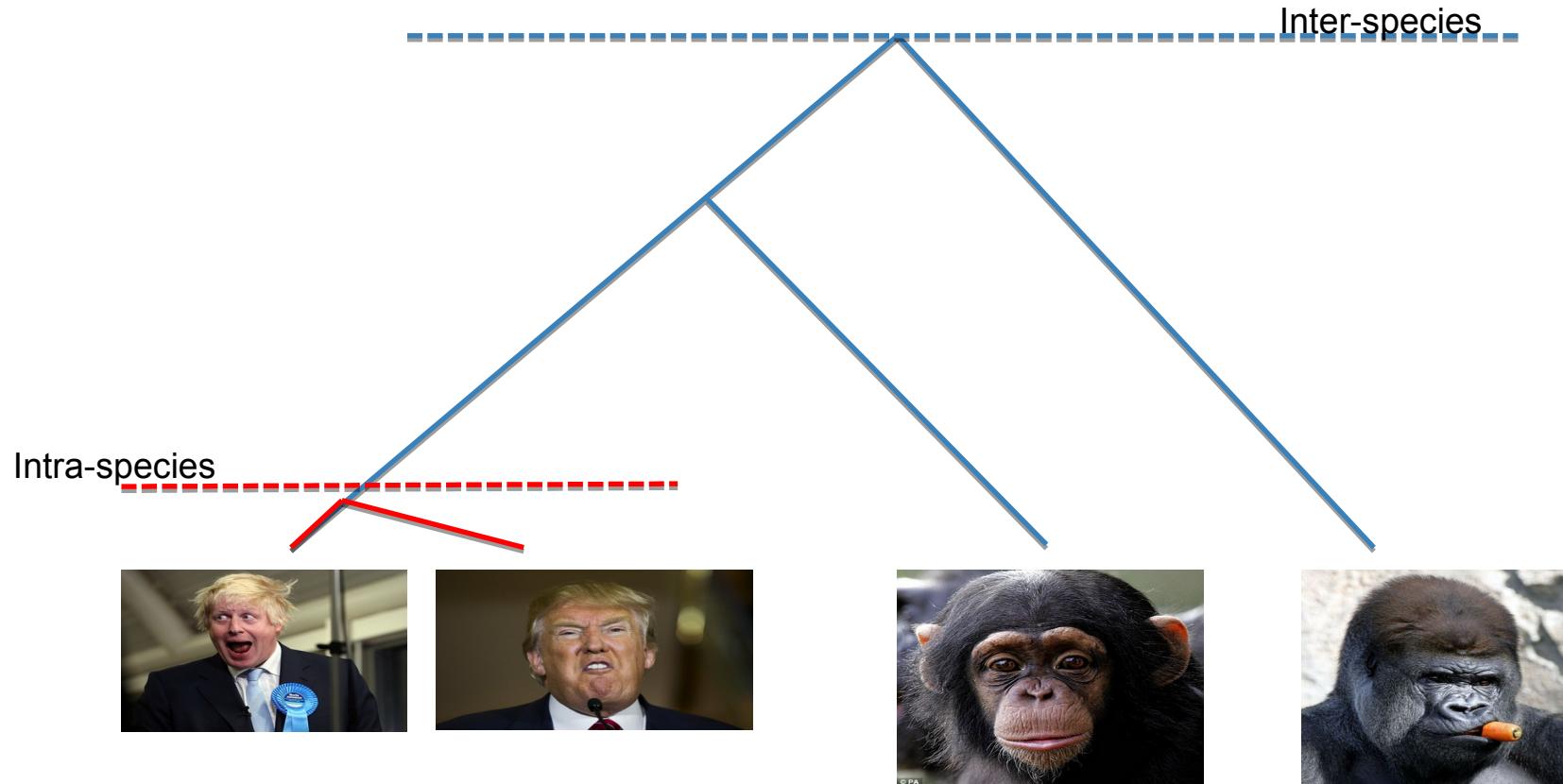


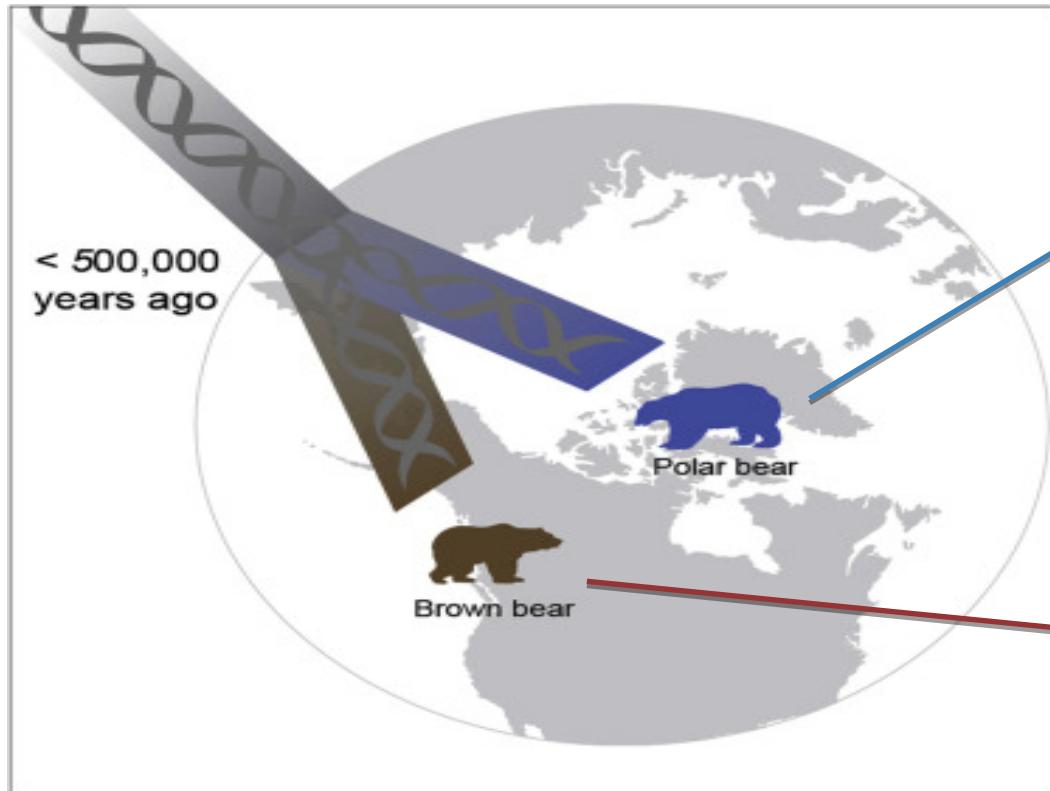
Selection (part 2)

Inter-species variation



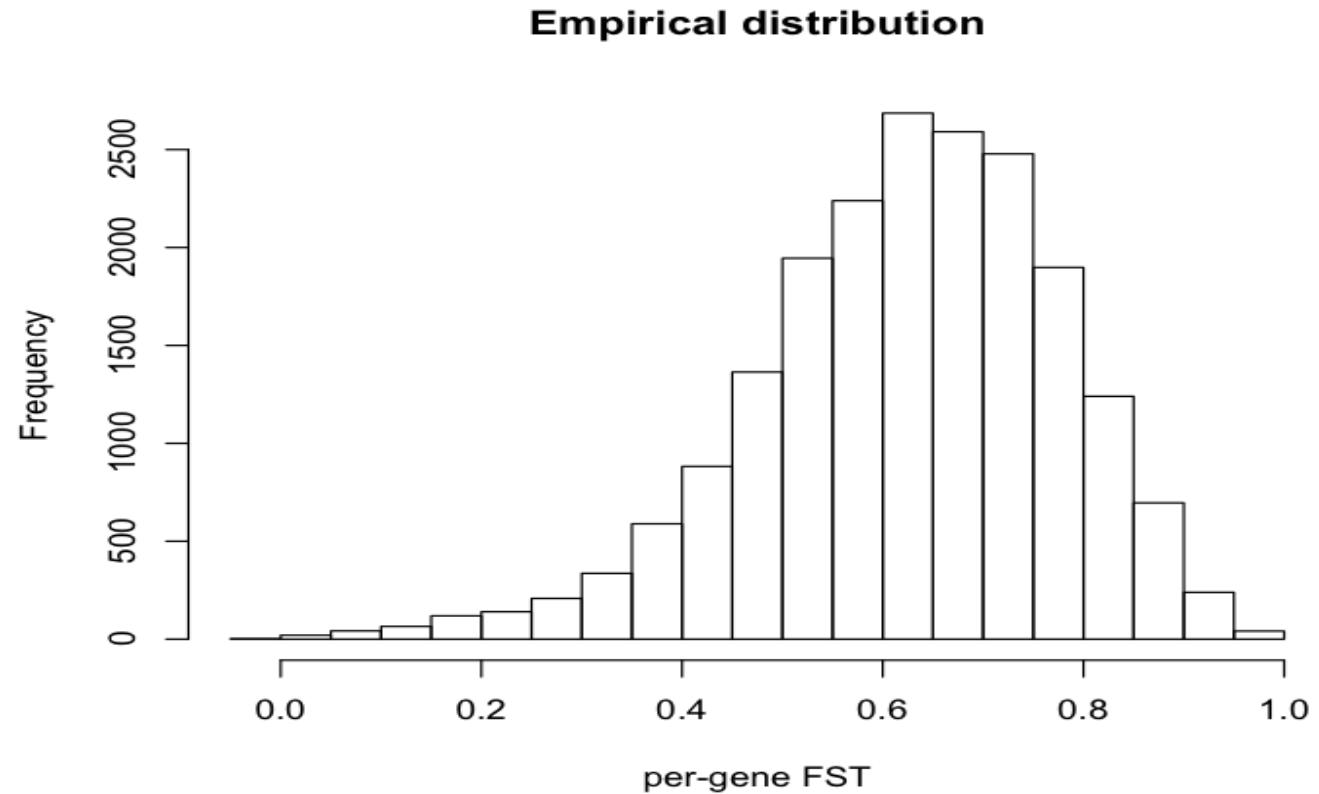
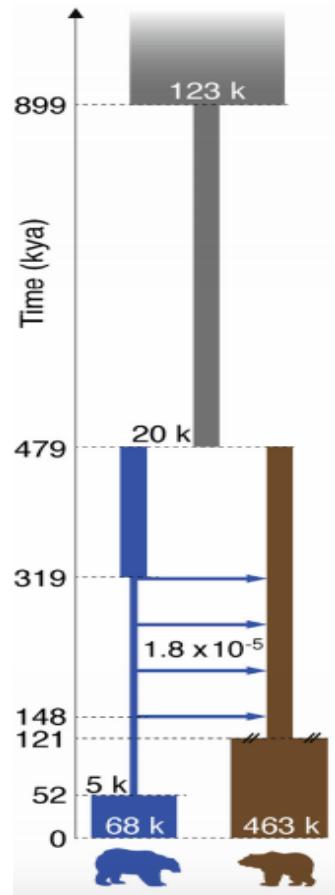
events in the deep past, macro-evolutionary trends, selection between species

Polar bears vs. Brown bears

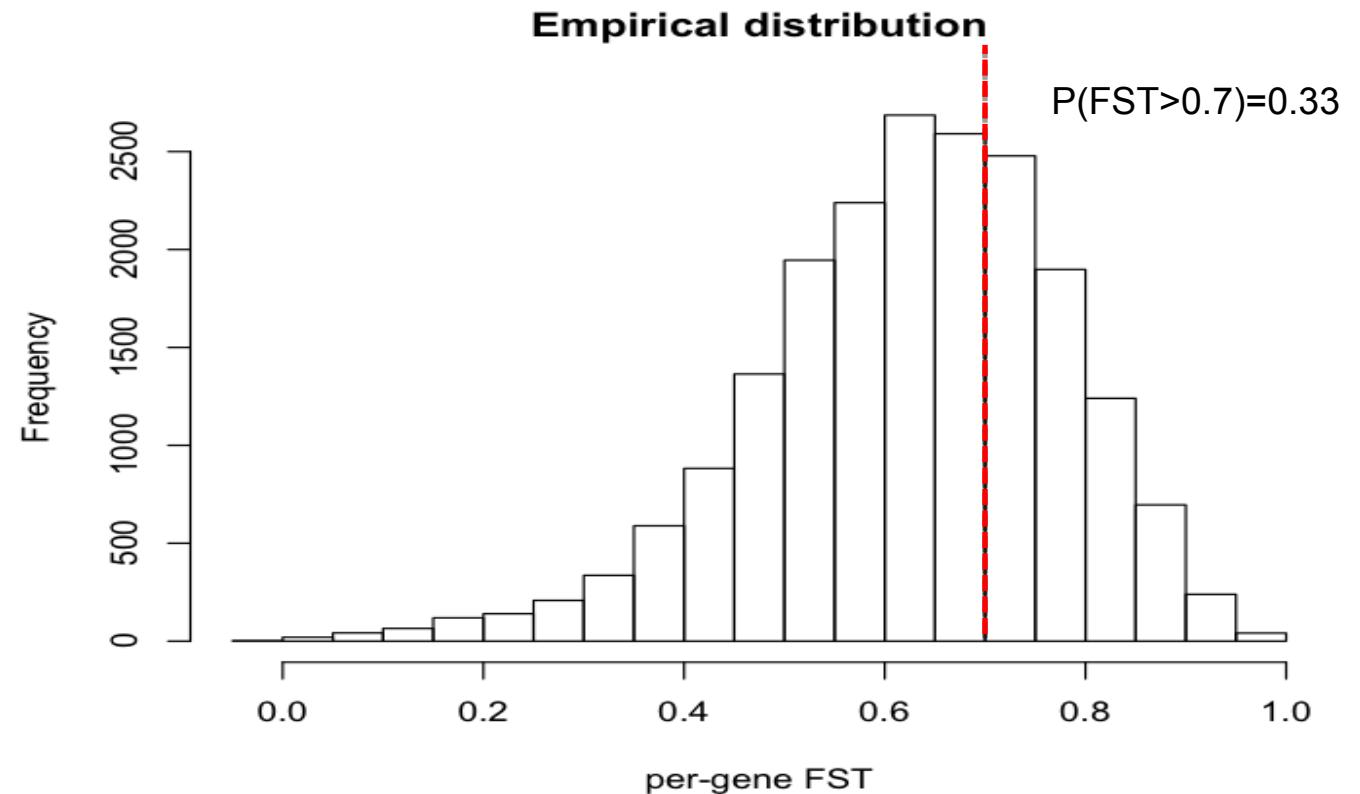
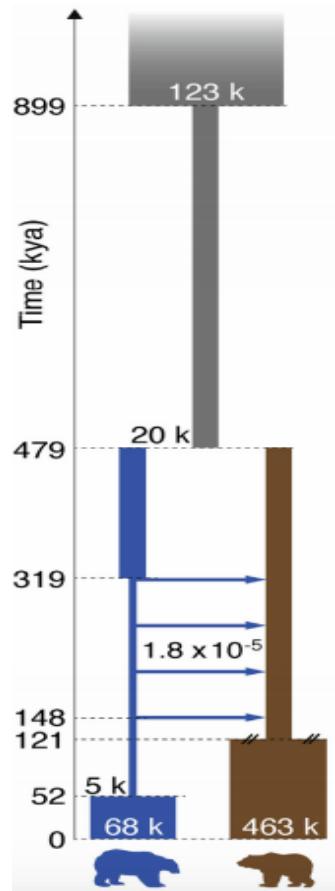


Question: what are the genetic signatures of polar bears' adaptation to the Arctic environment?

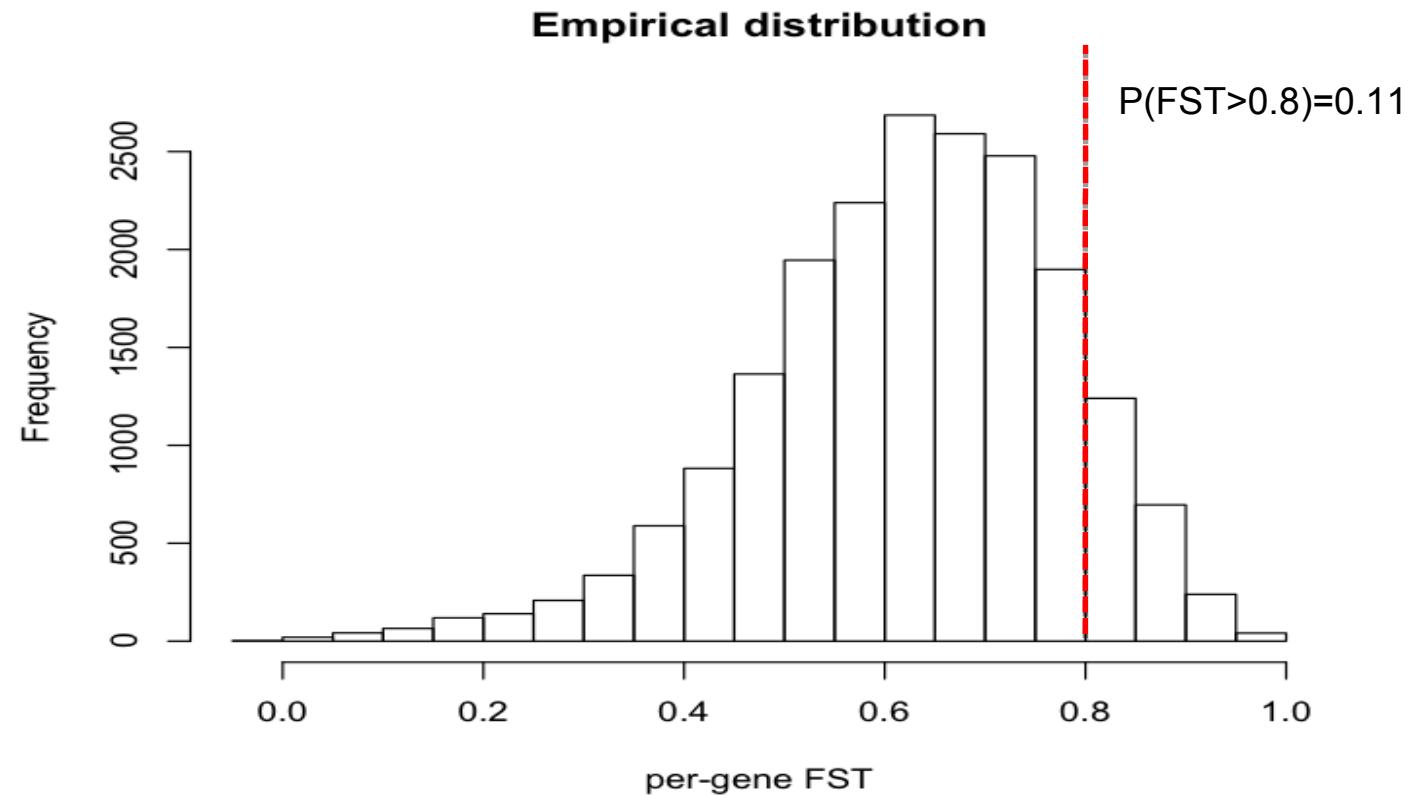
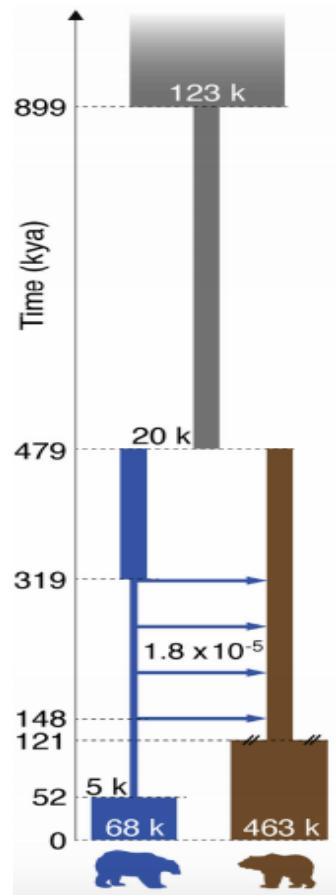
Expected genetic differentiation



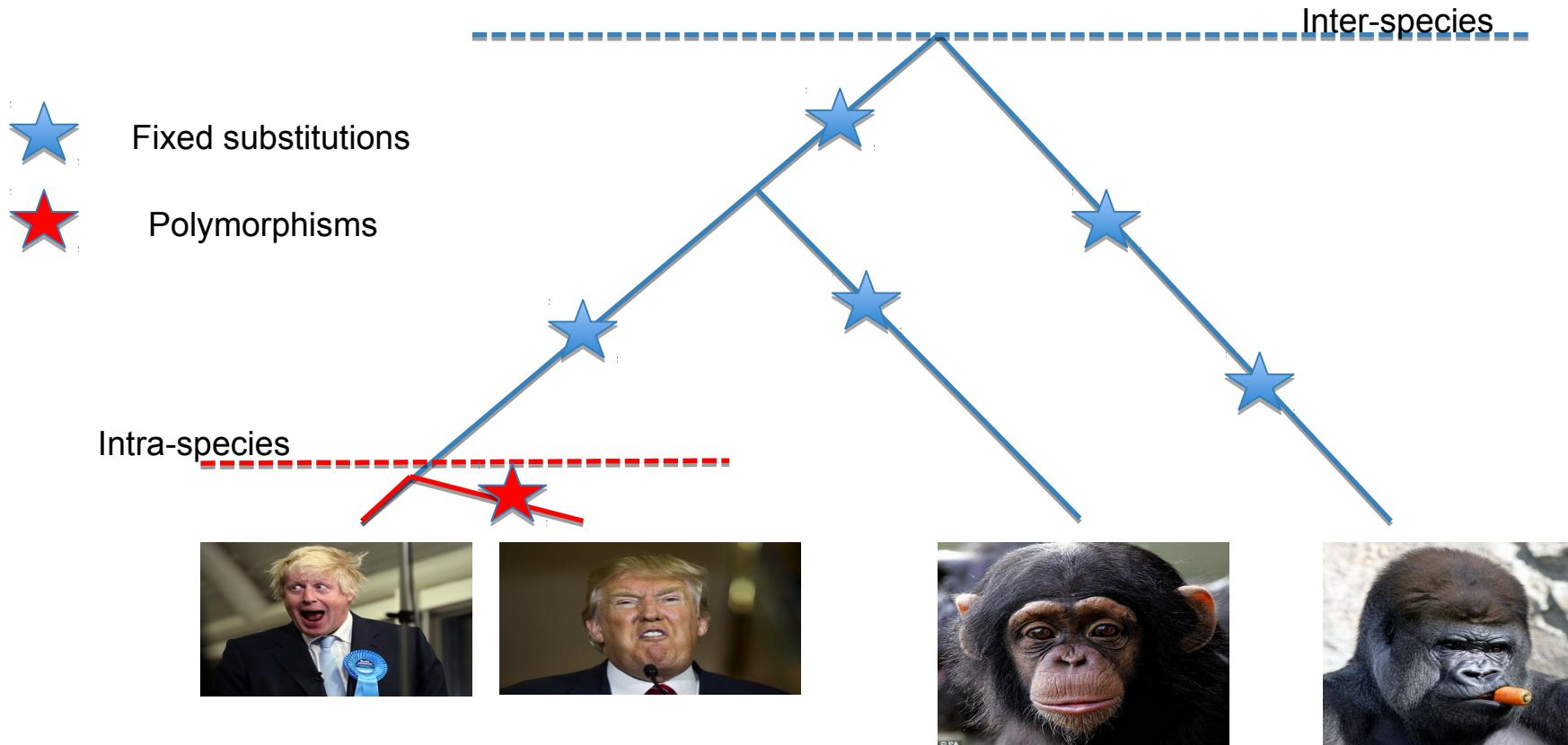
Expected genetic differentiation



Expected genetic differentiation



Inferring inter-species selection

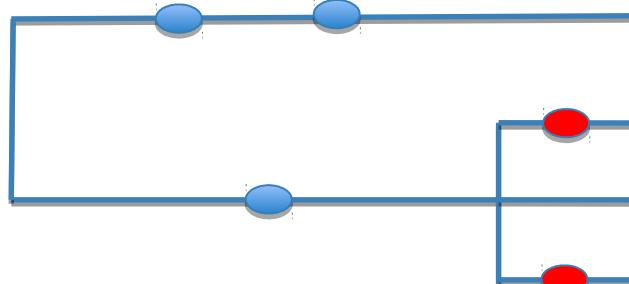


Polymorphisms and divergence

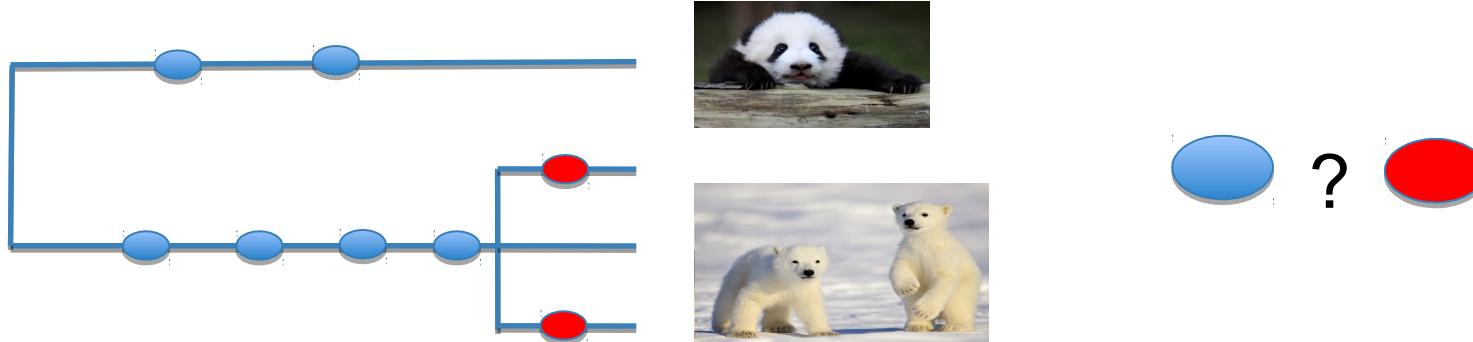
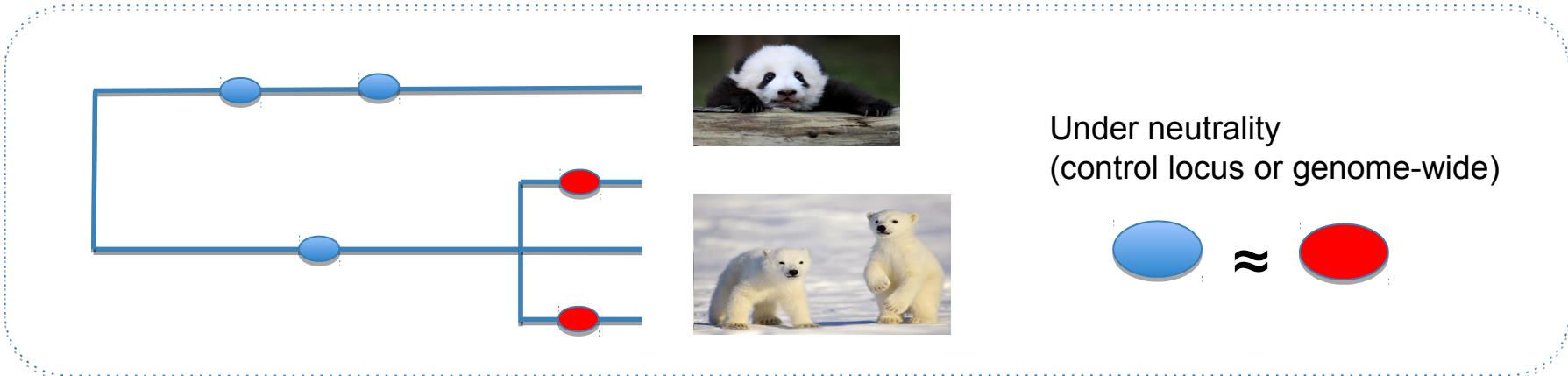
As both depend on mutation rates,
proportional.



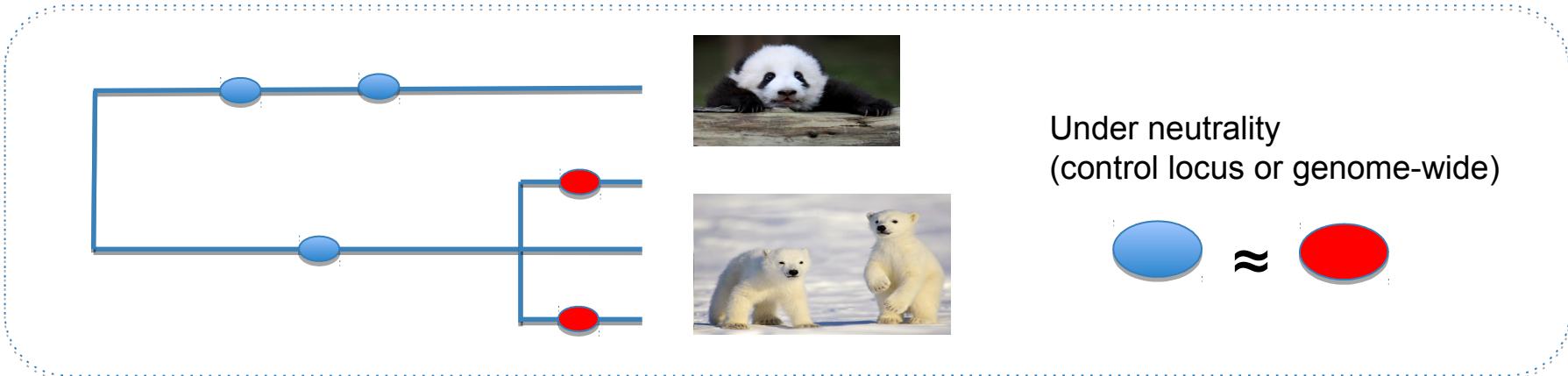
Levels are expected to be



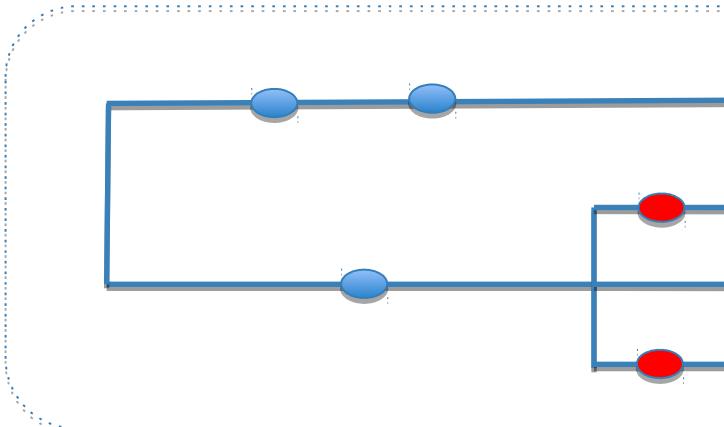
Polymorphisms and divergence



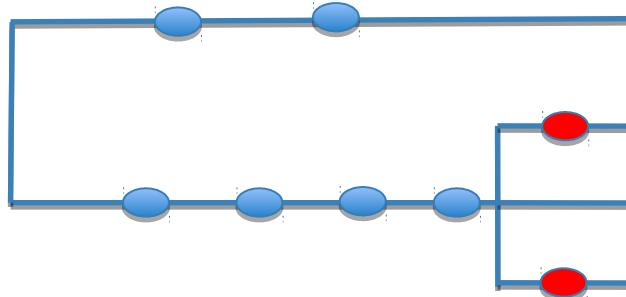
Polymorphisms and divergence



Polymorphisms and divergence



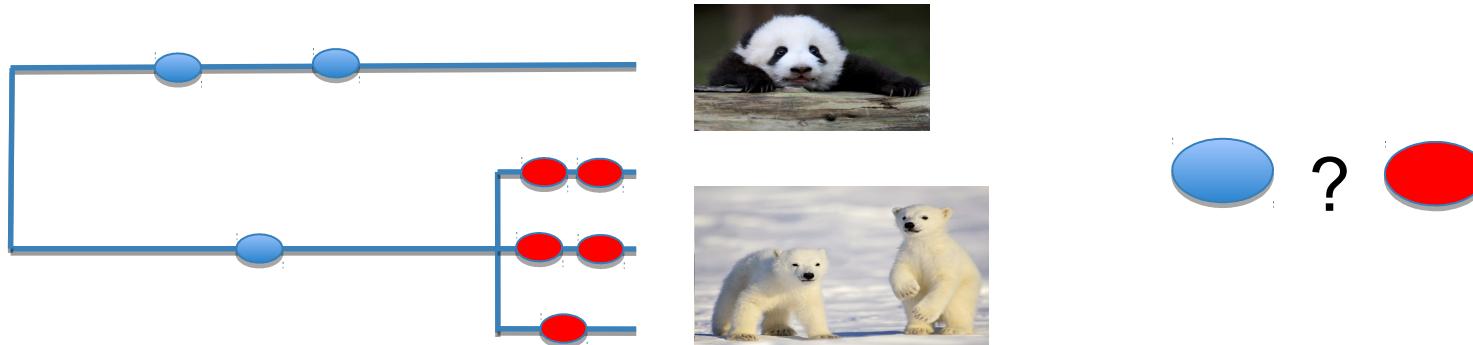
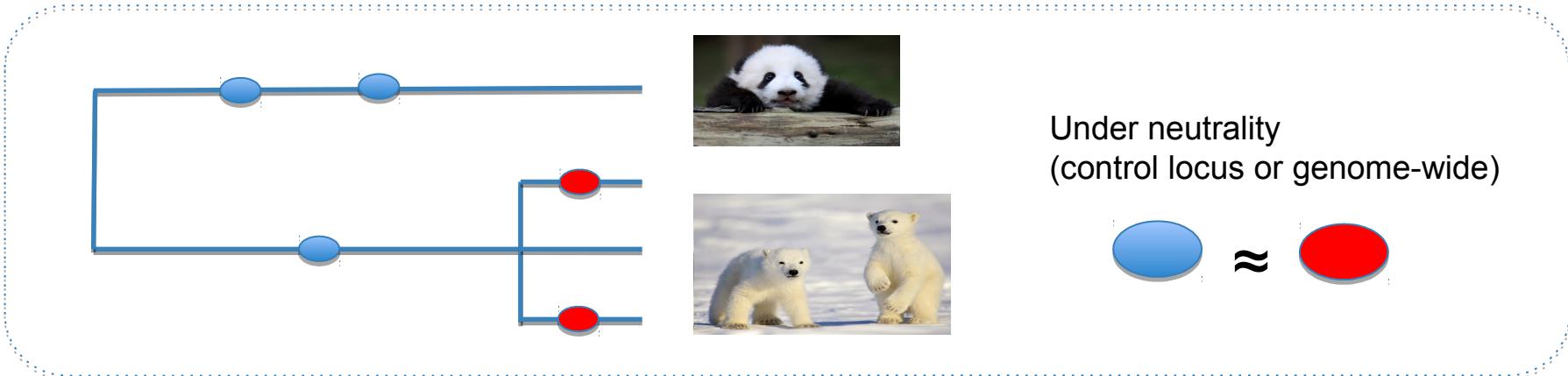
Under neutrality
(control locus or genome-wide)



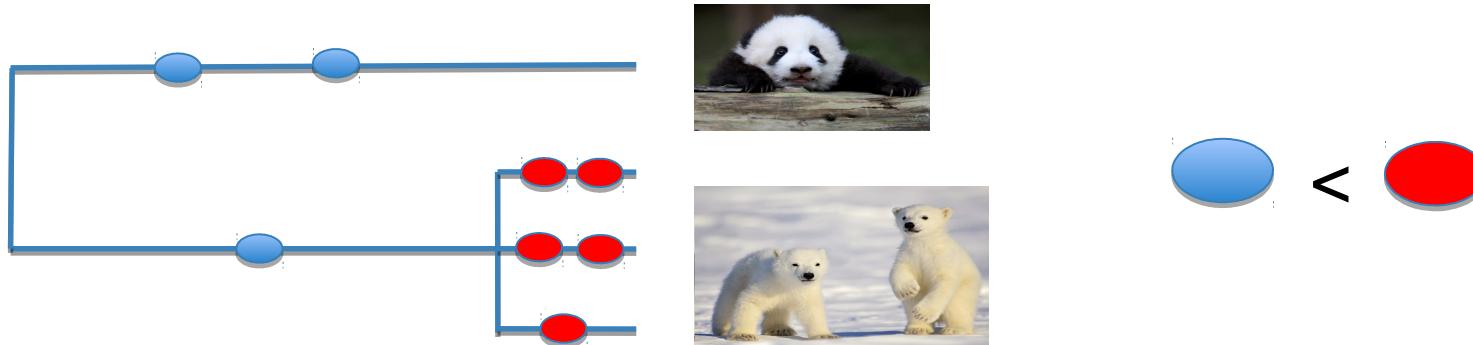
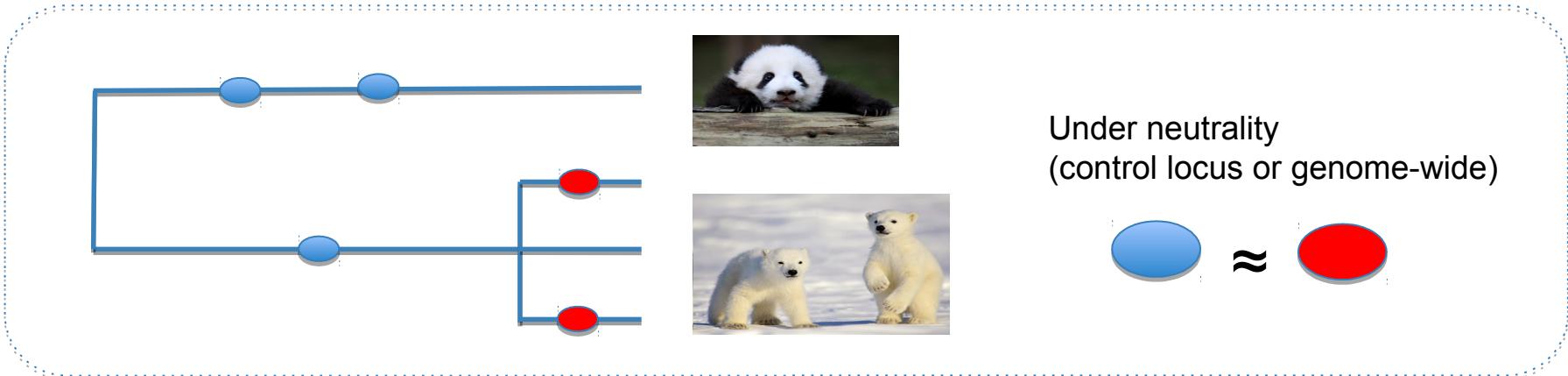
Positive selection
(or negative selection)



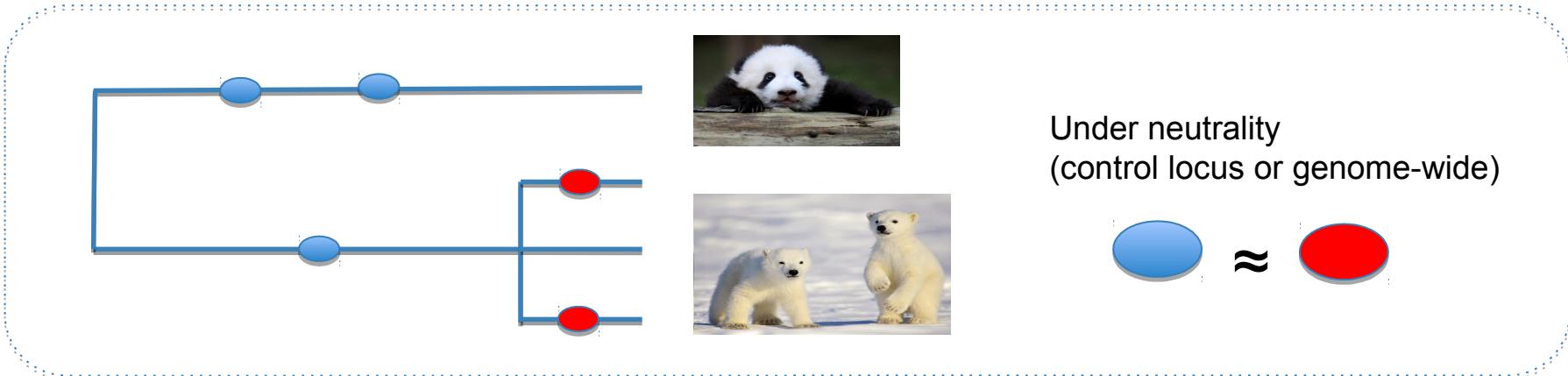
Polymorphisms and divergence



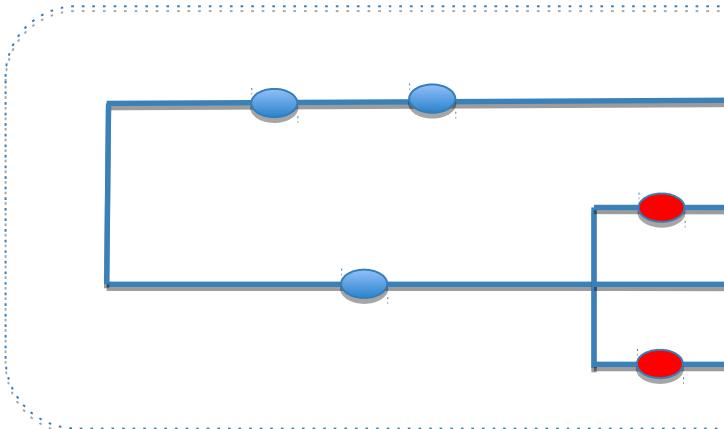
Polymorphisms and divergence



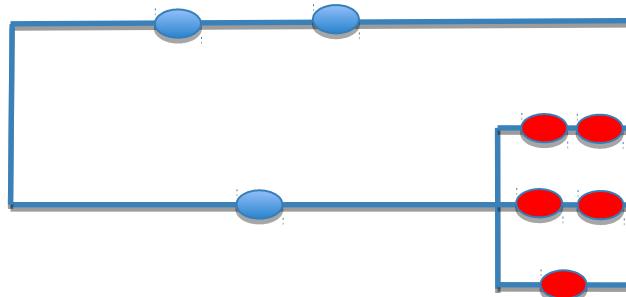
Polymorphisms and divergence



Polymorphisms and divergence



Under neutrality
(control locus or genome-wide)

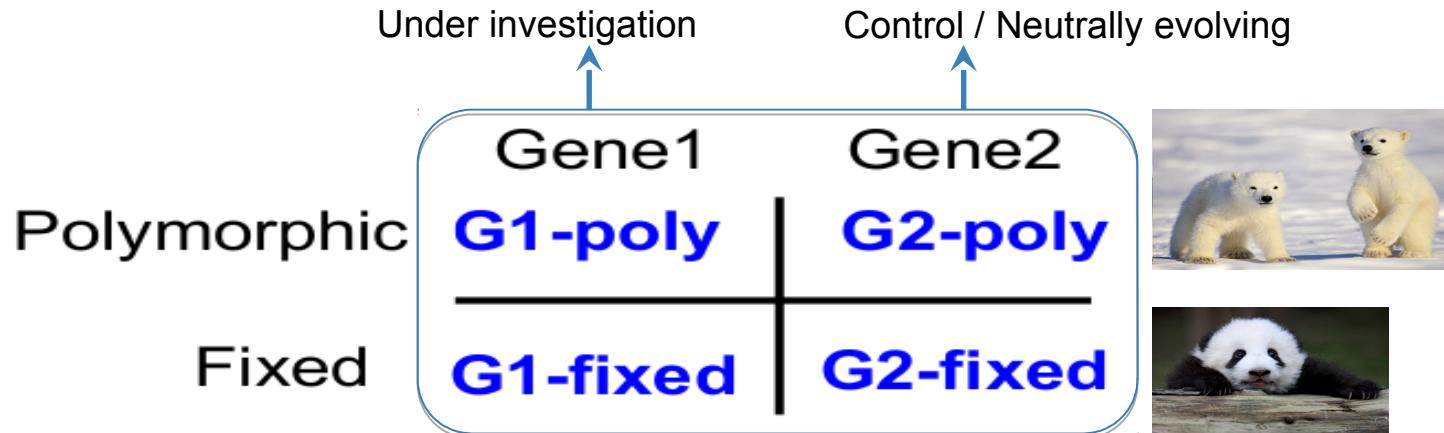


Balancing selection
(or relaxation of functional constraints)



HKA test

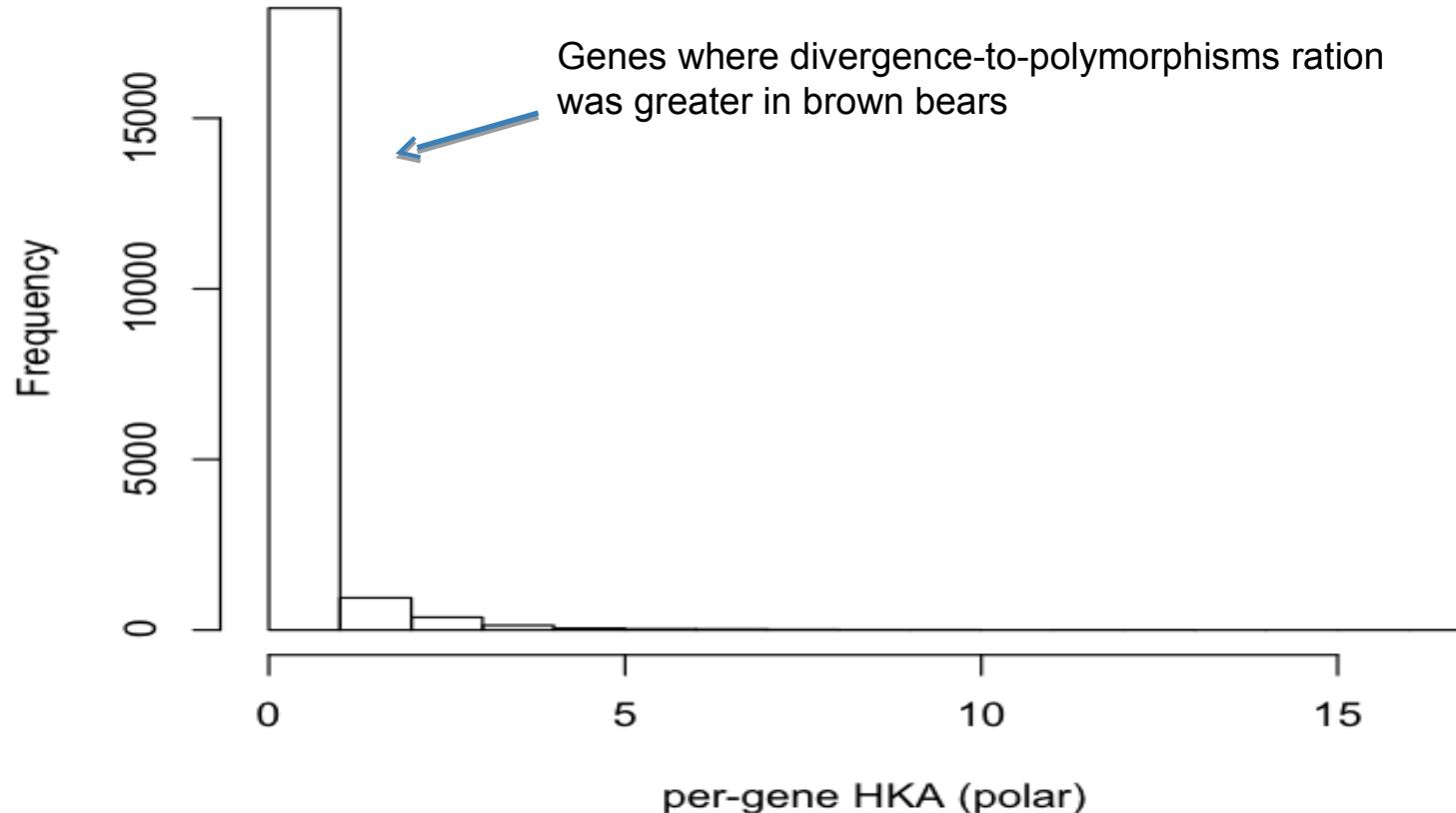
Hudson-Kreitman-Aguadè (HKA, Hudson et al. 1987) test



Contingency table 2x2: chi-square test

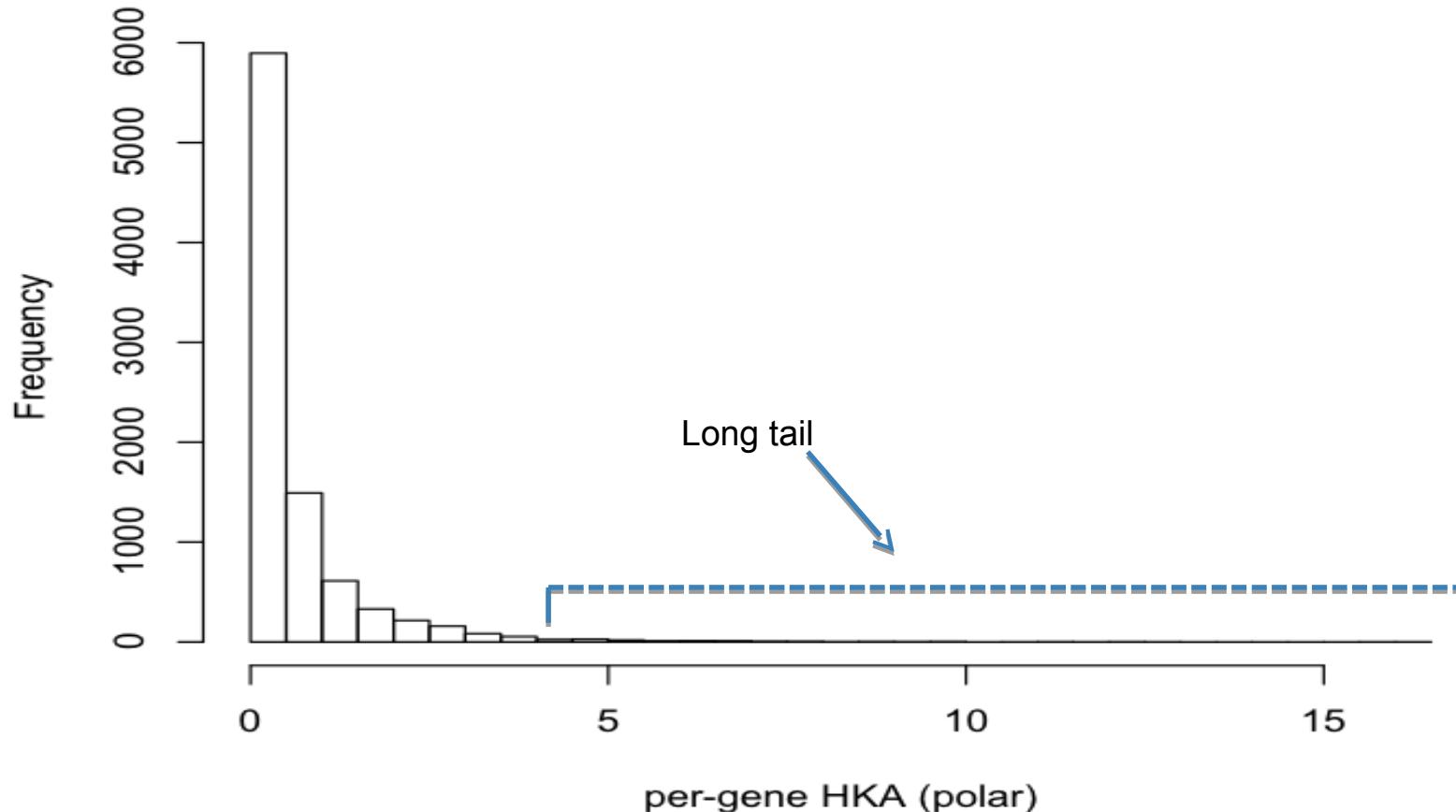
HKA test

Empirical distribution (-log10)



HKA test

Empirical distribution (-log10)



Coding polymorphisms

Substitutions in the coding regions may alter (non-synonymous) or not (synonymous) the protein sequence:

ATC CAA ...
I Q

Ancestral sequence



ATA GAA ...
I K

Species 1



ATG CAG ...
M Q

Species 2



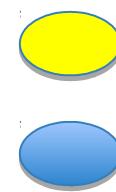
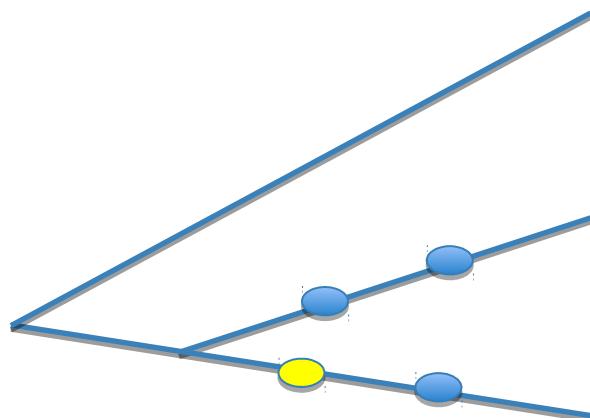
Non-synonymous



Synonymous

dN/ds

Comparison between rate of **nonsynonymous** substitutions and rate of **synonymous** substitutions (also called K_a/K_s or ω)



Non-synonymous



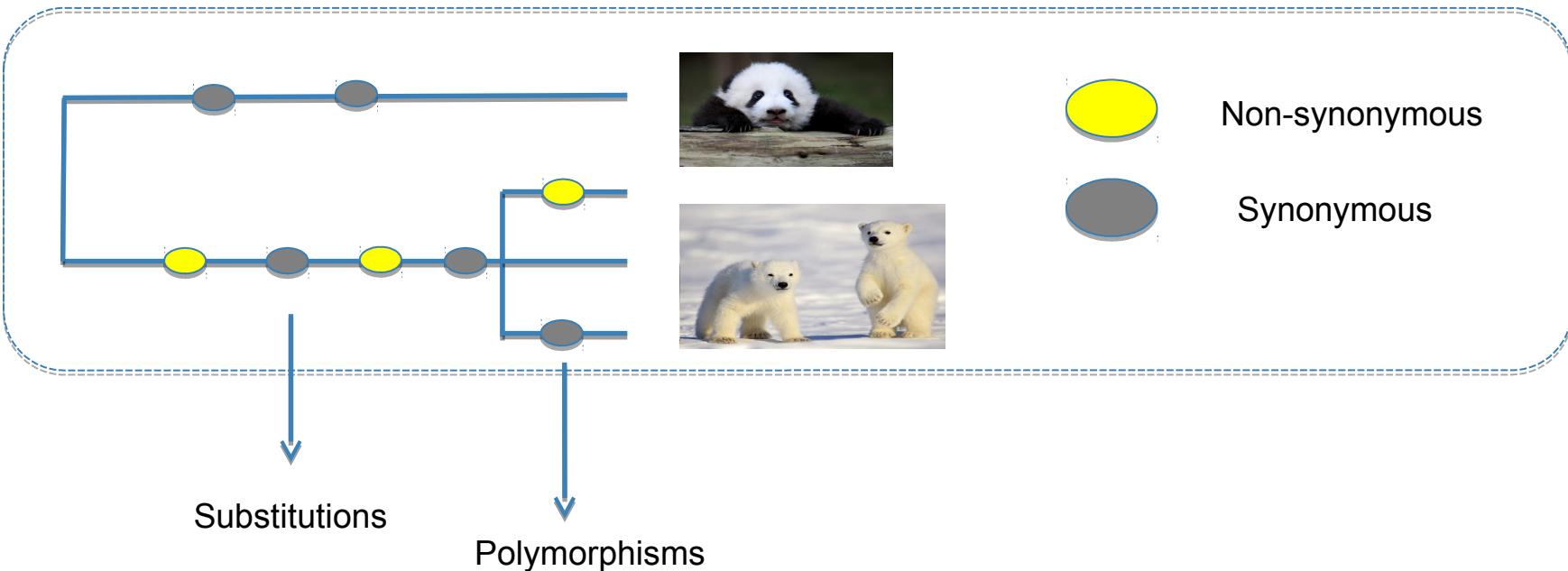
Synonymous

Positive selection
(novel proteins)
 $K_a/K > 1$

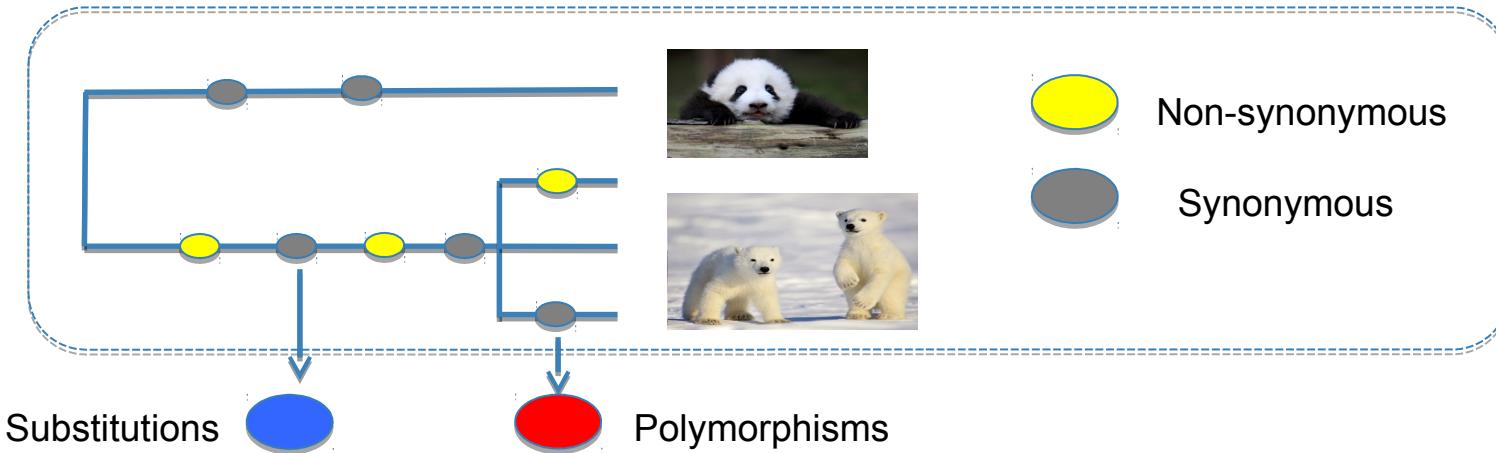
Negative selection
(against deleterious mutations)
 $K_a/K < 1$

Coding polymorphisms and divergence

Compare the amount of variation within a species to the divergence between species at non-synonymous and synonymous variants.

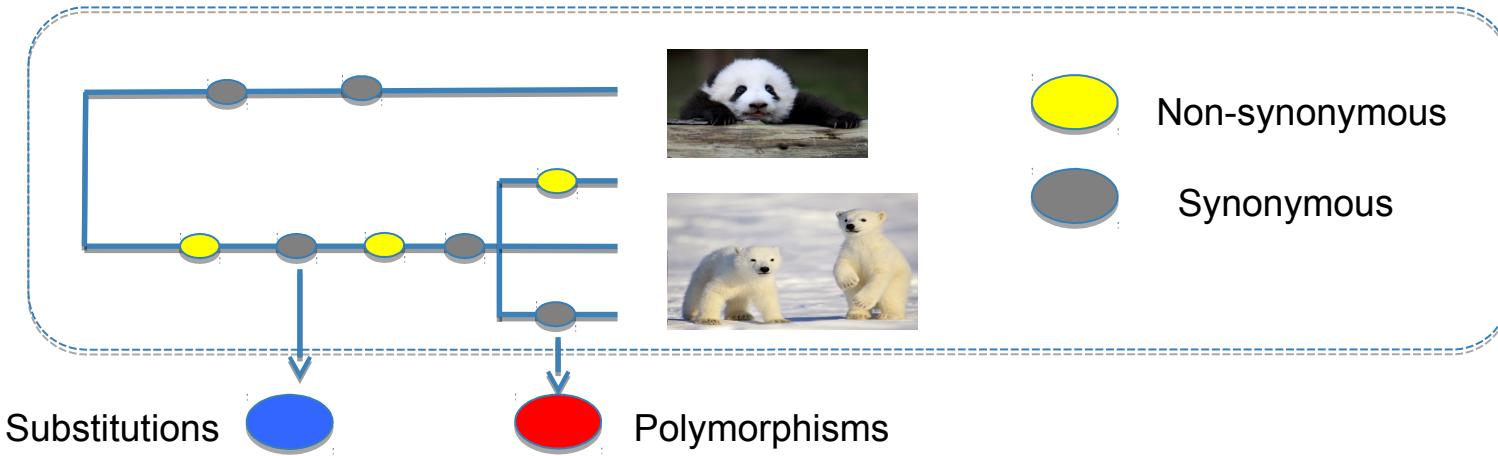


MK (McDonald–Kreitman) test



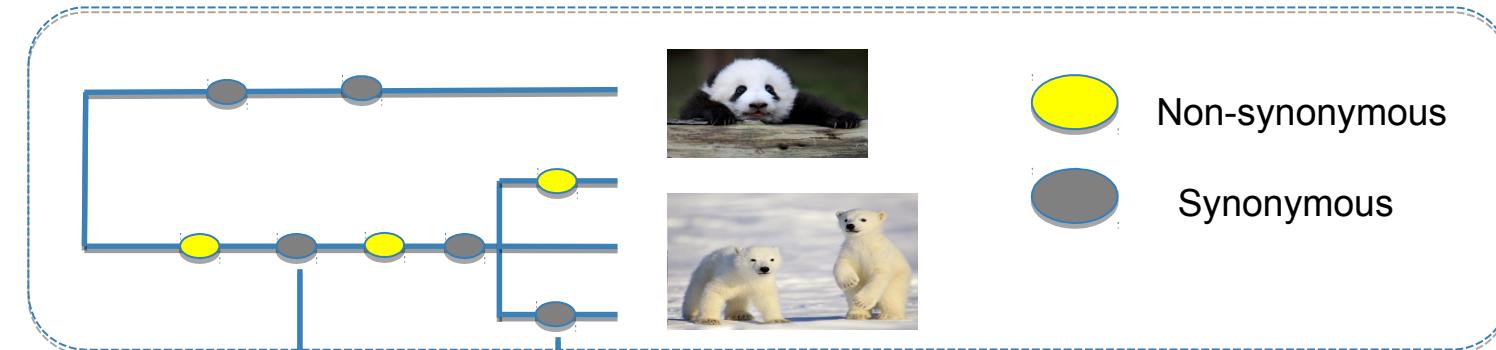
	Non-synonymous	Synonymous
Divergence		
Polymorphisms		

MK (McDonald–Kreitman) test



	Non-synonymous	Synonymous
Divergence	● (Blue)	● (Yellow)
Polymorphisms		
	dN/dS between species	

MK (McDonald–Kreitman) test



Substitutions



Polymorphisms



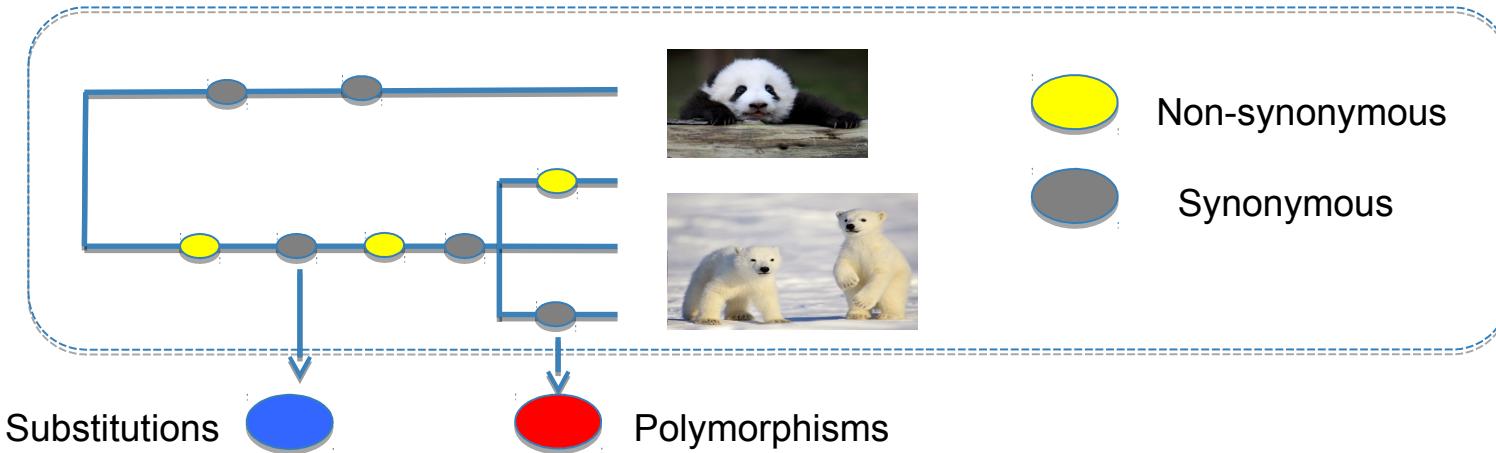
Non-synonymous



Synonymous

	Non-synonymous	Synonymous
Divergence	Substitutions (Blue)	Substitutions (Blue)
Polymorphisms	Polymorphisms (Red)	Polymorphisms (Red)
	dN/dS within species	

MK (McDonald–Kreitman) test



	Non-synonymous	Synonymous
Divergence		
Polymorphisms		

2x2 contingency table