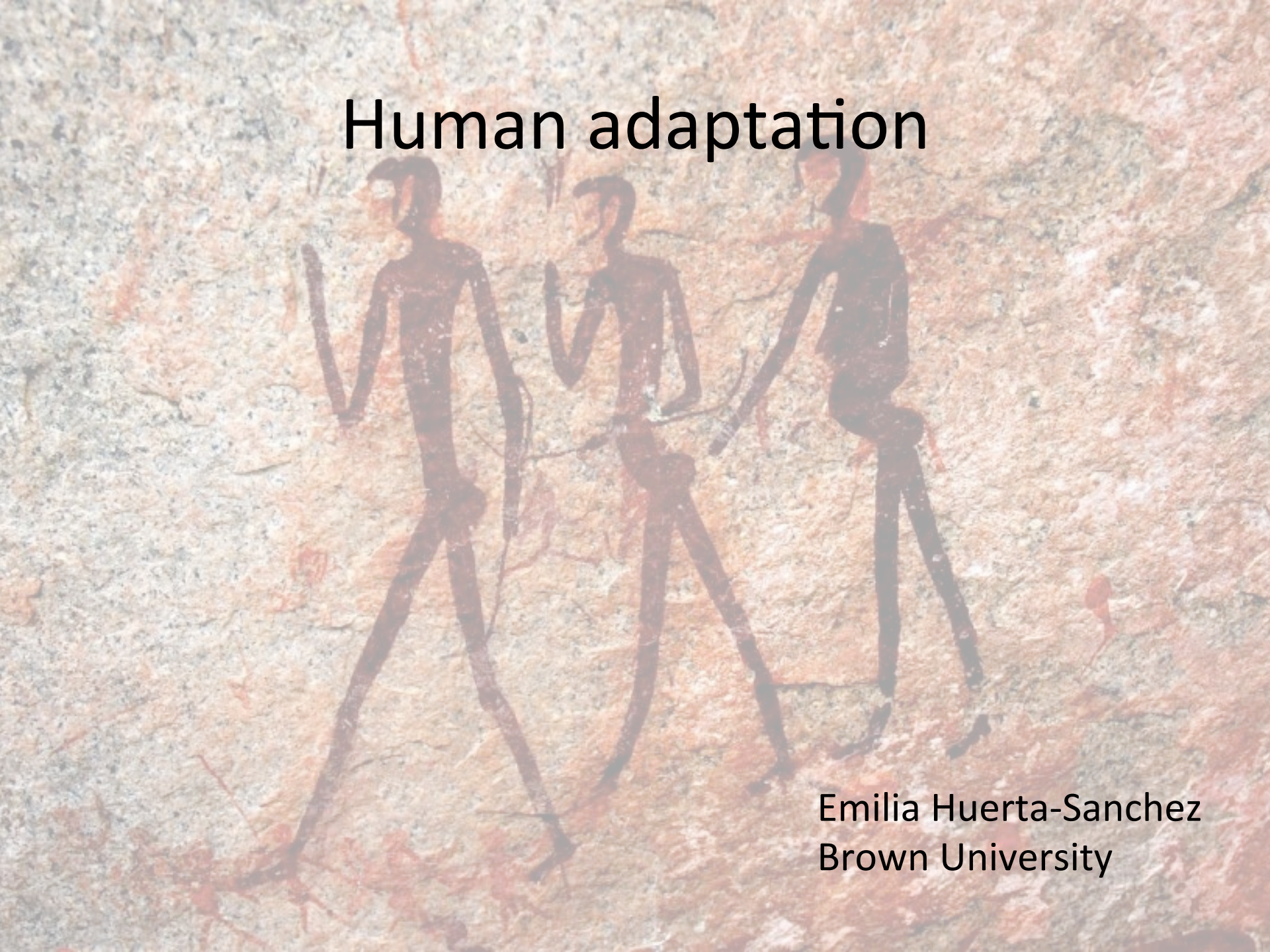
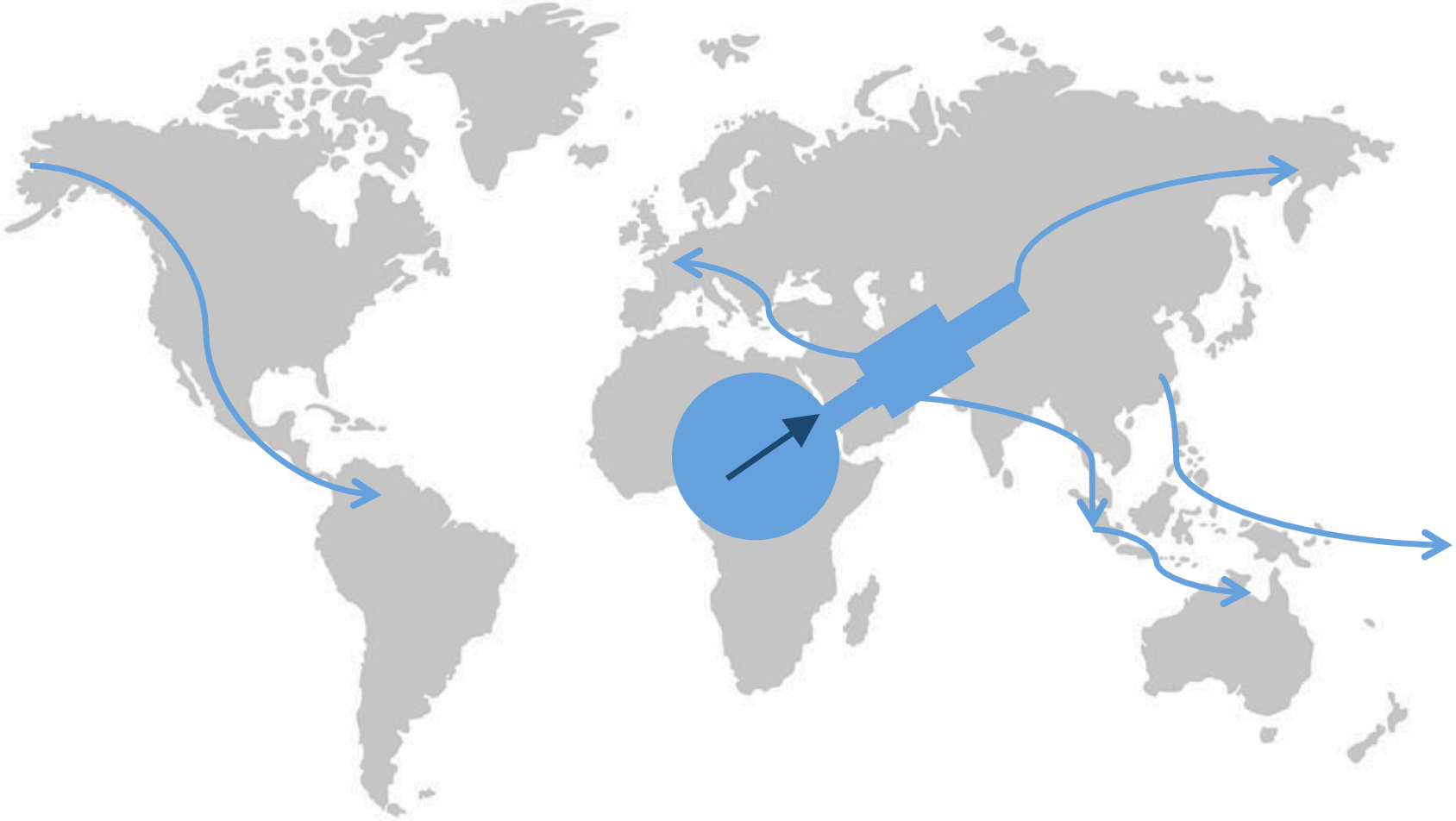
Human adaptation



Emilia Huerta-Sanchez
Brown University

Human dispersal



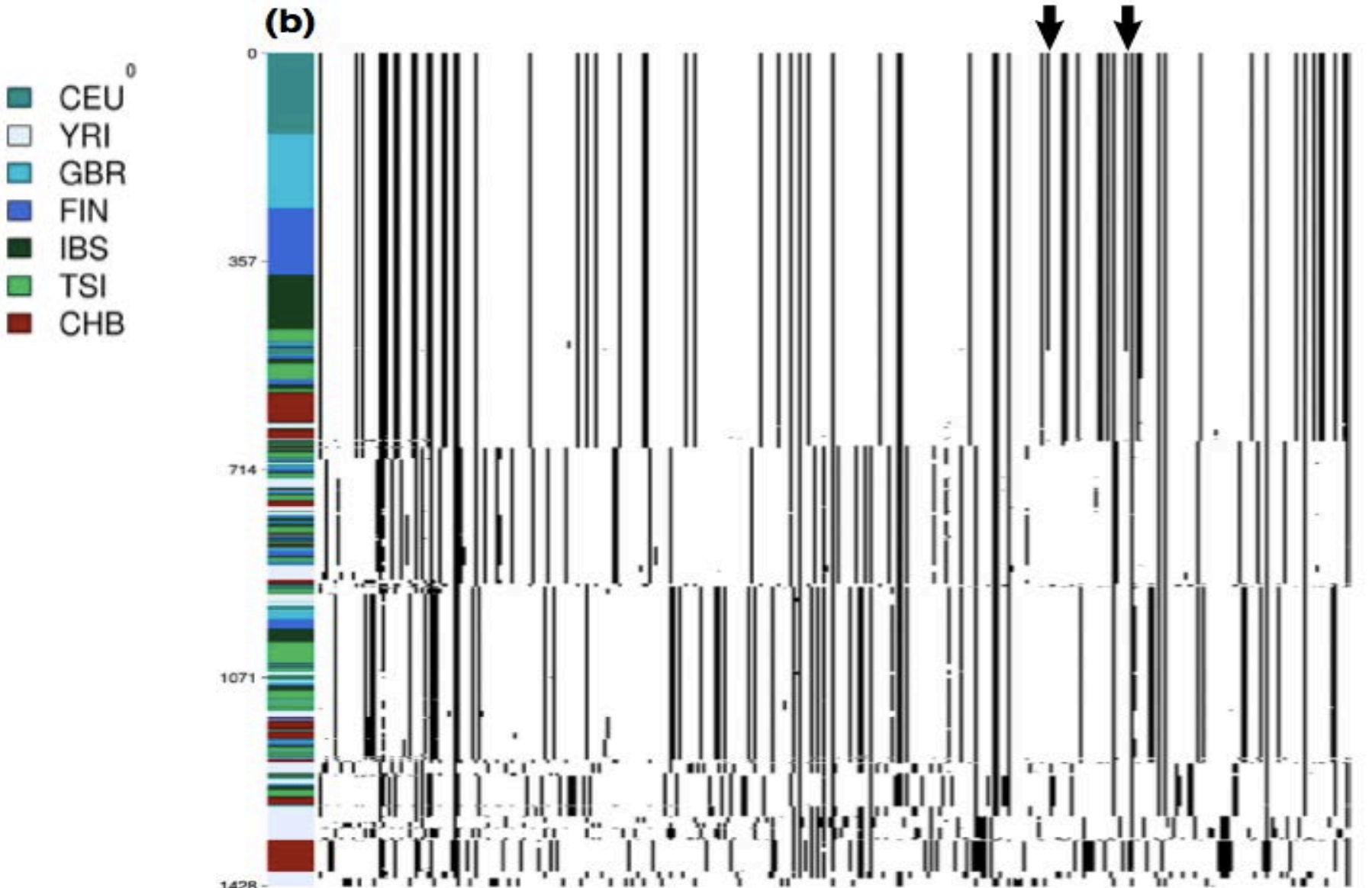
Humans have been exposed to different environments



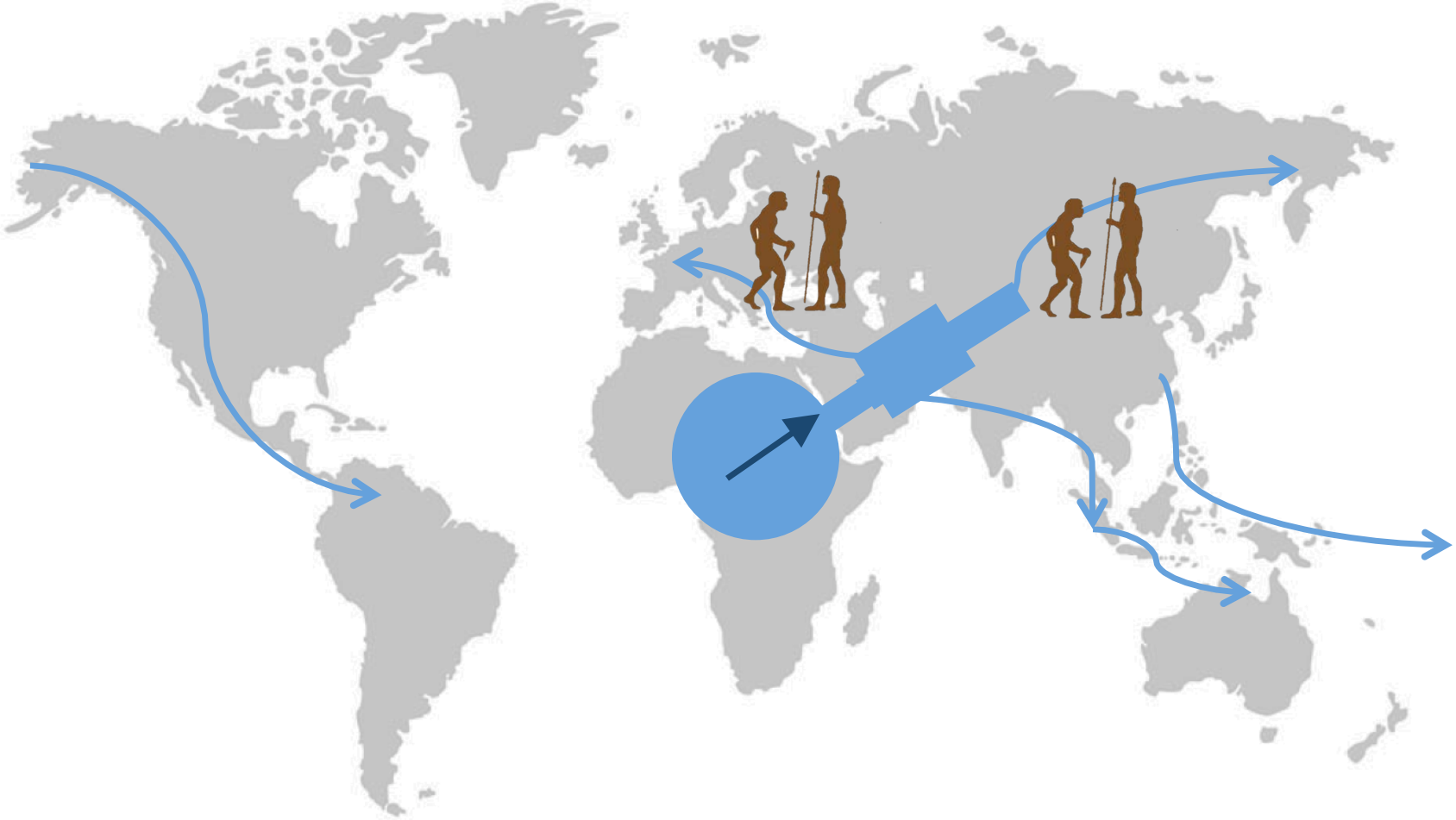



Graphic: Oliver Uberti and M. Brody Dittemore, NG Staff

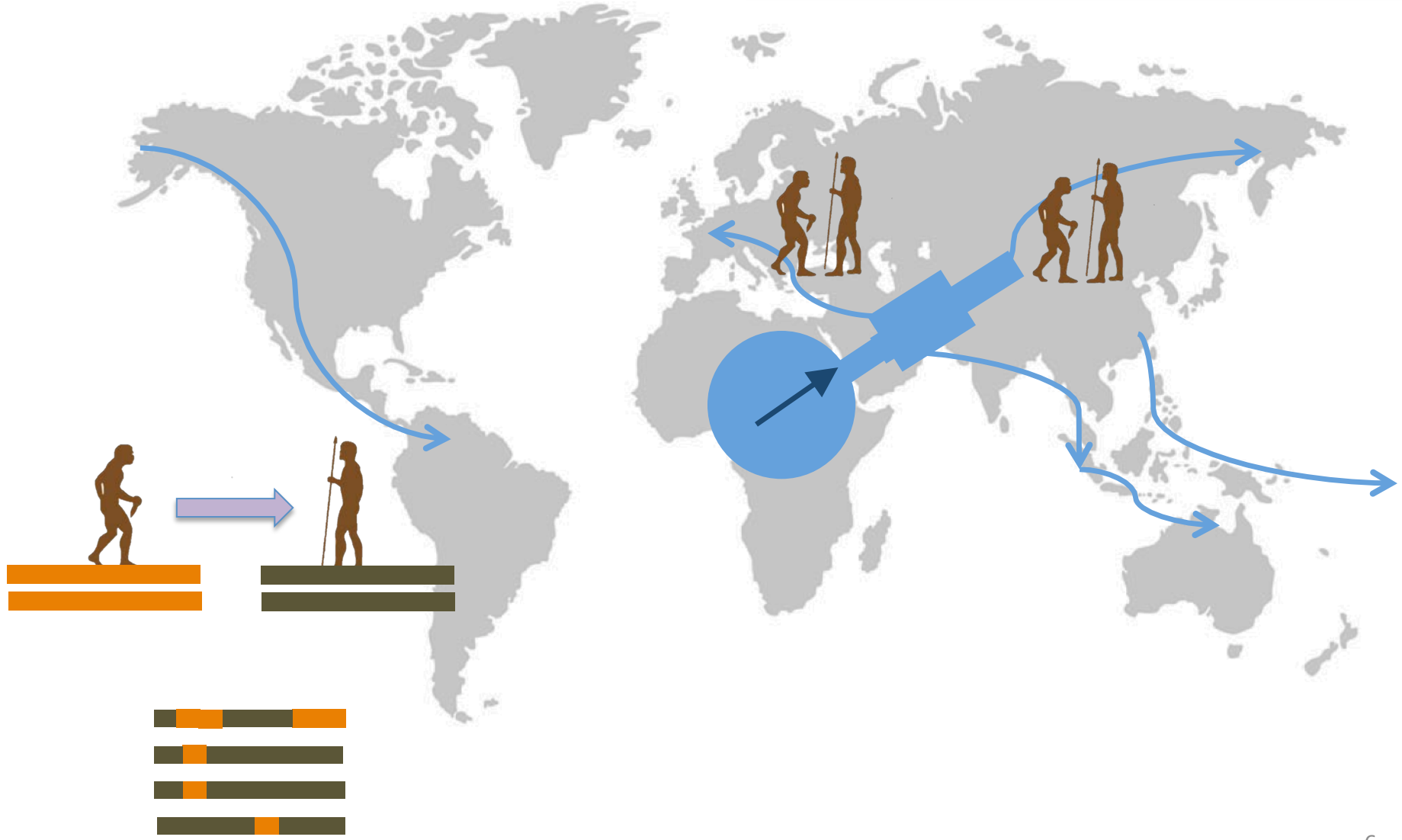
Lactase Persistence



Archaic humans

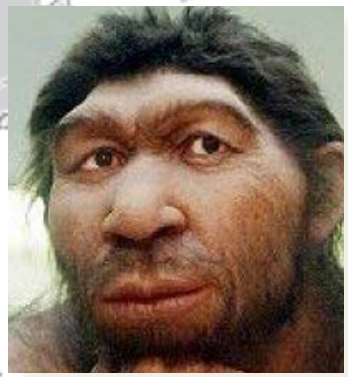


Archaic Admixture



Archaic Humans

Neanderthal bones

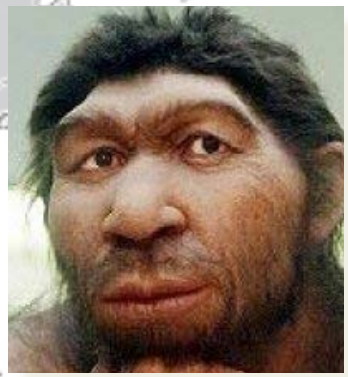


Denisova cave, Altai mountains

USAID MAP

Archaic Humans

Neanderthal bones

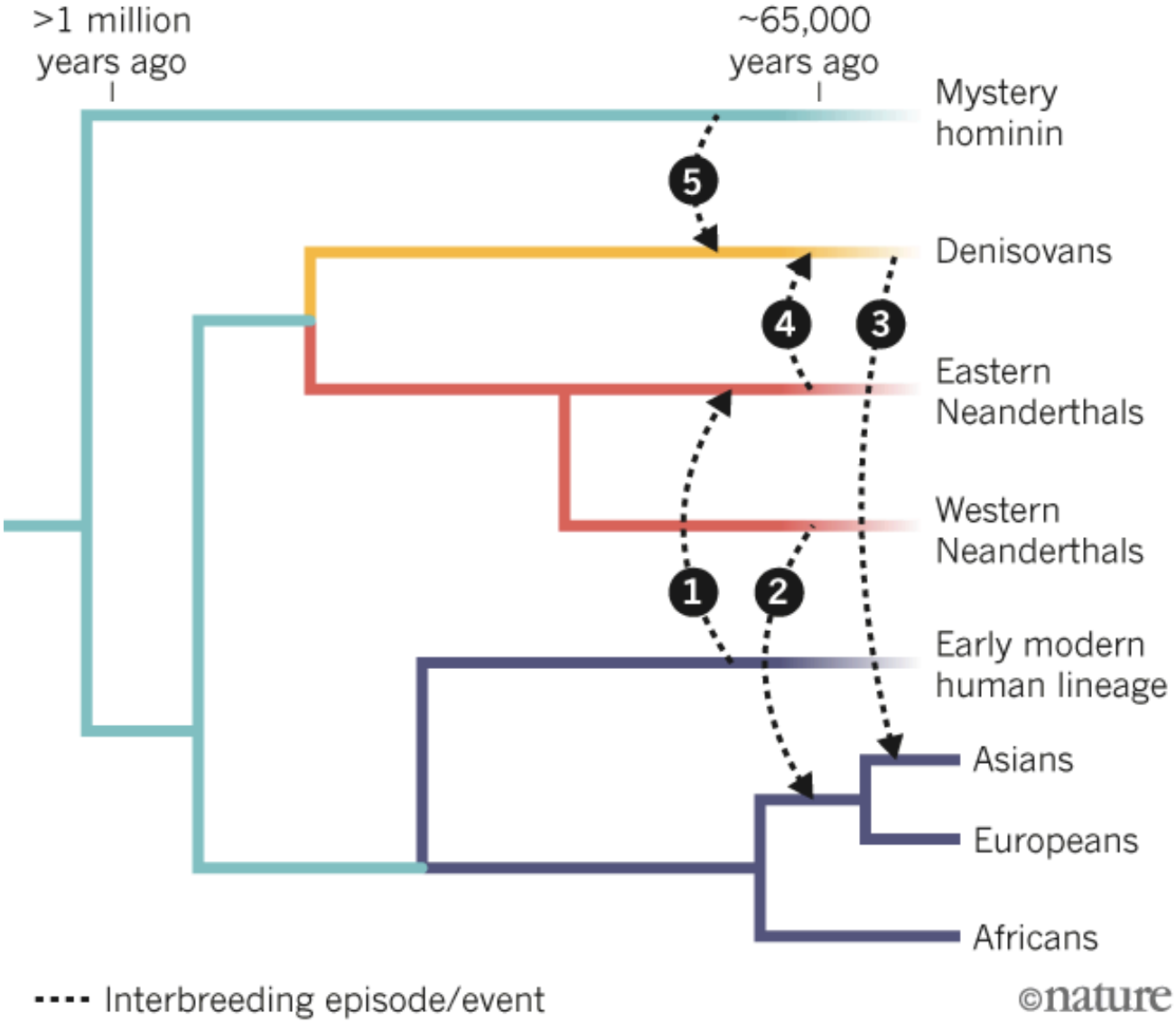


Denisova cave, Altai mountains

Papuans and Australians have largest amount of Denisovan admixture (~5%)

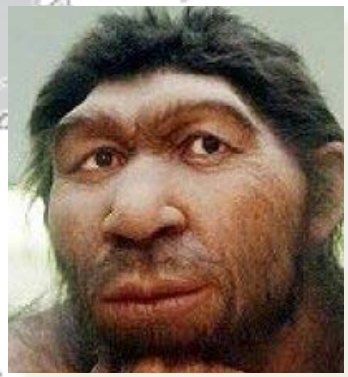
USAID MAP

Recent time scale



Archaic Humans

Neanderthal bones



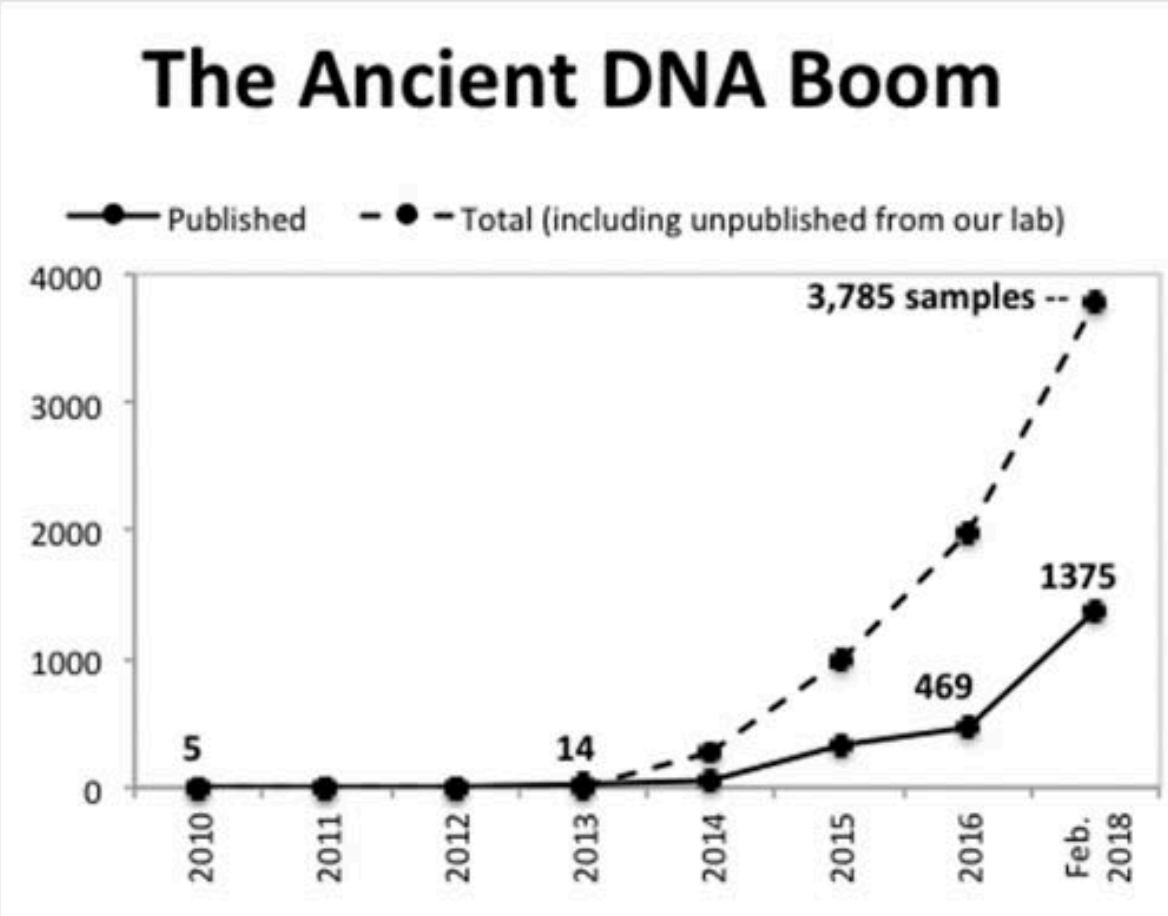
Denisova cave, Altai mountains

Papuans and Australians have largest amount of Denisovan admixture (~5%)

Ancient modern humans (100-40,000 years ago)

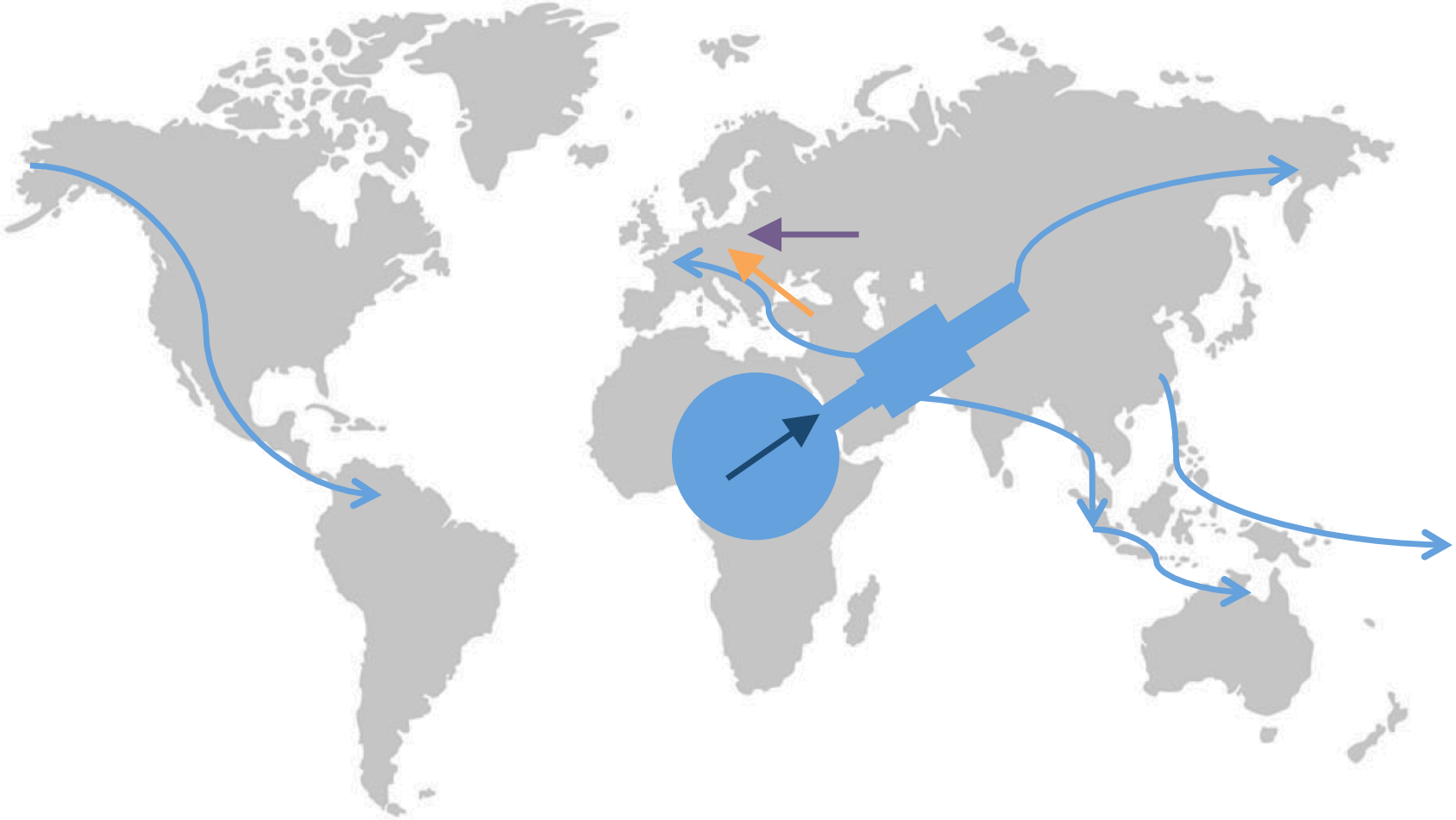
USAID MAP

Ancient Modern Human DNA

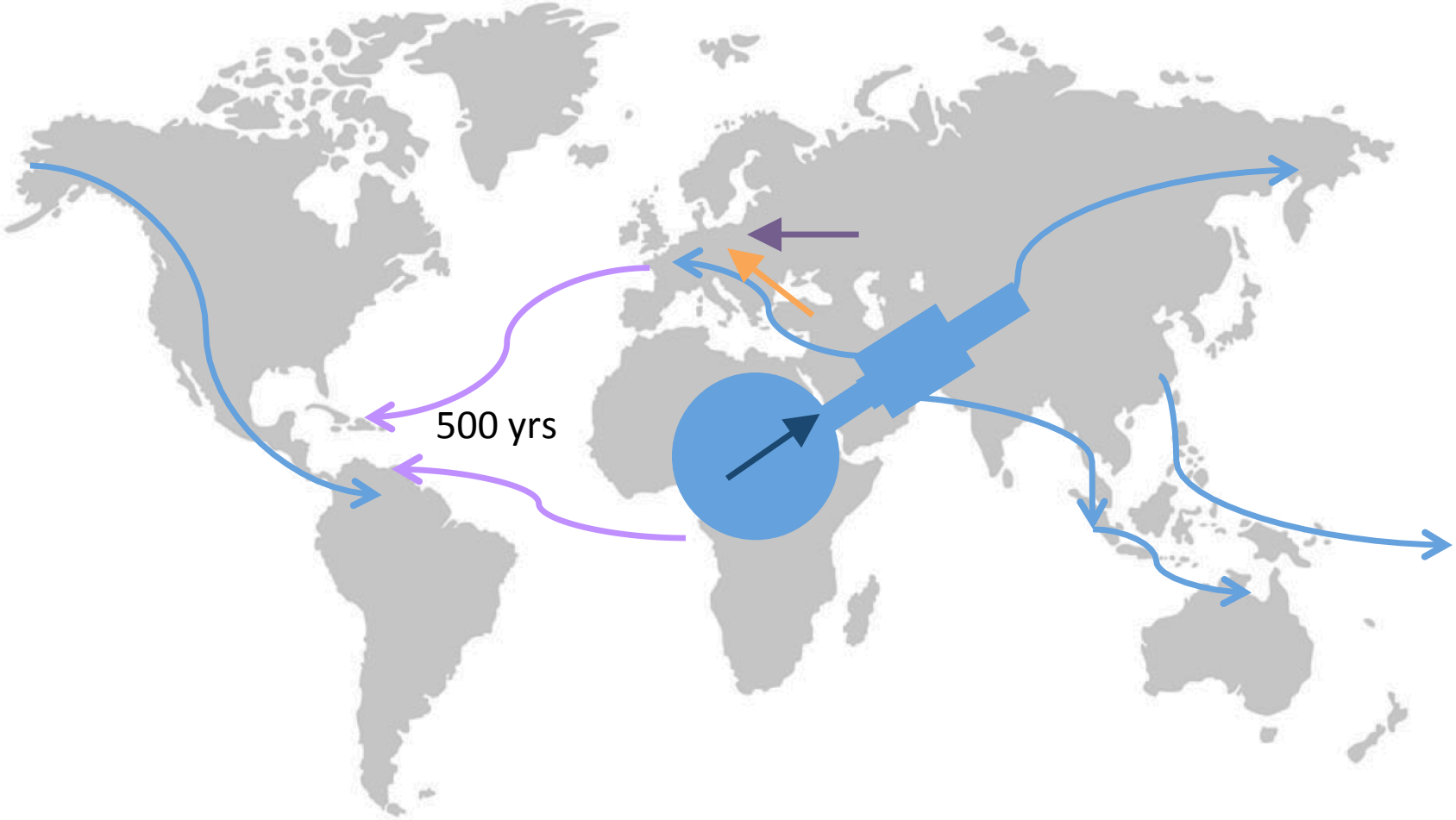


The first studies of ancient DNA were published in 2010. Since then, the number of ancient DNA samples that have been sequenced has grown exponentially. Credit: David Reich.

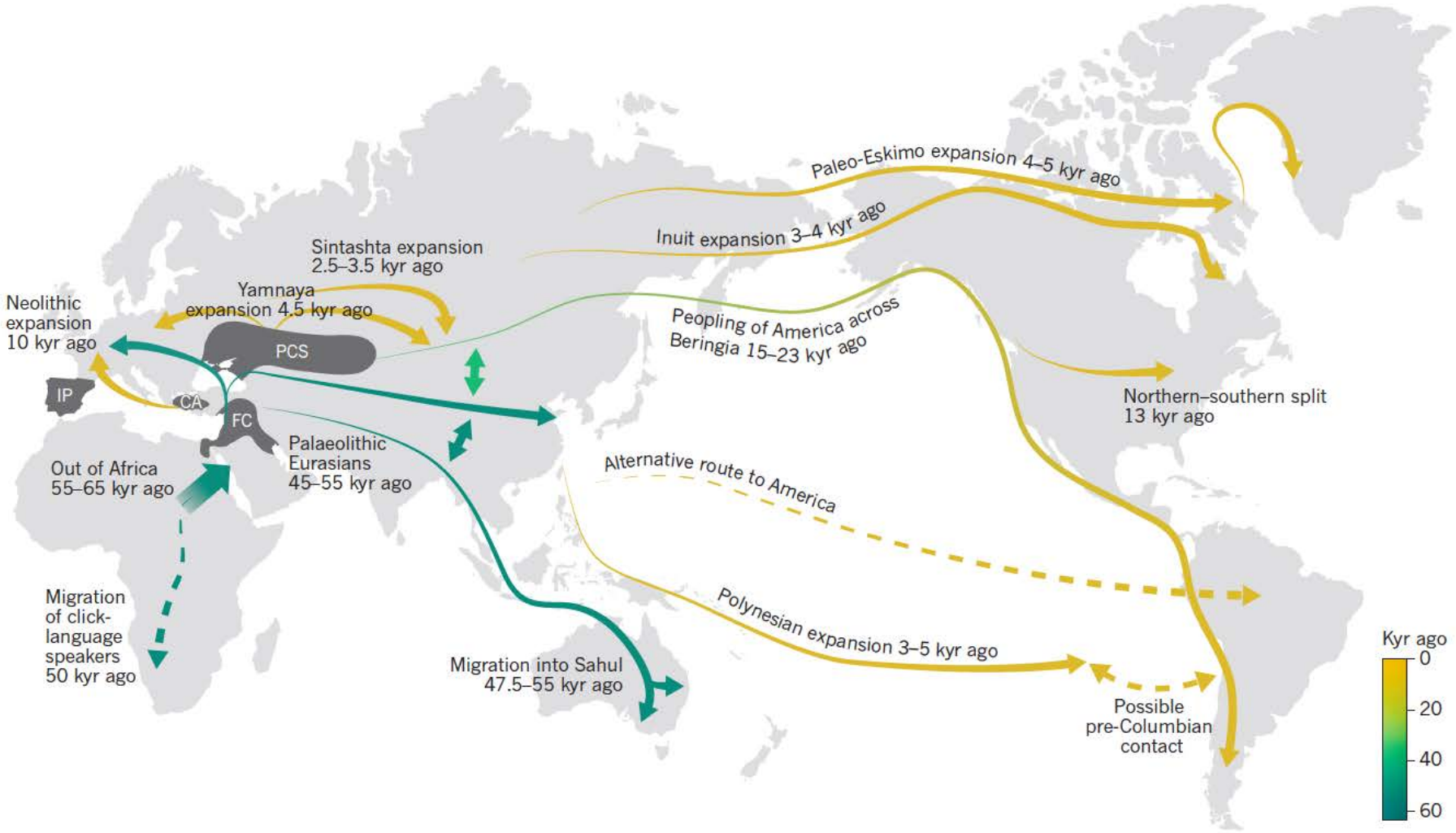
Three waves of migration into Europe



European colonization in the Americas



Population Movements



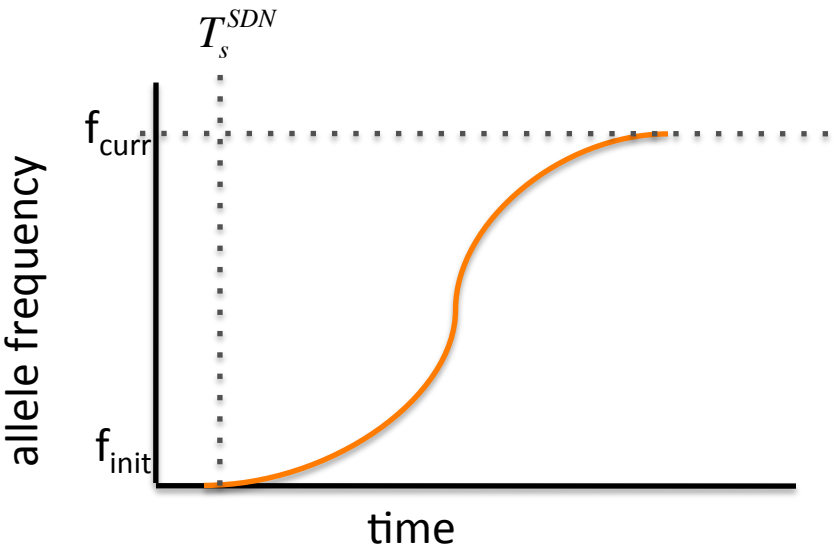
From Nielsen *et al.* 2017

Hypothesis

Admixture has played a *central role* in

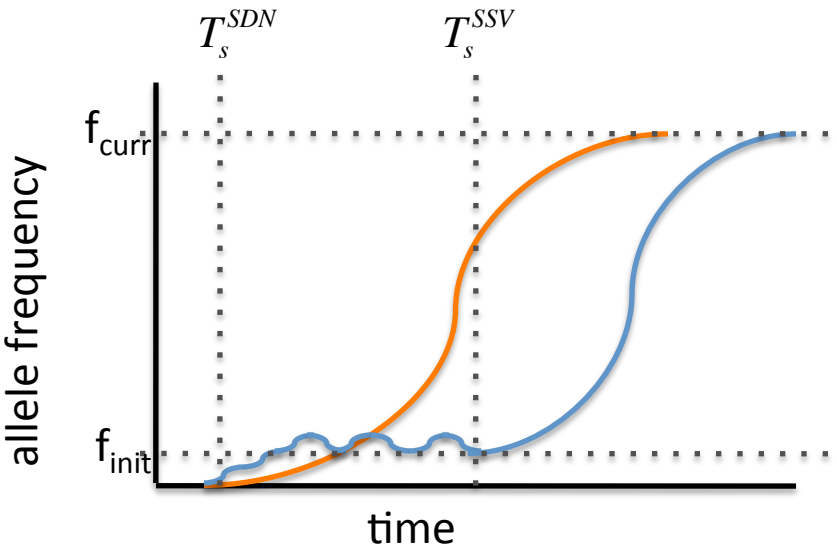
- shaping patterns of genetic variation

Positive Selection



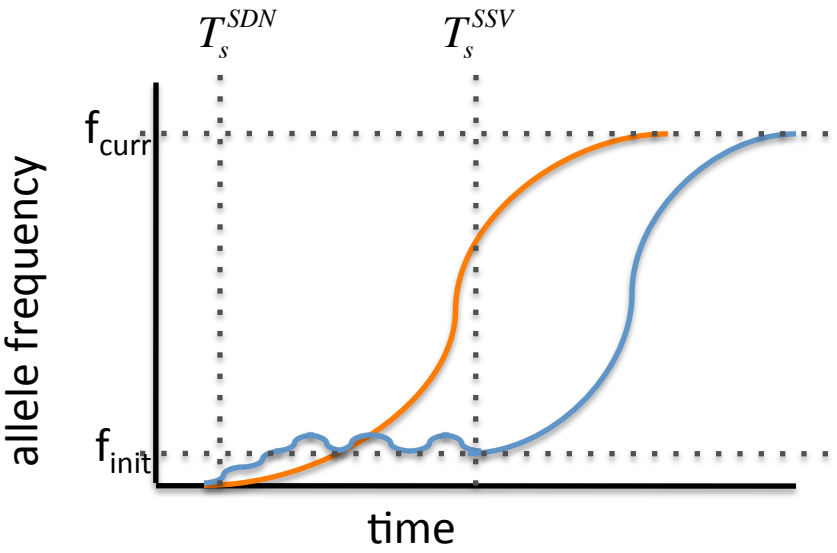
- Beneficial allele rises to high frequency

Positive Selection from standing genetic variation



- Environment changes, some of the existing genetic variation is beneficial

Positive Selection from standing genetic variation



- Timing and strength of selection
- Patterns of genetic variation differ

Figs from book chapter on Directional selection and adaptation Encyclopedia of Evolutionary Biology Racimo et al. 2016

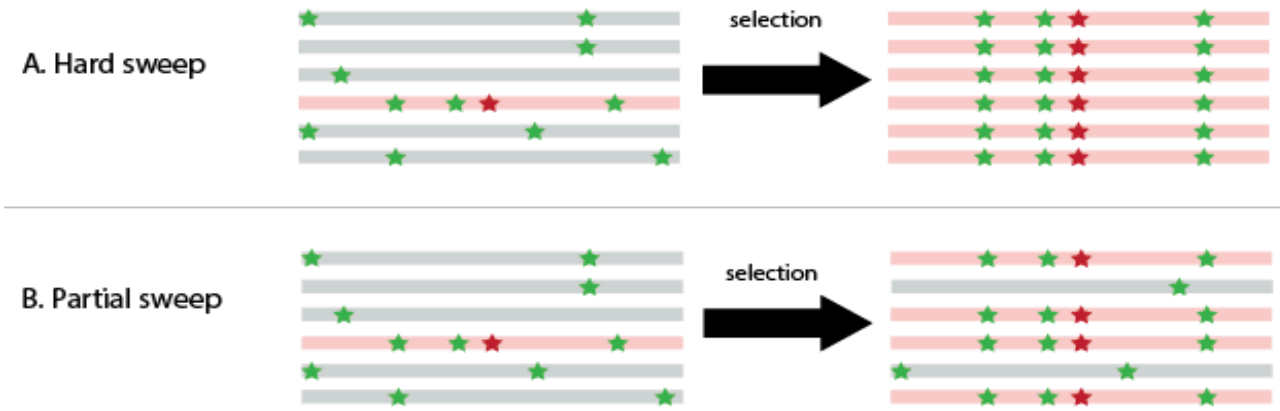
A. Hard sweep

Figs from book chapter on Directional selection and adaptation Encyclopedia of Evolutionary Biology Racimo et al. 2016

A. Hard sweep

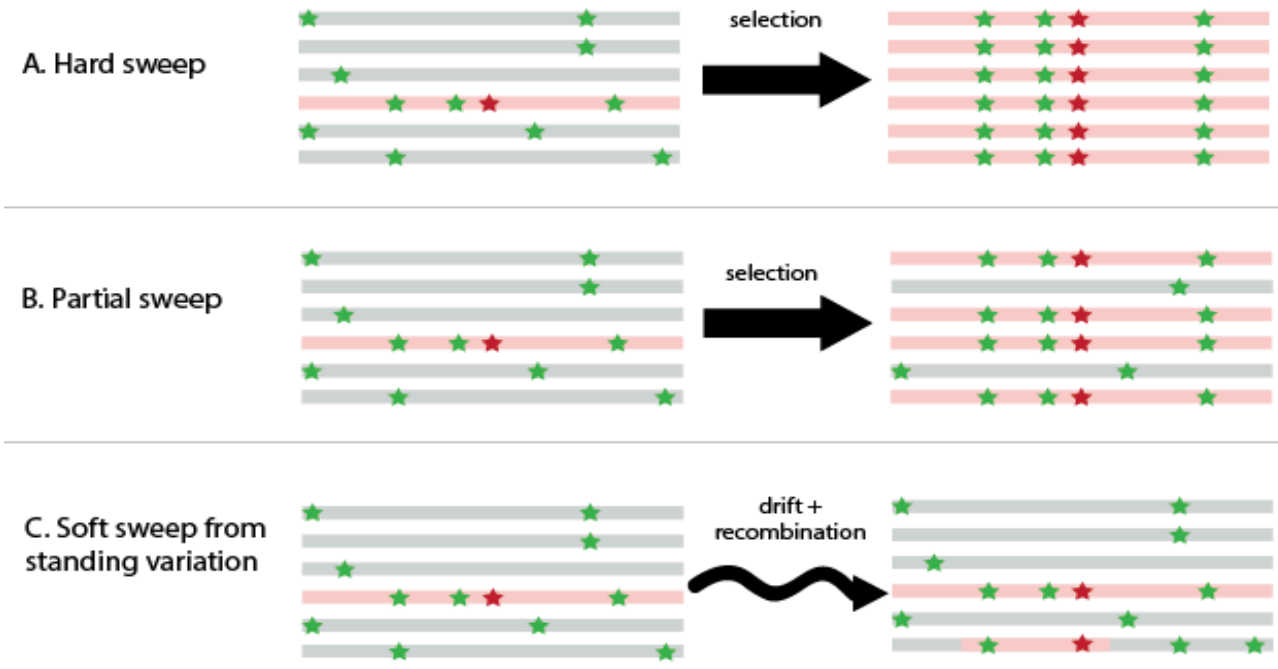
B. Partial sweep

Figs from book chapter on Directional selection and adaptation Encyclopedia of Evolutionary Biology Racimo et al. 2016



Tajima's D
iHH (Voight et al.)
EHH (Sabeti et al.)

Figs from book chapter on Directional selection and adaptation Encyclopedia of Evolutionary Biology Racimo et al. 2016



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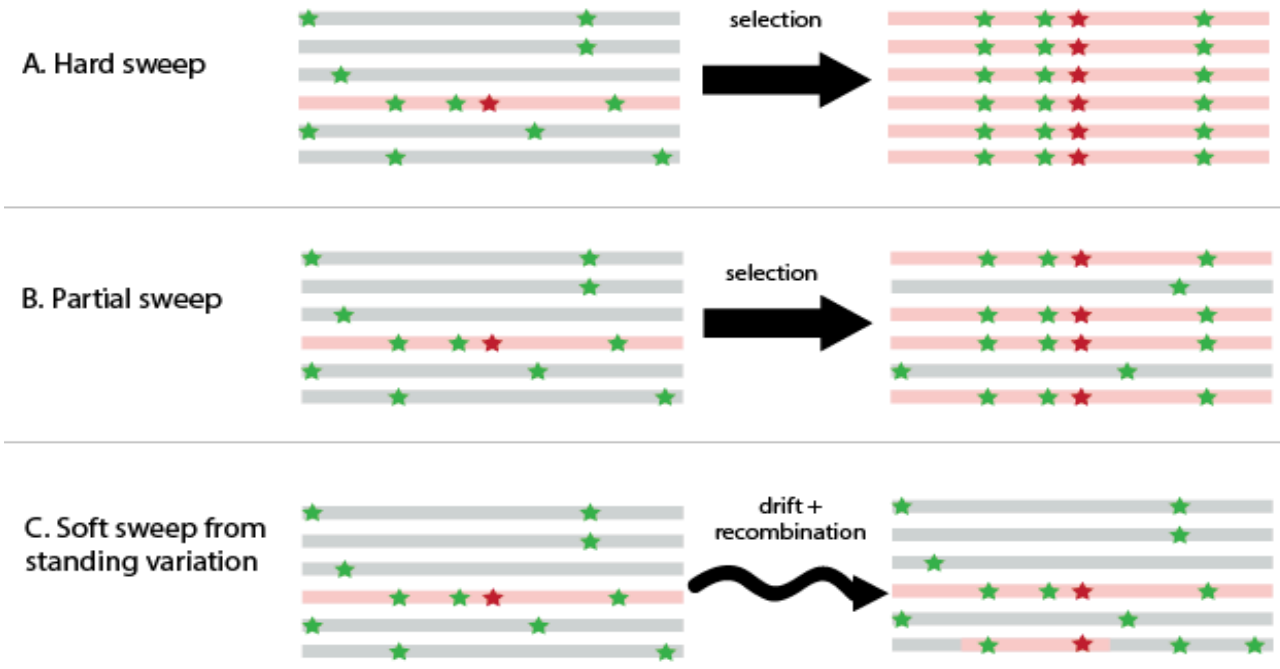
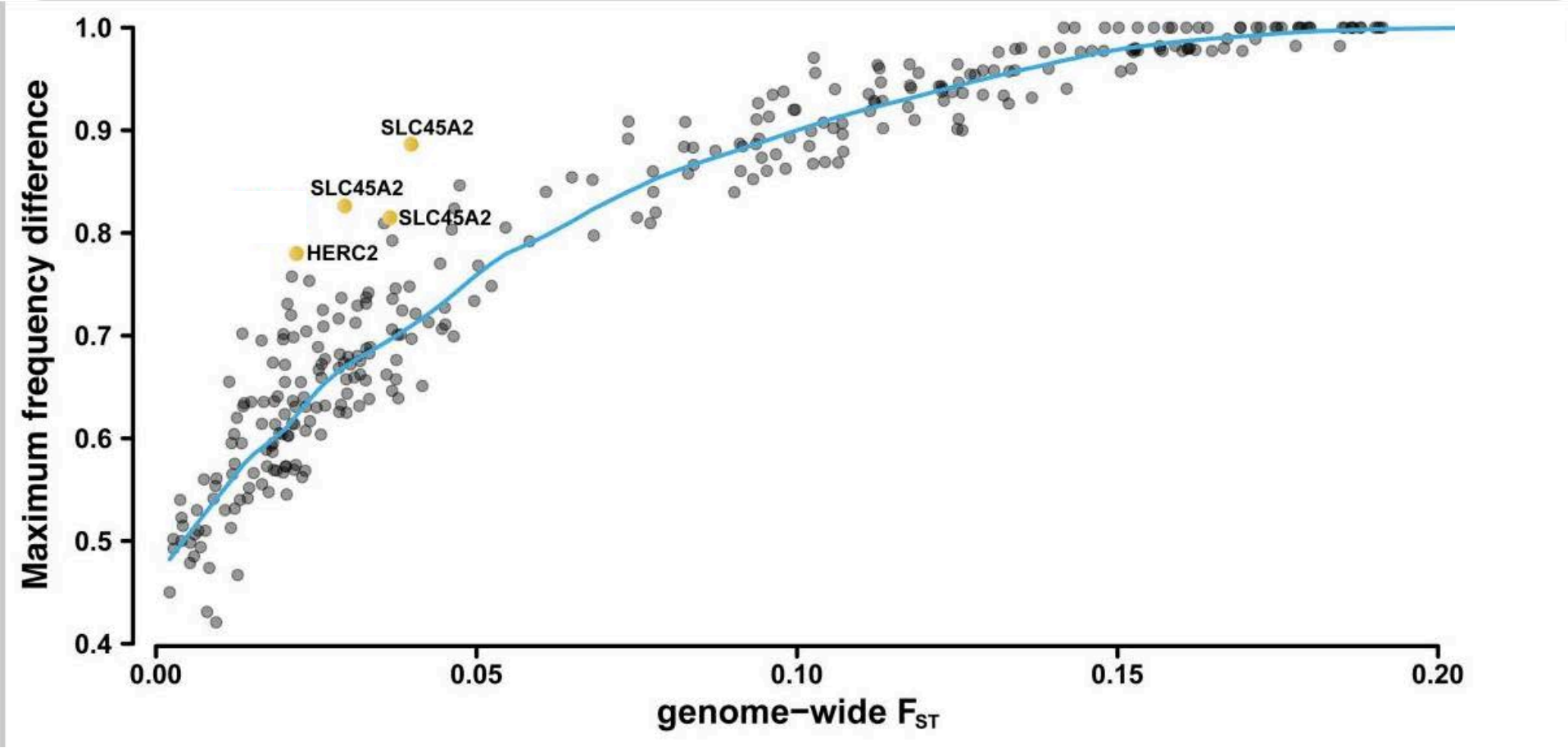


Tajima's D
iHH (Voight et al.)
EHH (Sabeti et al.)
NSL (Ferrer-Admetlla et. al)

Test in within a single population.
Can use FST for two populations

Genes involved in Skin pigmentation, local adaptation



Redrawn from Coop et al. 2009

local adaptation, 3-population test

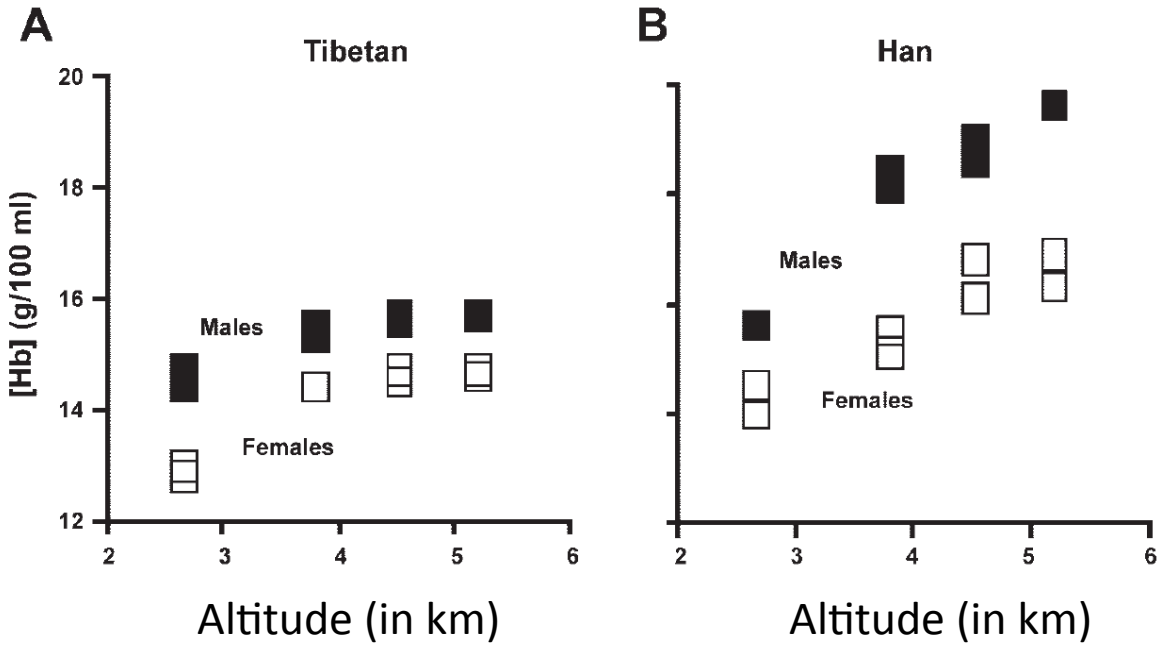
50 Tibetan exomes
50 Danish Exomes
40 Han exomes

Yi* X. et al. (2010) Science

Response to high altitude environments in Tibetans

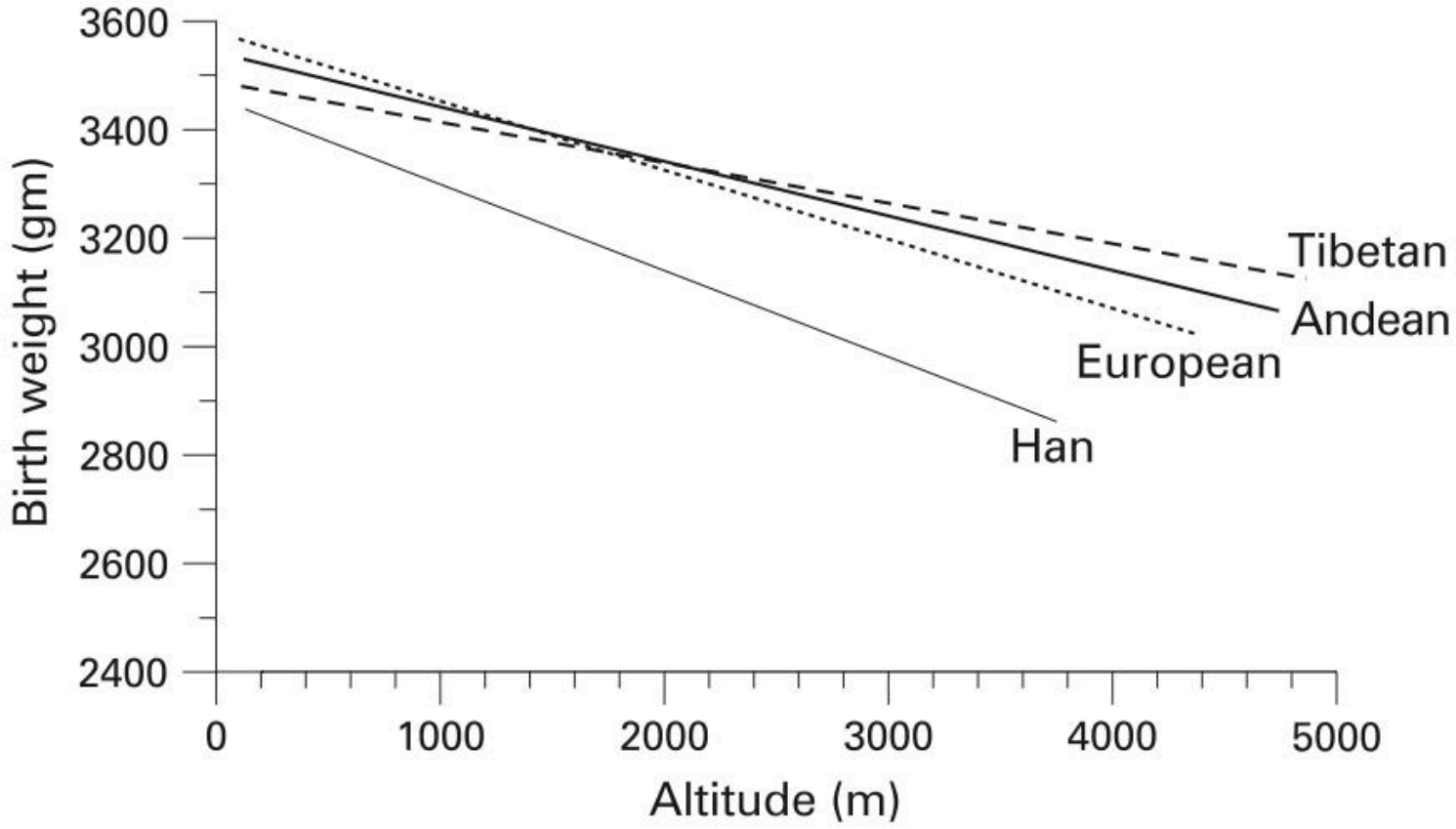
In the 70s, studies showed that Tibetans had a different physiological response

Tibetan Plateau



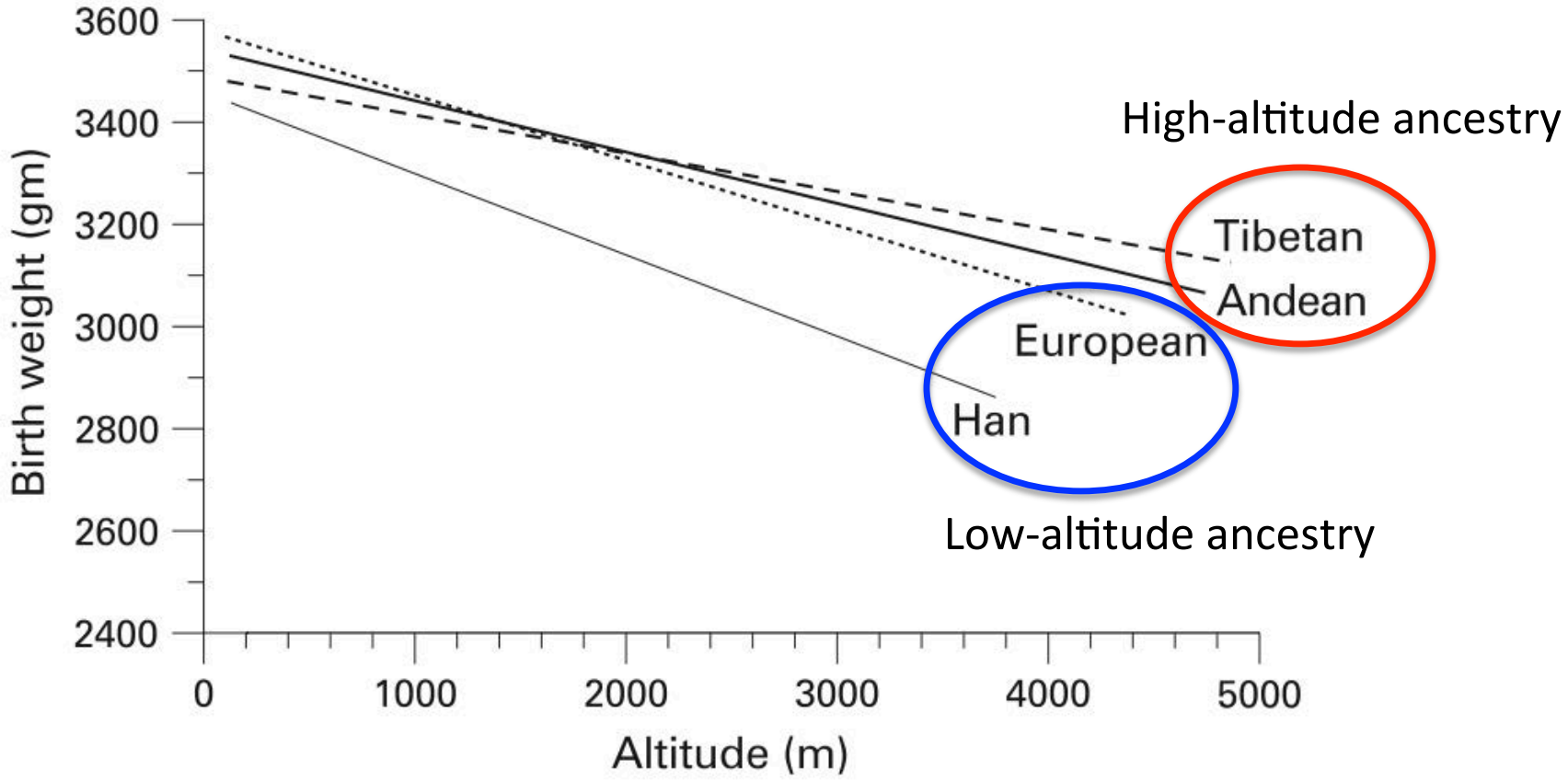
Wu et al. (2005) Journal of Applied Physiology

Higher fertility and lower infant mortality rate in high altitude natives than in acclimatized low altitude natives



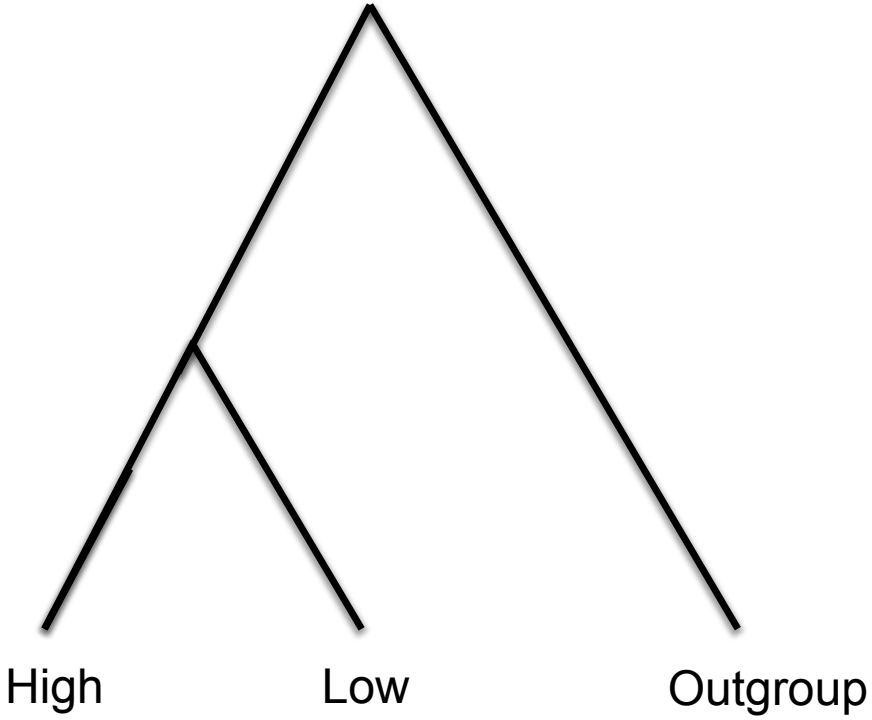
Niermeyer et al. (2009) *Arch. Dis. Child*

Higher fertility and lower infant mortality rate in high altitude natives than in acclimatized low altitude natives



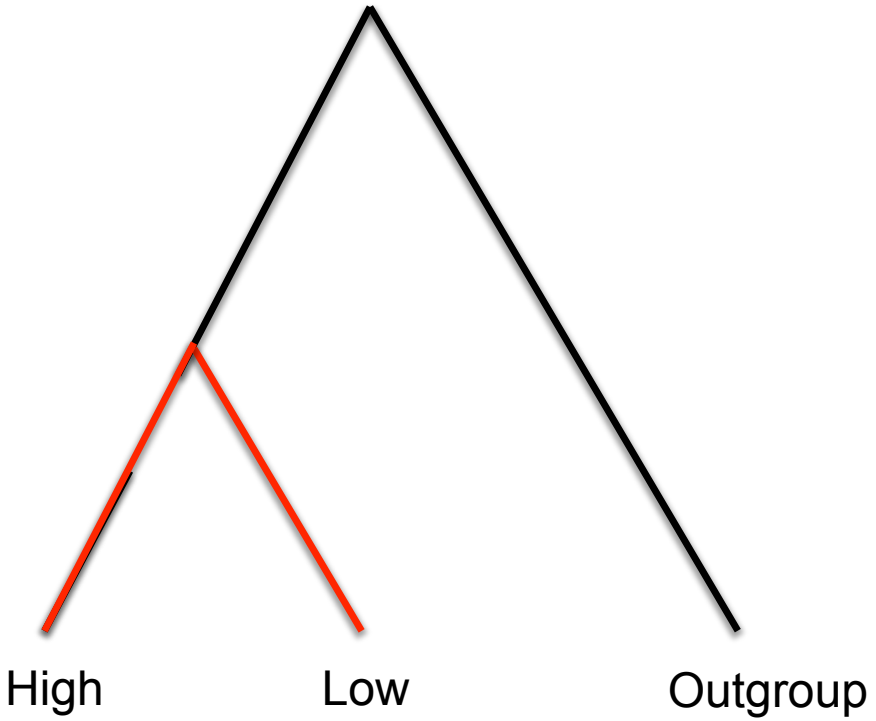
Niermeyer et al. (2009) *Arch. Dis. Child.*

Identifying signatures of positive selection



Yi* X. et al. (2010) Science

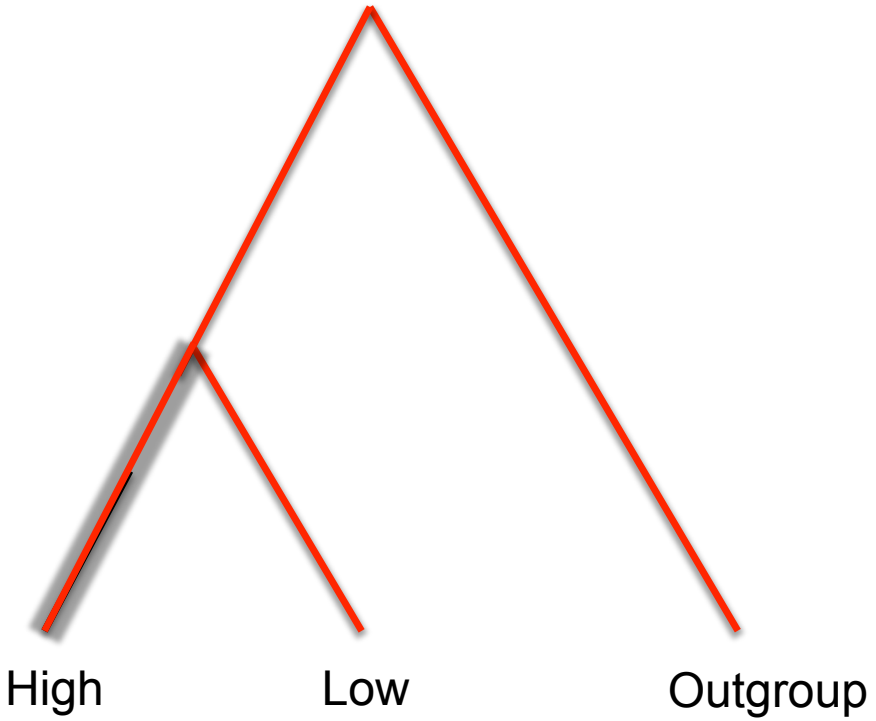
Identifying signatures of positive selection



$$PBS_{High} = \quad T_{High,Low}$$

Yi* X. et al. (2010) Science

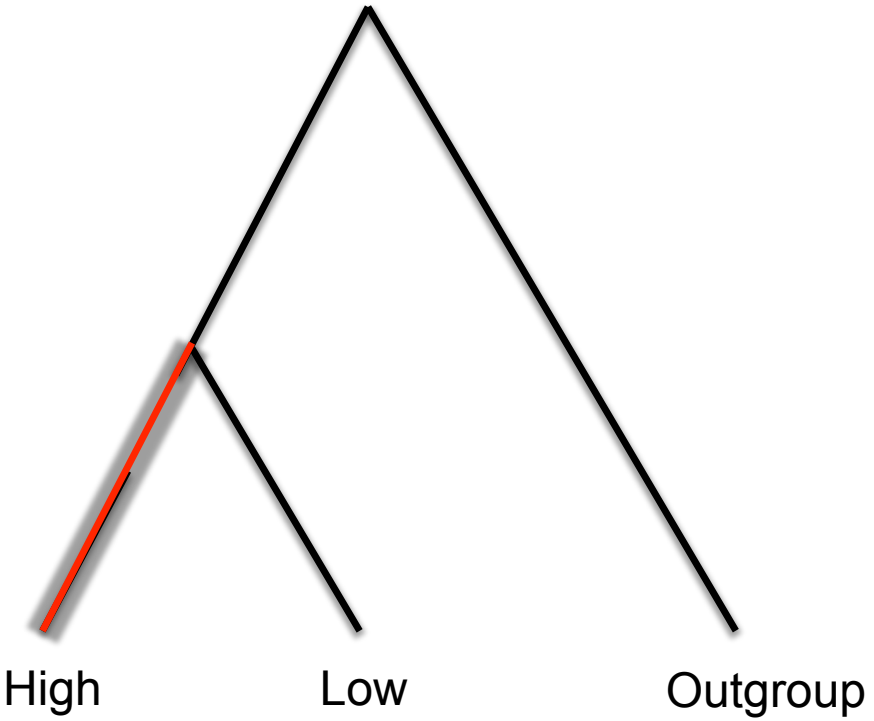
Identifying signatures of positive selection



$$PBS_{High} = T_{High,Low} + T_{High,Outgroup}$$

Yi* X. et al. (2010) Science

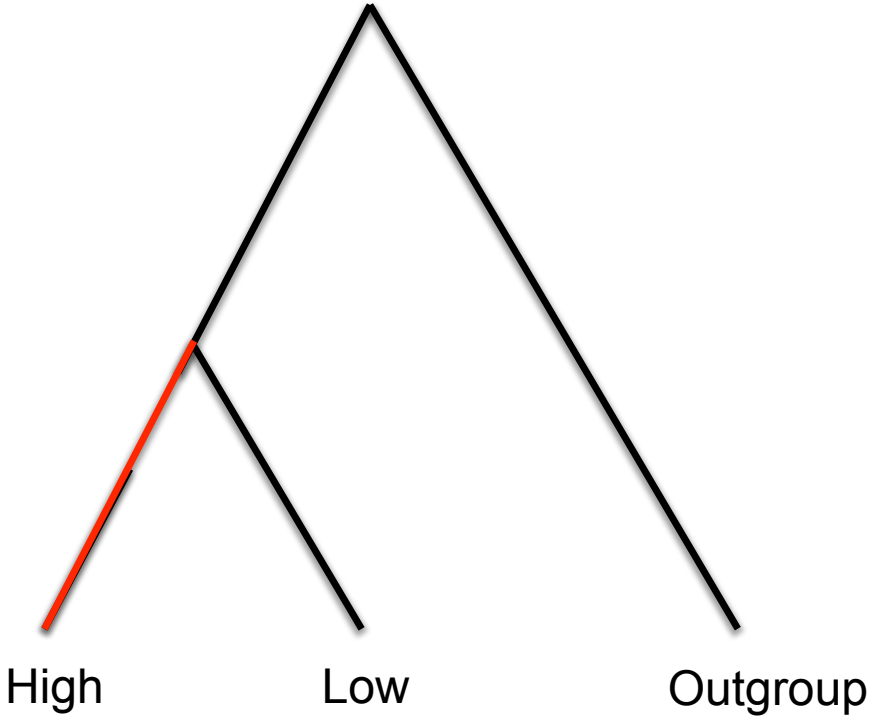
Identifying signatures of positive selection



$$PBS_{High} = T_{High,Low} + T_{High,Outgroup} - T_{Low,Outgroup}$$

Yi* X. et al. (2010) Science

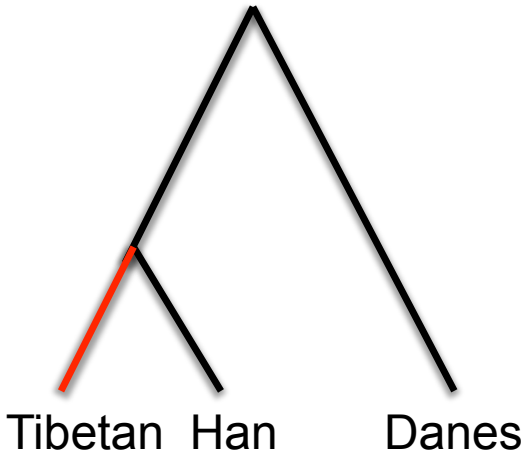
Identifying signatures of positive selection



$$PBS_{High} = \frac{1}{2}\left[T_{High,Low} + T_{High,Outgroup} - T_{Low,Outgroup}\right]$$

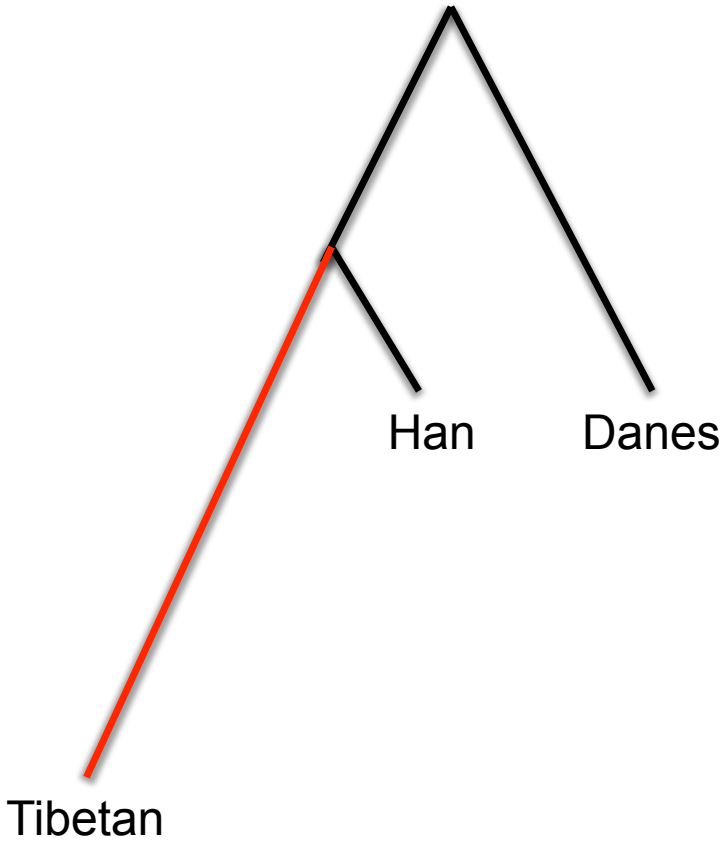
Yi* X. et al. (2010) Science

PBS under neutrality



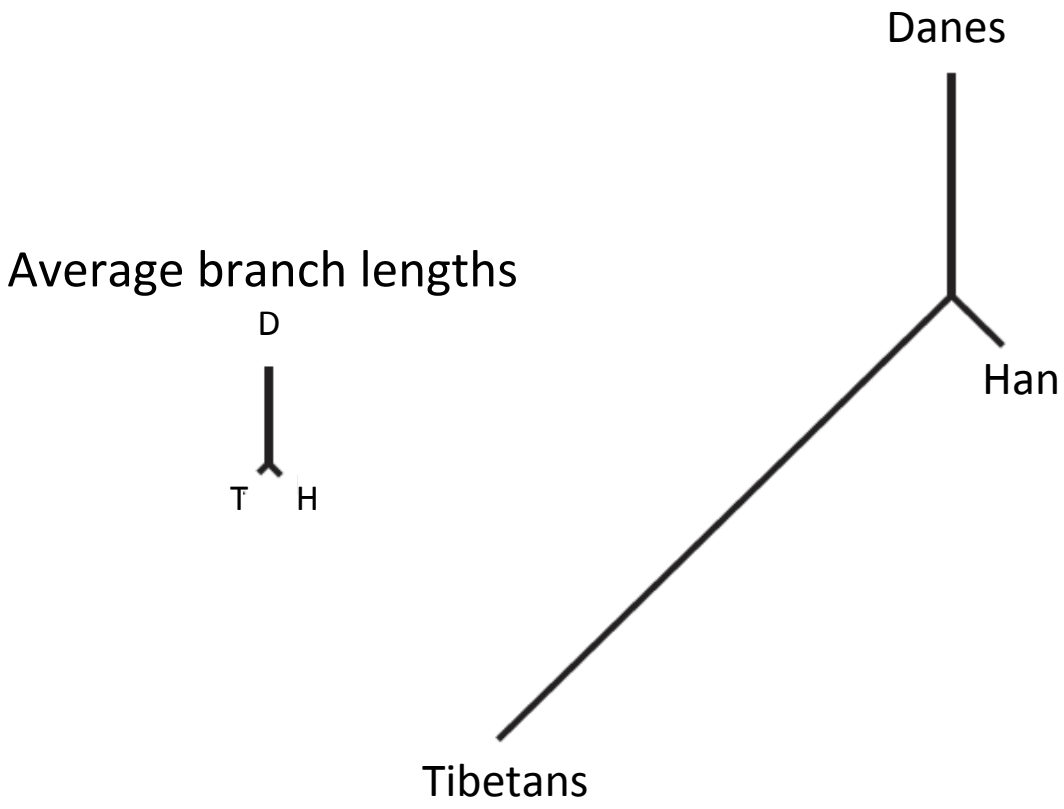
Yi* X. et al. (2010) Science

PBS under positive selection



Yi* X. et al. (2010) Science

Largest PBS: *EPAS1*



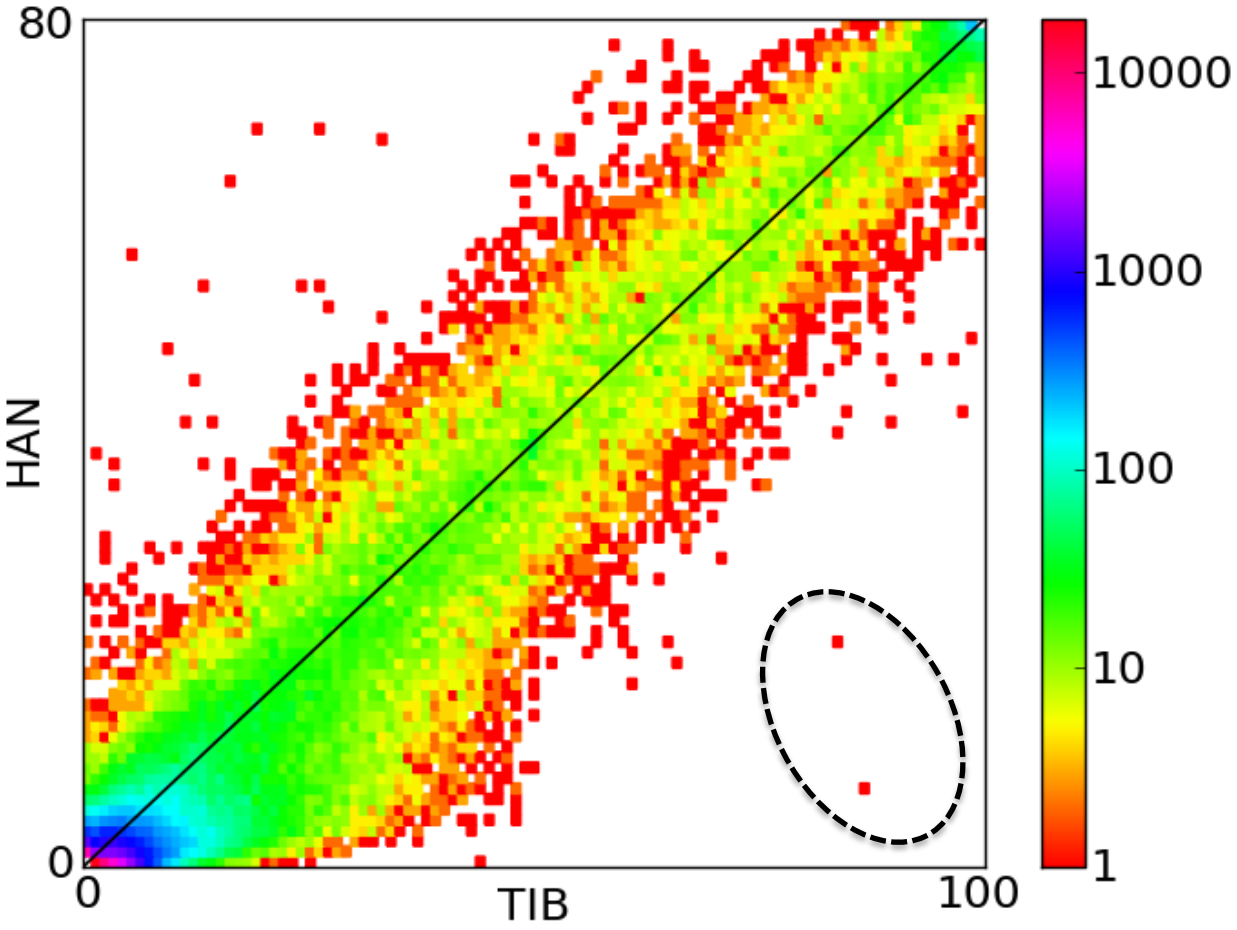
Yi* X. et al. (2010) Science

EPAS1: Hypoxia inducible factor 2

- Major Transcription factor that orchestrates response to low oxygen levels
- Regulates several genes involved in red blood cell production
- SNPs in *EPAS1* have been associated with super-athlete performances
- Highly expressed in the adult and fetal lung and placenta

Yi* X. et al. (2010) Science

EPAS1: large frequency differences.



Yi* X. et al. (2010) Science

Significant association with phenotype?

Genotype	Tibetan frequency	Mean hemoglobin concentration
CC	10	178
CG	84	178.9
GG	272	167.5

- Individuals with GG genotypes have ***LOWER*** hemoglobin concentration

Yi* X. et al. (2010) Science

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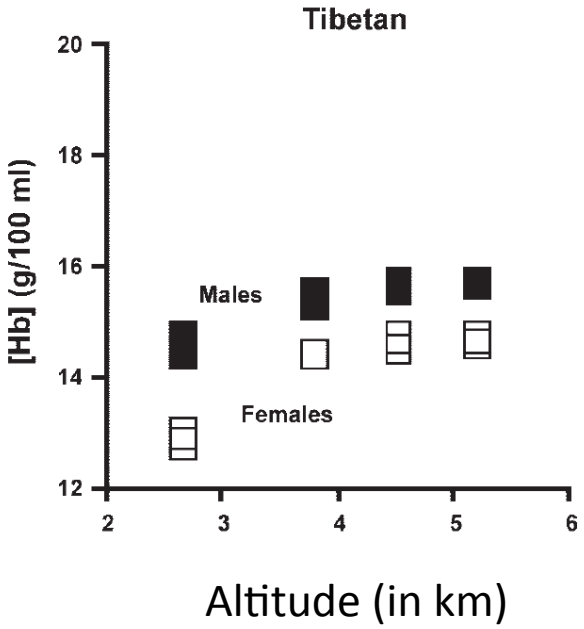

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Yi* X. et al. (2010) Science

Figs from book chapter on Directional selection and adaptation Encyclopedia of Evolutionary Biology Racimo et al. 2016

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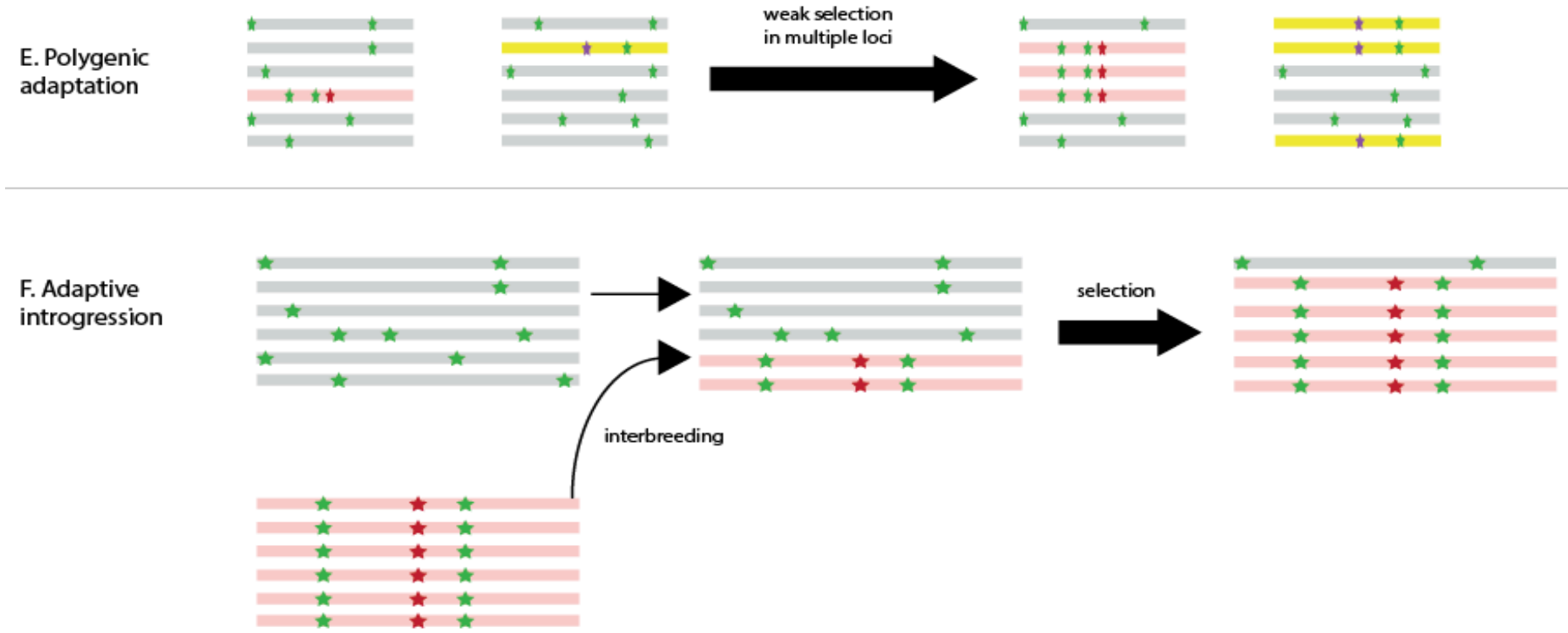
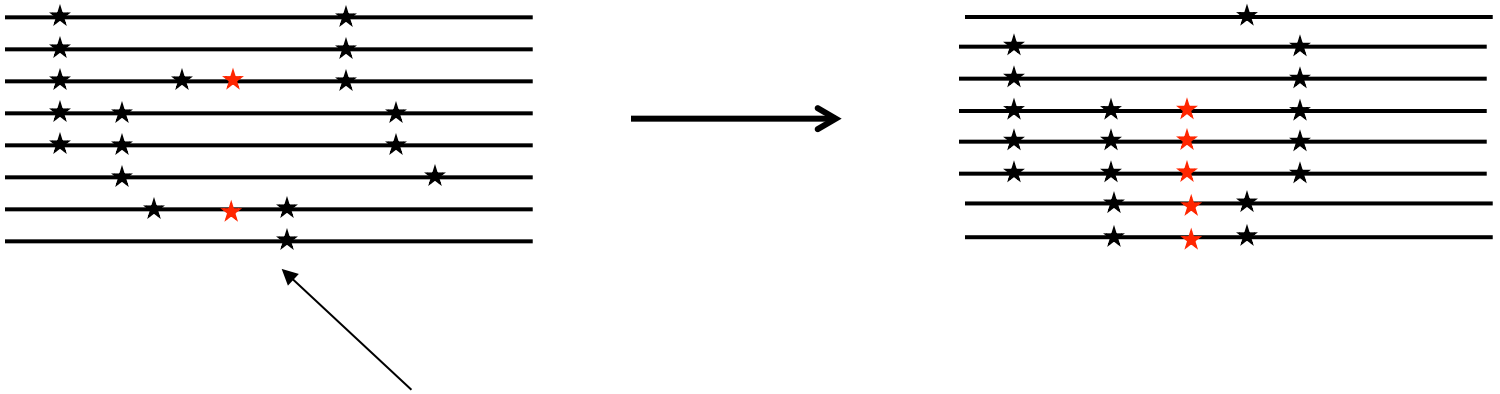
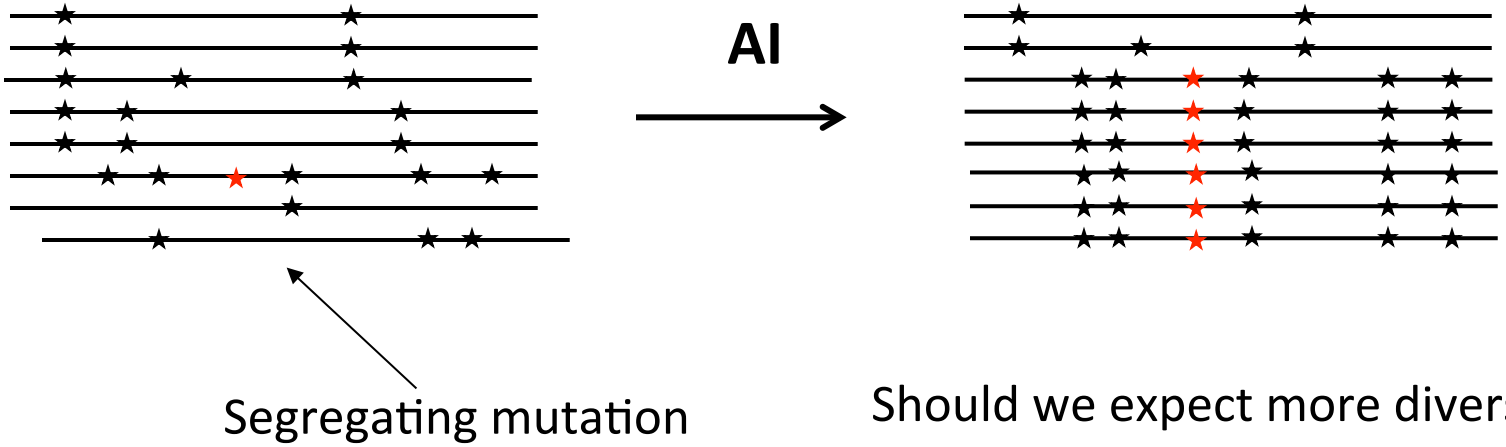


Will pattern be different from selection on standing variation?

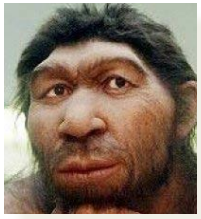




Should we expect more diversity on the Selected haplotype?

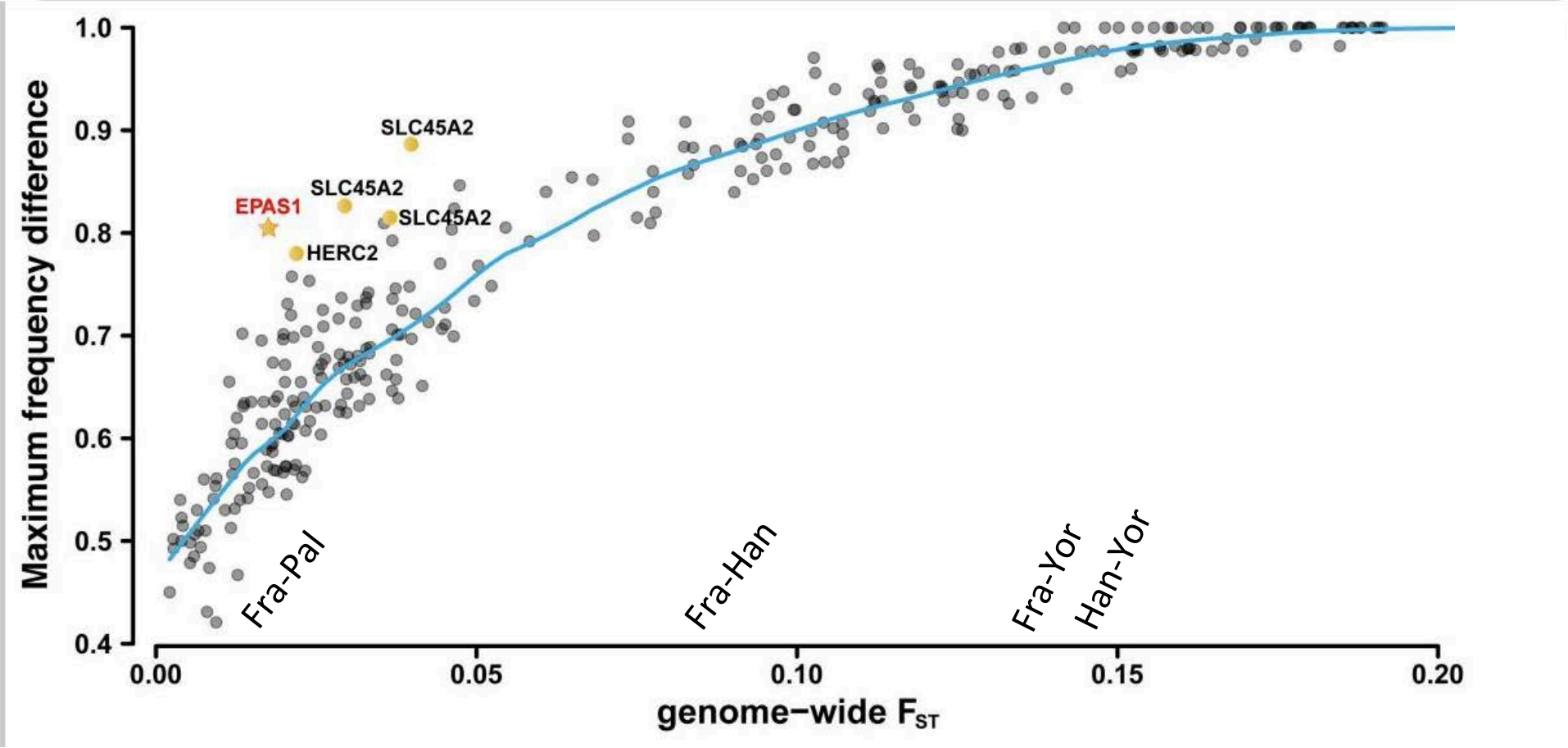
Admixed haplotypes can have a tremendous evolutionary advantage

EPAS1



Huerta-Sanchez et al. *Nature* (2014)
Yi*, Liang*, Huerta-Sanchez* *et al. Science* (2010)

Genetic Differentiation



Redrawn from Coop et al. 2009