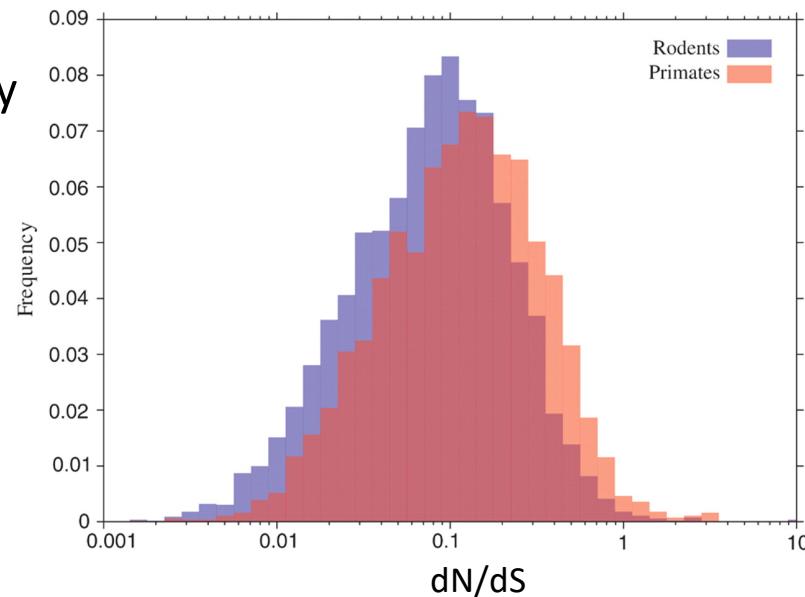


Levels of constraint

- Neutral theory claims most new mutations are deleterious and are lost immediately. Only neutral mutations contribute to substitution.
- $dN = \text{nonsynonymous subst./site}$
- $dS = \text{synonymous subst./site}$
- Expected dN/dS for a “typical” gene. < 1

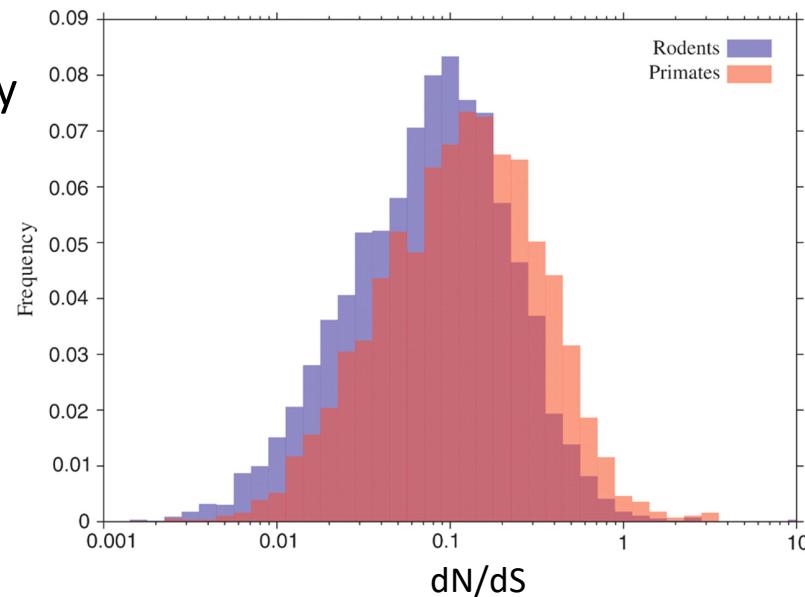
Consistent with neutral theory
slower rate of substitution at
more constrained sites.



Levels of constraint

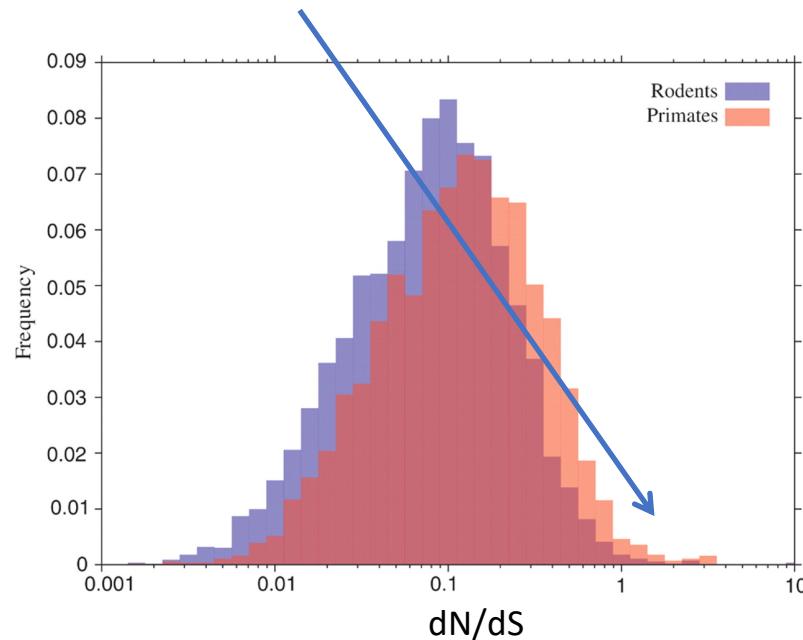
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Consistent with neutral theory
slower rate of substitution at
more constrained sites.



Adaptive protein divergence and the dN/dS ratio

- dN = nonsynonymous subst./site
- dS = synonymous subst./site
- Expected dN/dS for a “typical” gene. < 1
- Expected dN/dS for a gene coding for an unconstrained protein = 1
- Recurrent directional selection, dN/dS > 1 *



* This is a very conservative test.

An example

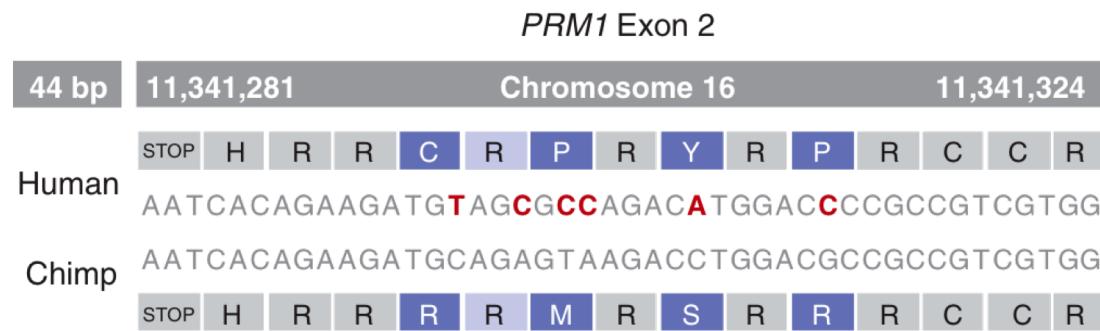
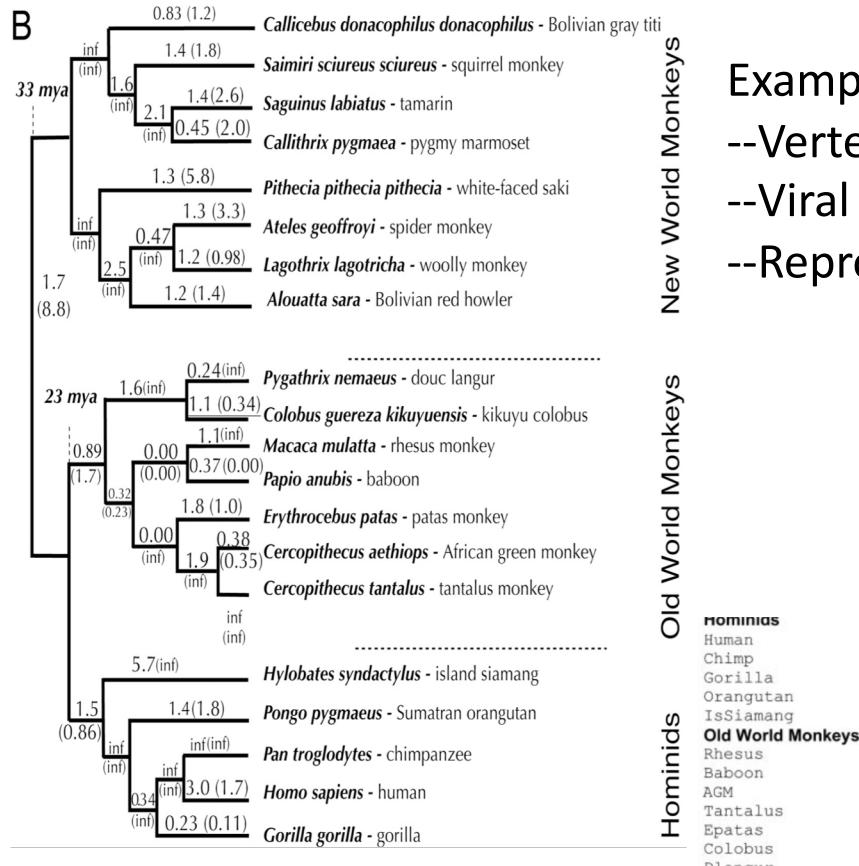


Fig. 2. Excess of function-altering mutations in *PRM1* exon 2. The *PRM1* gene exon 2 contains six differences between humans and chimpanzees, five of which alter amino acids (7, 8).

Sabeti et al 2007

TRIM5 α gene involved in primate retrovirus defense. dN/dS > 1 for the majority of branches in phylogeny



Sawyer et al 2005

Examples of genes showing dN/dS > 1

- Vertebrate immune system
- Viral coat proteins in viruses
- Reproduction related genes

Invertebrate gamete
recognition proteins
Vertebrate gametogenesis

Nomines

Human
Chimp
Gorilla
Orangutan
Issiamang

Old World Monkeys

Rhesus
Baboon
AGM
Tantalus
Epatas
Colobus
Dlanguar

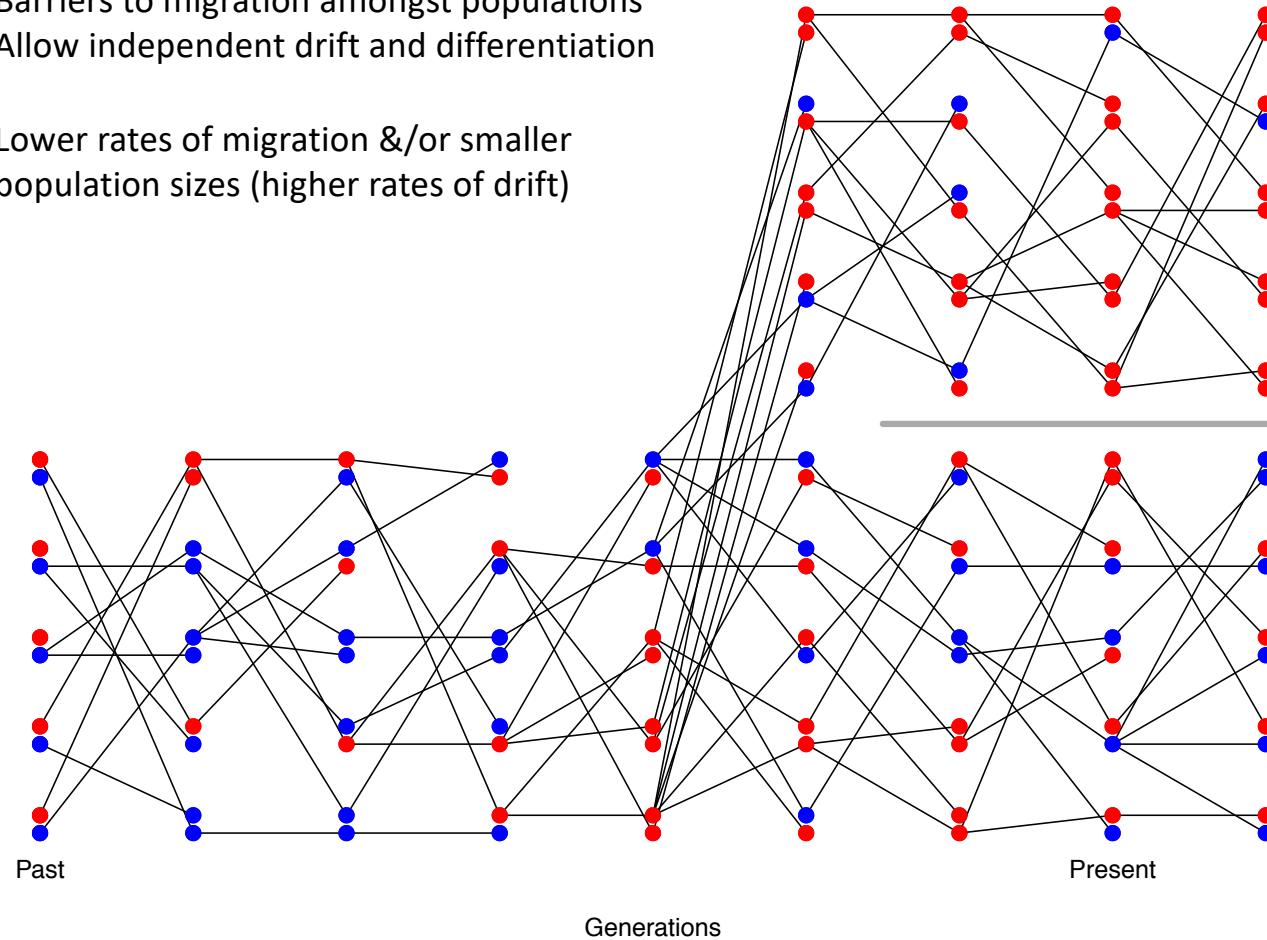
New World Monkeys

VDVTVPNNISCAVISED**R**QVSSPKPQIIY**G**ARGTRYQT--FVNFN~~Y~~CTGILGSQSITS**G**K
VDVTVPNNISCAVISED**M**RQVSSPKPQIIY**G**ARGTRYQT--FVNFN~~Y~~CTGILGSQSITS**G**K
VDVTVPNNISCAVISED**D**MRQVSSPKPQIIY**G**ARGTRYQT--FVNFN~~Y~~CTGILGSQSITS**G**K
VDVTVPNDISXAVISE**D**MRQVSC**P**EPQIIY**G**AQGT~~T~~YQT--FVNFN~~Y~~CTGILGSQSITS**G**K
VDVTVPNNIS**Y**AVISE**D**MRQVSS**P**E**P**QII**F**EAQGT**I**SQ**T**--FVNFN~~Y~~CTGILGSQSITS**G**K

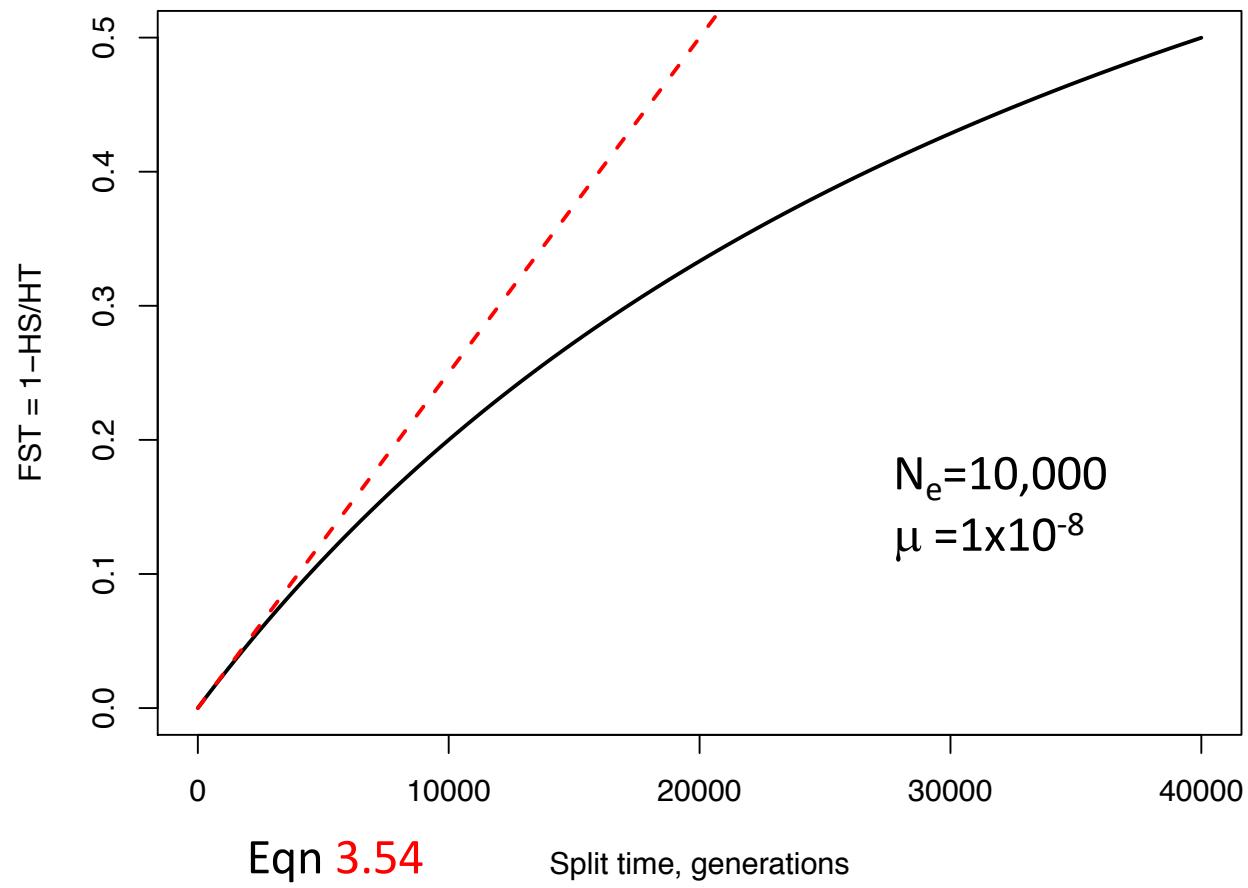
<----4-5---->

Barriers to migration amongst populations
Allow independent drift and differentiation

Lower rates of migration &/or smaller
population sizes (higher rates of drift)

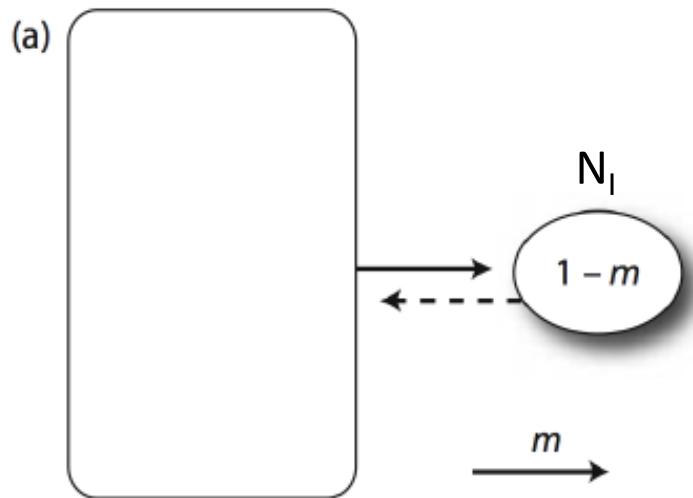


$$F_{ST} = 1 - H_S / H_T = (H_T - H_S) / H_T$$



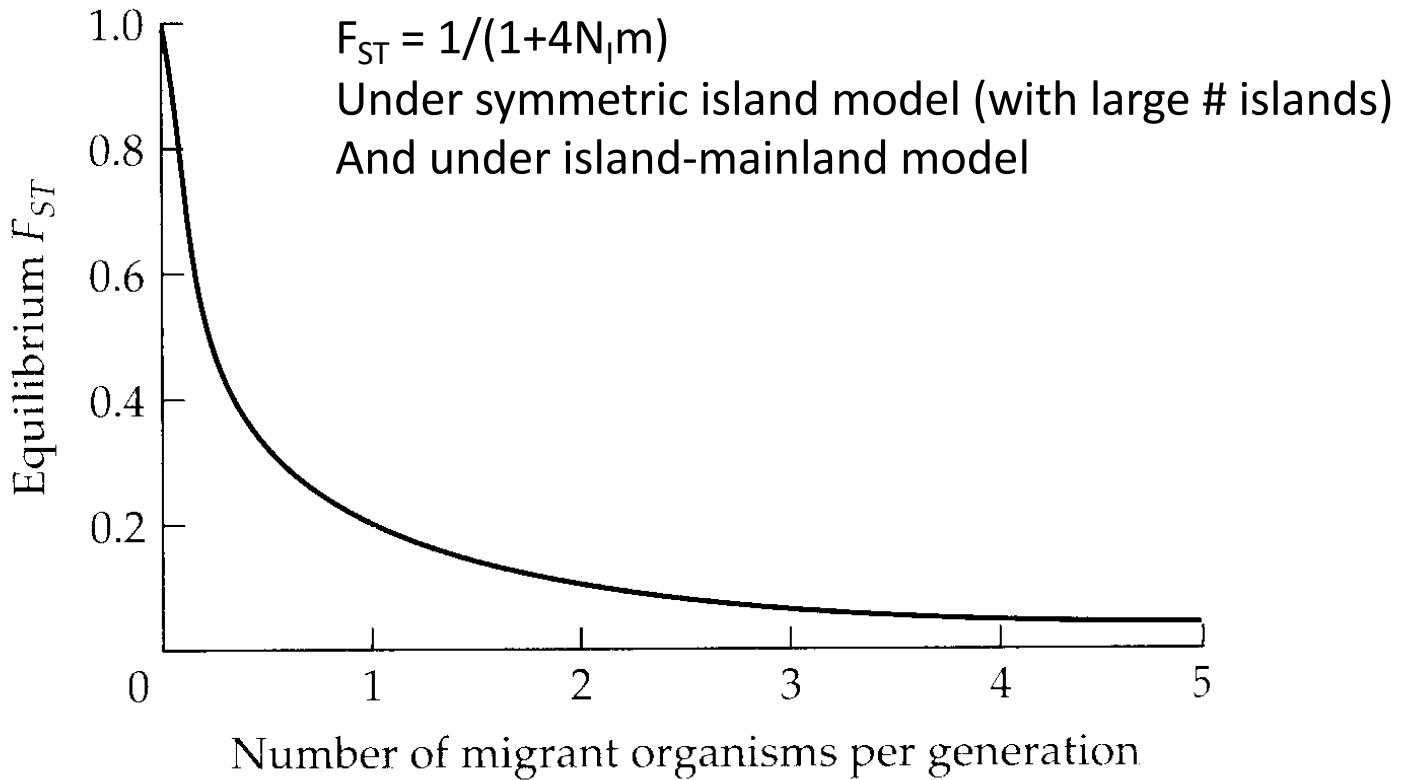
Eqn 3.54

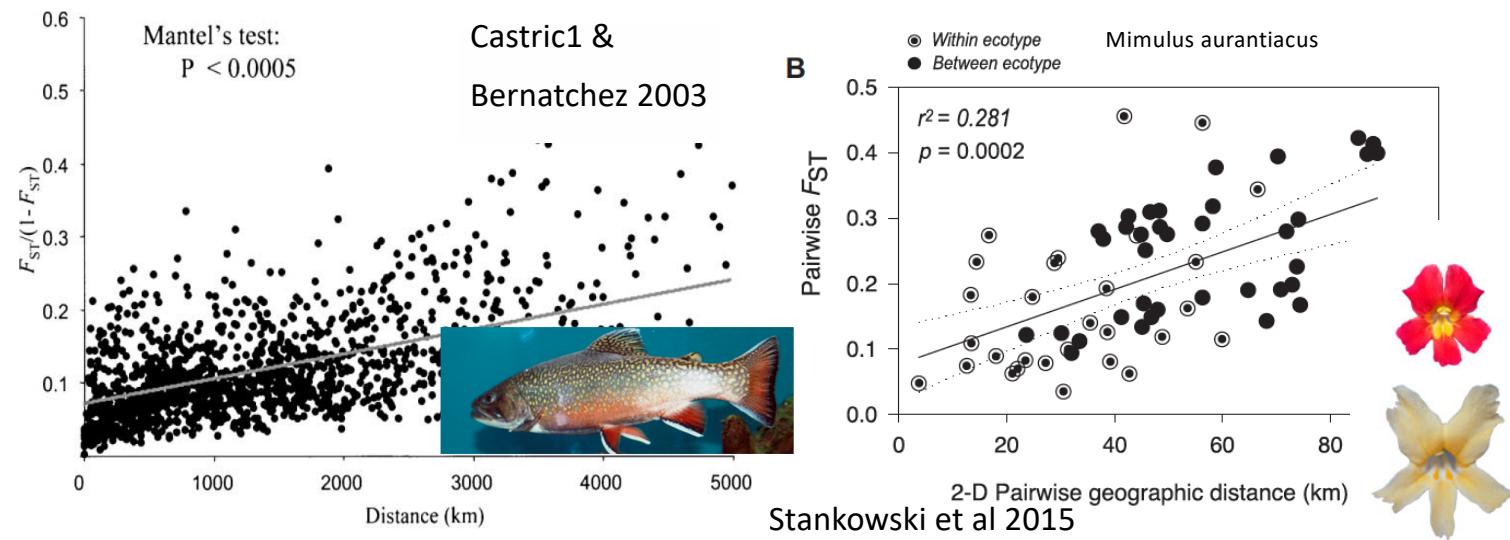
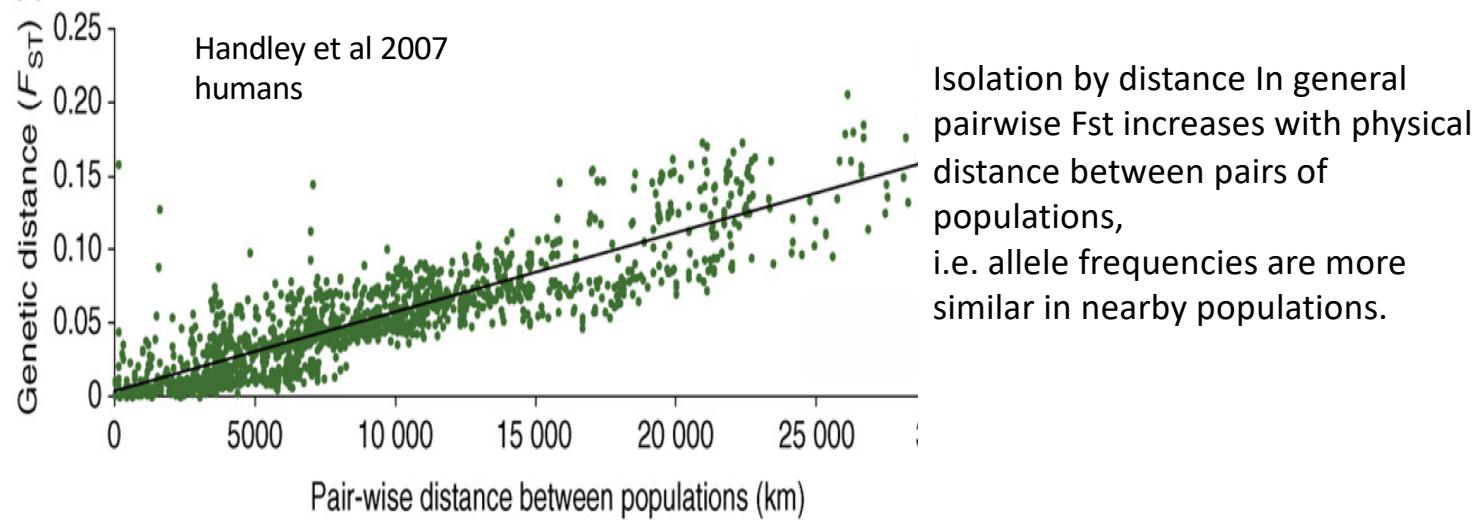
Island-Mainland model

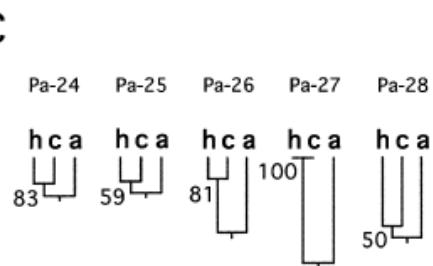
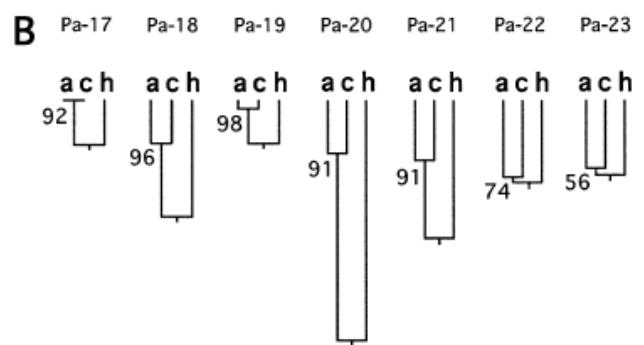
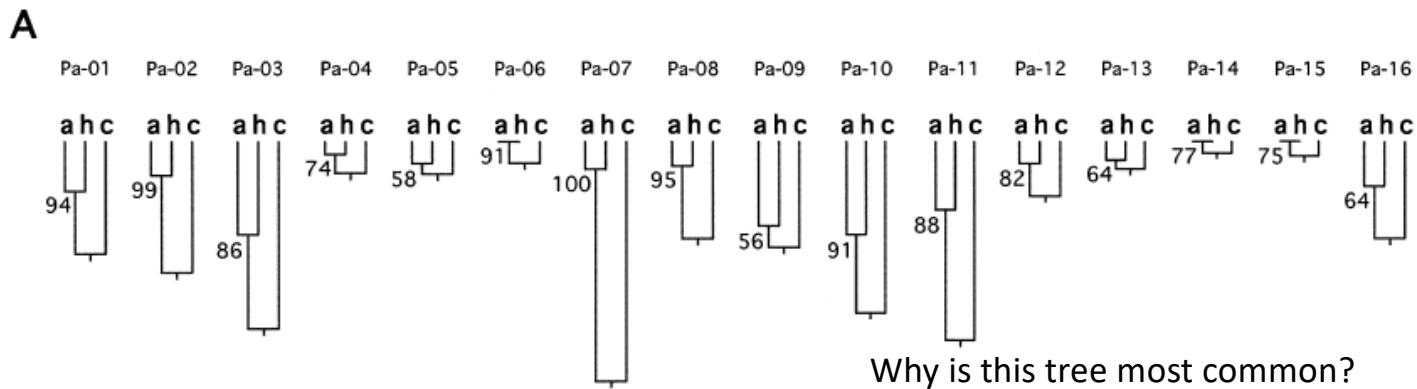


$$\begin{aligned} F_{ST} &= 1 - (H_{island}/H_T) \\ &= 1/(1 + 4N_I m) \end{aligned}$$

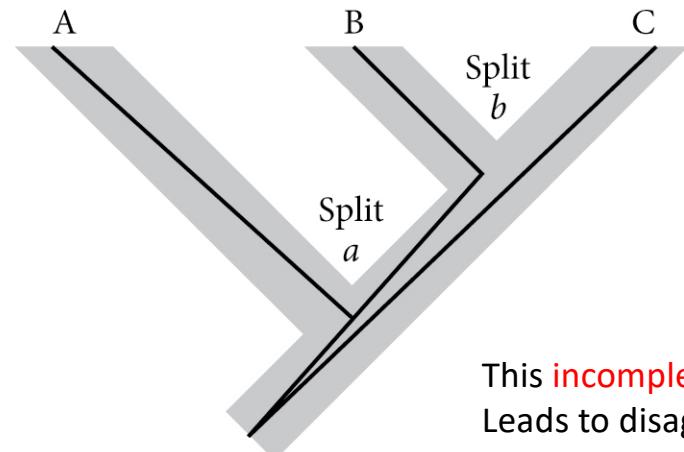
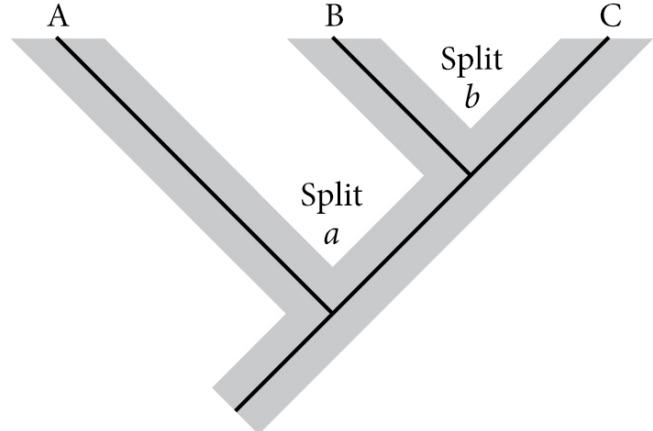
Eqn 3.59



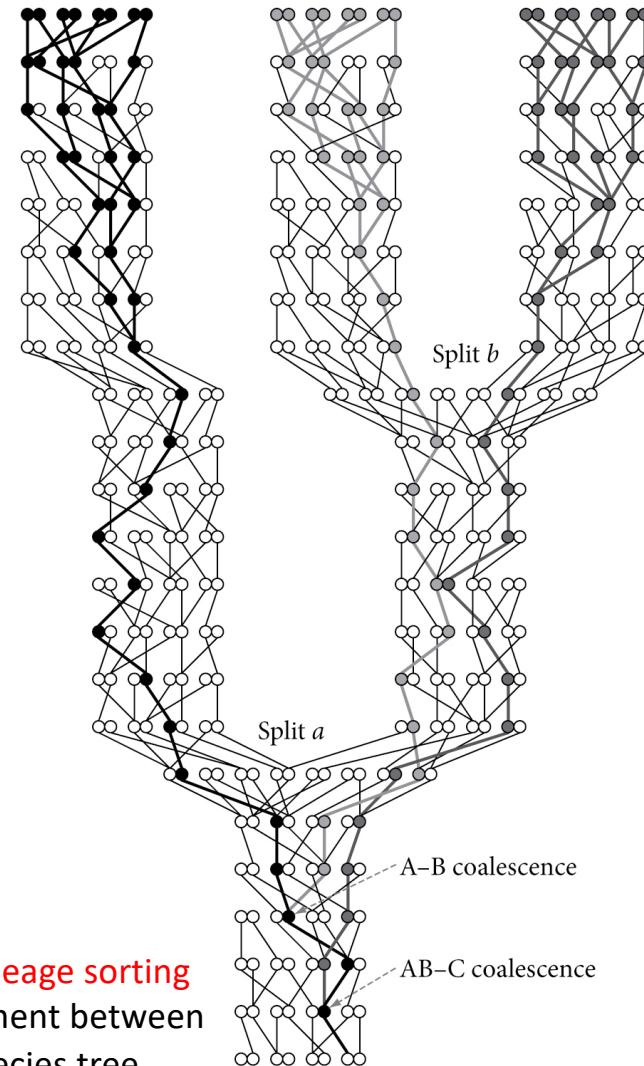




28 gene trees for 3
AUSTRALIAN
GRASS FINCHES (*POEPHILA*) Scale
JENNINGS & EDWARDS 2005 | 0.5 subst



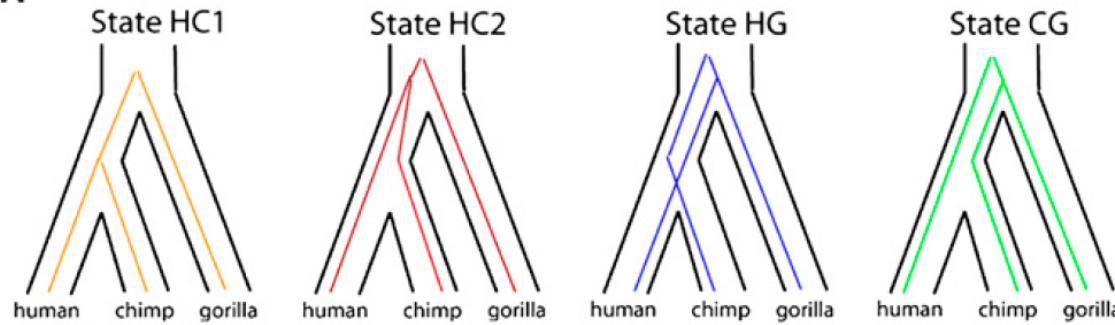
This **incomplete lineage sorting**
Leads to disagreement between
Gene trees and species tree.



Baum & Smith book

Human-Chimp-Gorilla incomplete lineage sorting

A



Species tree:

Uninformative

Agrees

Two speciation events

$n = 3$



5 patterns

Disagrees

1	0	0	1	0
0	1	0	1	0
0	0	1	1	0

1 pattern

1

2 patterns

0 | 1

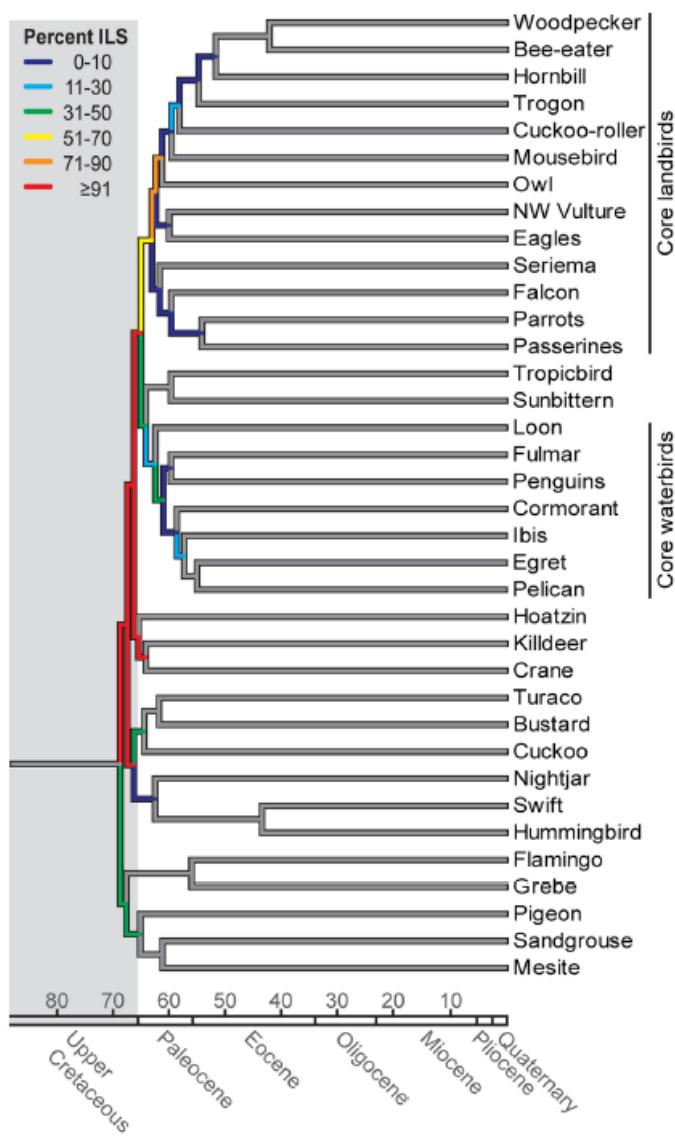
1 | 0

1 | 1

Project
overview

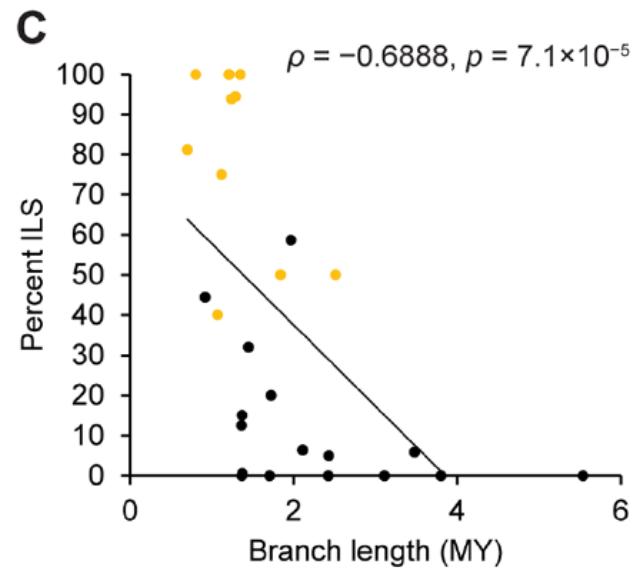


© Jon Fjeldså

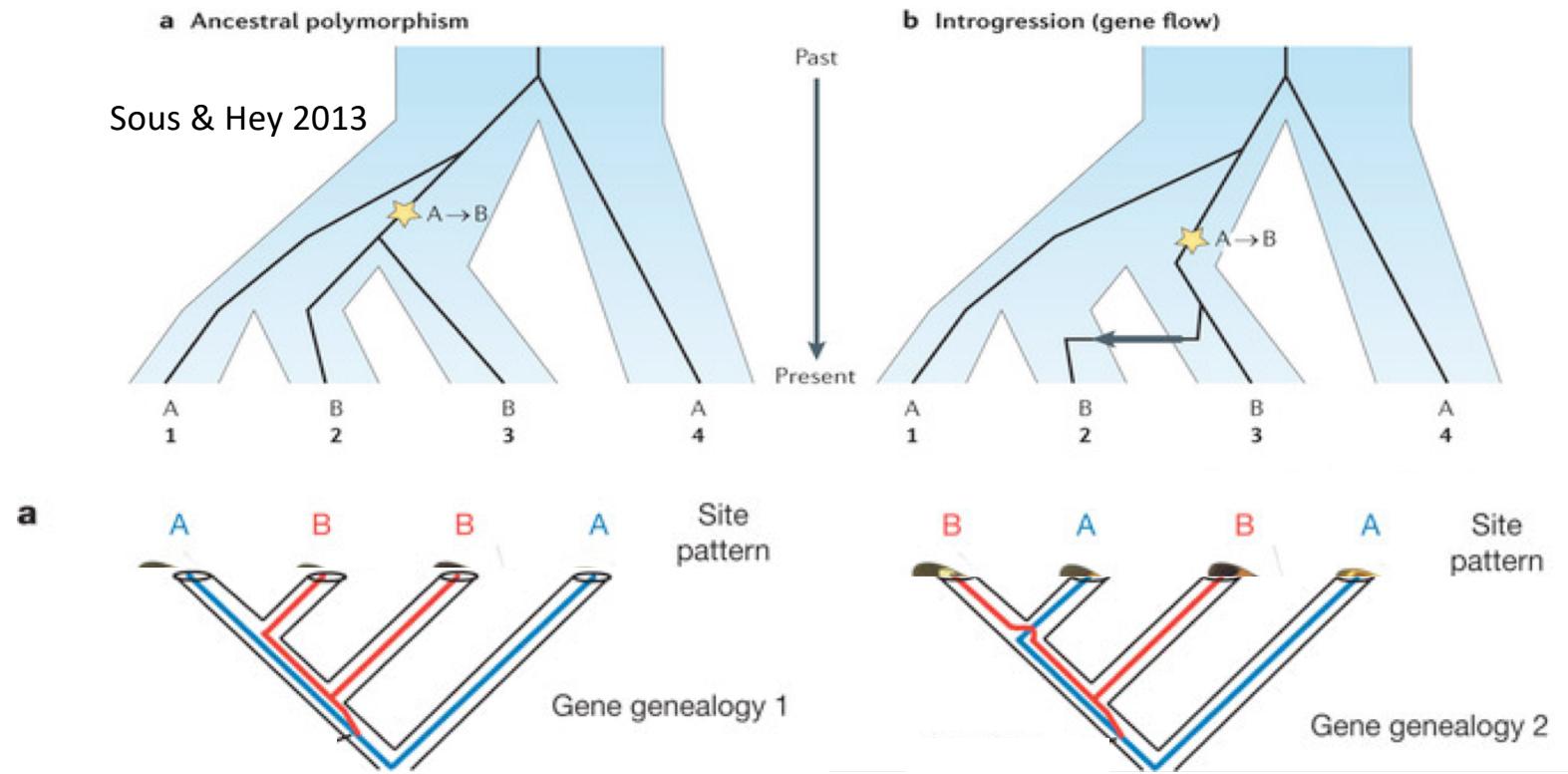


The Dynamics of Incomplete Lineage Sorting across the Ancient Adaptive Radiation of Neoavian Birds

Alexander Suh*, Linnéa Smeds, Hans Ellegren



Gene tree-species tree conflict can result from introgression or incomplete lineage sorting



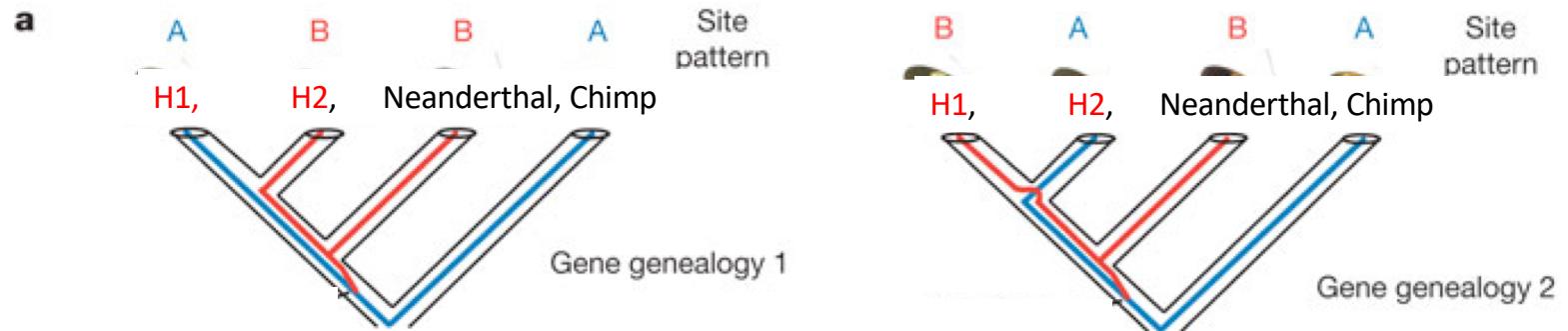
Distinguishing incomplete lineage sorting from introgression (ABBA-BABA statistic)

Under incomplete lineage sorting & no introgression

Number of ABBA loci = Number of BABA loci

$$D = (\#(BABA) - \#(ABBA))/C, \quad C = \#(ABBA) + \#(BABA)$$

Green et al 2010, Nature



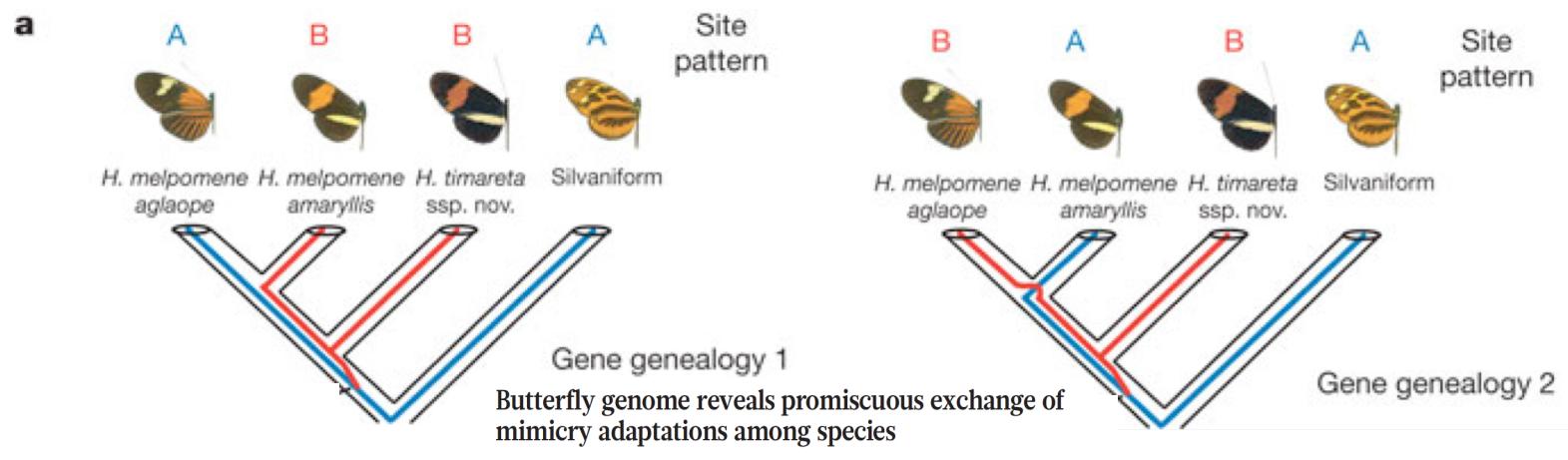
Under incomplete lineage sorting & no introgression
 Number of ABBA loci =Number of BABA loci
 $D = (\#(BABA) - \#(ABBA))/C; C = \#(ABBA) + \#(BABA)$

Genetic history of an archaic hominin group from Denisova Cave in Siberia

David Reich^{1,2*}, Richard E. Green^{3,4*}, Martin Kircher^{5*}, Johannes Krause^{3,5*}, Nick Patterson^{6*}, Eric V. Durand^{6*}, Bence Viola^{3,7*}, Adrian W. Briggs^{3,7}, Udo Stenzel³, Philipp L. F. Johnson⁸, Tomislav Maricic⁹, Jeffrey M. Good¹⁰, Tomas Marques-Bonet^{10,11}, Can Alkan¹⁰, Qiaomei Fu^{3,12}, Swapna Mallick^{1,2}, Heng Li¹³, Matthias Meyer¹⁴, Evan E. Eichler¹⁵, Mark Stoneking¹⁶, Michael Richards^{17,18}, Sahra Talamo¹⁹, Michael V. Shunkov¹⁴, Anatoli P. Derevianko¹⁴, Jean-Jacques Hublin¹⁹, Janet Kelso³, Montgomery Slatkin⁶ & Svante Pääbo³

Table 1 | Sharing of derived alleles between present-day and archaic hominins

Sample H ₁	Sample H ₂	D(H ₁ , H ₂ , Neanderthal, chimpanzee)					D(H ₁ , H ₂ , Denisova, chimpanzee)					Z-score	
		n _{BABA}	n _{ABBA}	D (%)	s.e. (%)	Z-score	n _{BABA}	n _{ABBA}	D (%)	s.e. (%)	Z-score		
African/African*													
San	Yoruba	23,690	23,855	-0.3	0.6	-0.6	39,042	39,019	0.0	0.5	0.1		0.1
Eurasian/African*													
French	San	25,242	22,982	4.7	0.6	7.6†	39,838	38,495	1.7	0.5	3.4†		3.4†
French	Yoruba	21,794	19,890	4.6	0.7	6.9†	34,262	33,078	1.8	0.5	3.6†		3.6†
Han	San	25,081	22,470	5.5	0.6	8.5†	38,815	37,439	1.8	0.5	3.4†		3.4†
Han	Yoruba	21,741	19,412	5.7	0.7	7.9†	33,182	32,184	1.5	0.5	2.8		2.8
Eurasian/Melanesian*													
French	Papuan	15,523	15,548	-0.1	0.8	-0.1	23,509	25,470	-4.0	0.7	-5.7†		-5.7†
Han	Papuan	15,059	14,677	1.3	0.9	1.5	22,262	24,198	-4.2	0.7	-5.8†		-5.8†
Melanesian/African*													
Papuan1	San	21,985	20,366	3.8	0.7	5.1†	35,923	32,841	4.5	0.6	7.2†		7.2†
Papuan1	Yoruba	19,107	17,646	4.0	0.8	4.9†	30,995	28,186	4.7	0.6	7.4†		7.4†



The Heliconius Genome Consortium*

Under incomplete lineage sorting

$$D = (\#(BABA) - \#(ABBA))/C$$

$$D=0.037 \pm 0.003 \text{ (two-tailed } D = 0, P = 1 \times 10^{-40})$$

