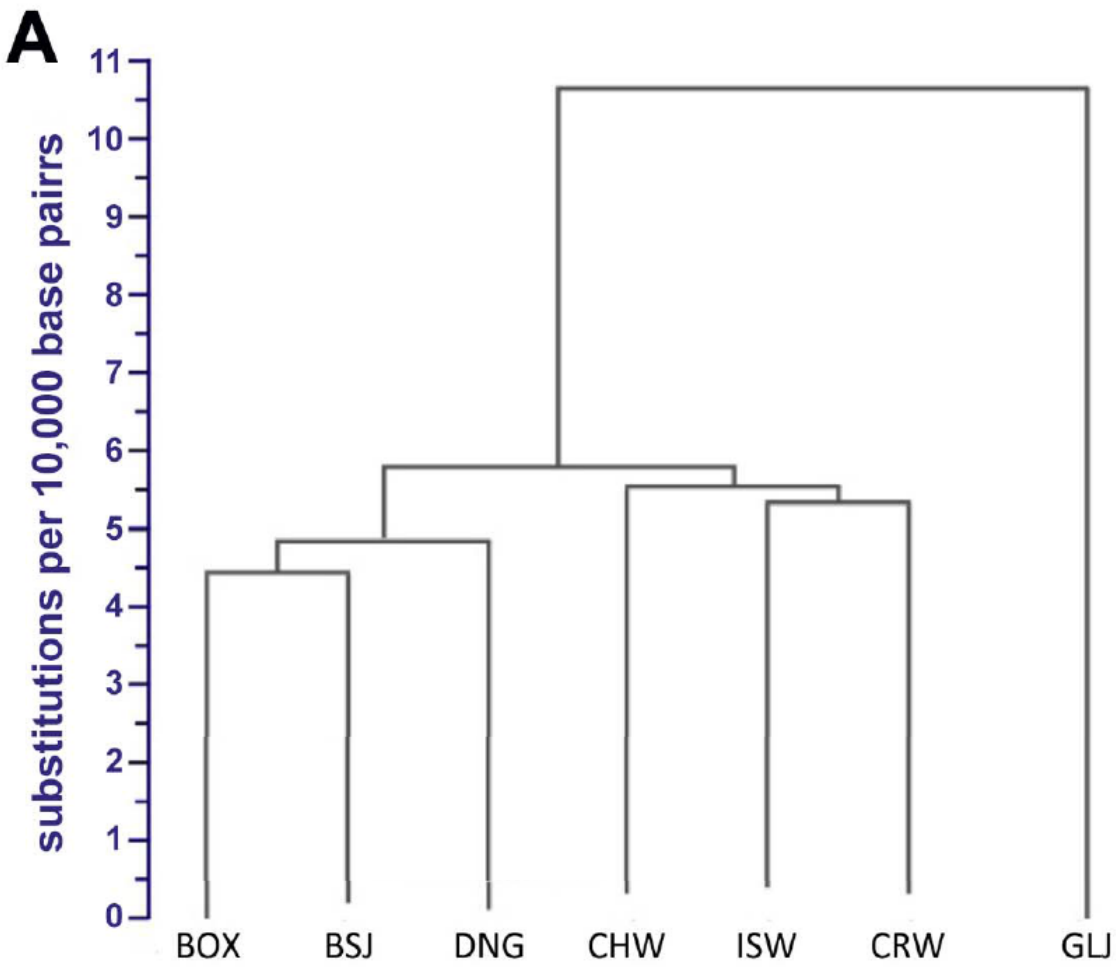
Basenji (Congolese hunting dog)

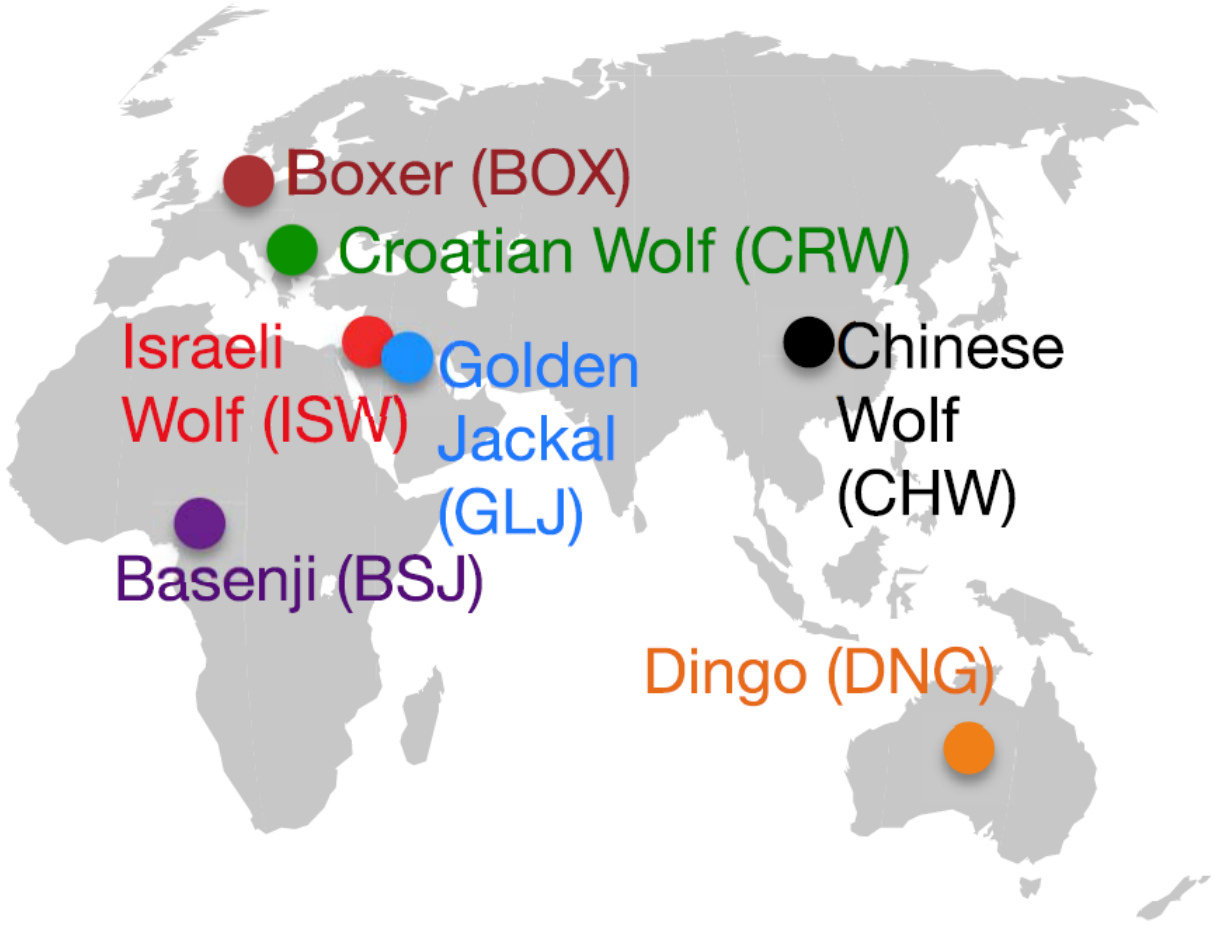
Dingo (Australian wild dog)

Israeli Wolf

Croatian Wolf

Let’s test who hybridized with whom using ADMIXTOOLS and treemix





Results by Freedman et al., 2014, PLoS Genetics