

Demographic inferences and the genetics of admixture

November 2020

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Imperial College
London

Human genetic diversity



Robin Hammond



Robin Hammond



3.2 billion nucleotides



10 million SNPs



Human population genetics

- **Describe** the genetic diversity within and between populations
- **Explain** the origin of the observed diversity
 - Demography
 - Natural Selection

Population

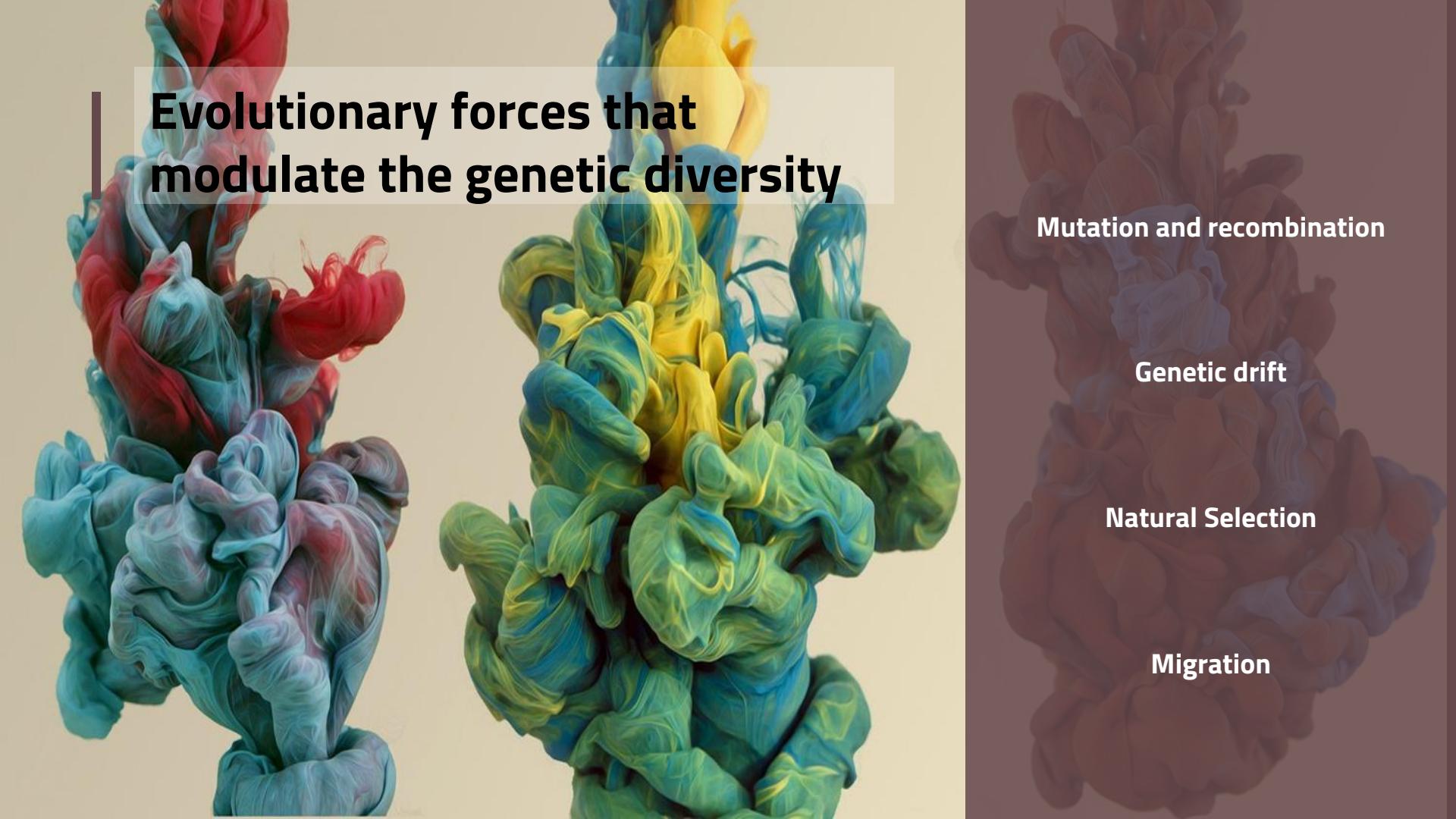


Human genetic diversity

Evolutionary forces that modulate the genetic diversity

A large, abstract 3D visualization composed of three distinct, colorful, organic shapes. The left shape is primarily red, blue, and purple. The middle shape is primarily green, yellow, and blue. The right shape is primarily orange, red, and blue. These shapes resemble stylized, flowing clouds or complex molecular structures.

Evolutionary forces that modulate the genetic diversity

The background of the slide features three abstract, organic shapes composed of swirling, translucent ink or paint. The left shape is primarily red, blue, and purple. The middle shape is primarily yellow, green, and blue. The right shape is primarily brown and blue. These shapes overlap and flow into each other against a light beige background.

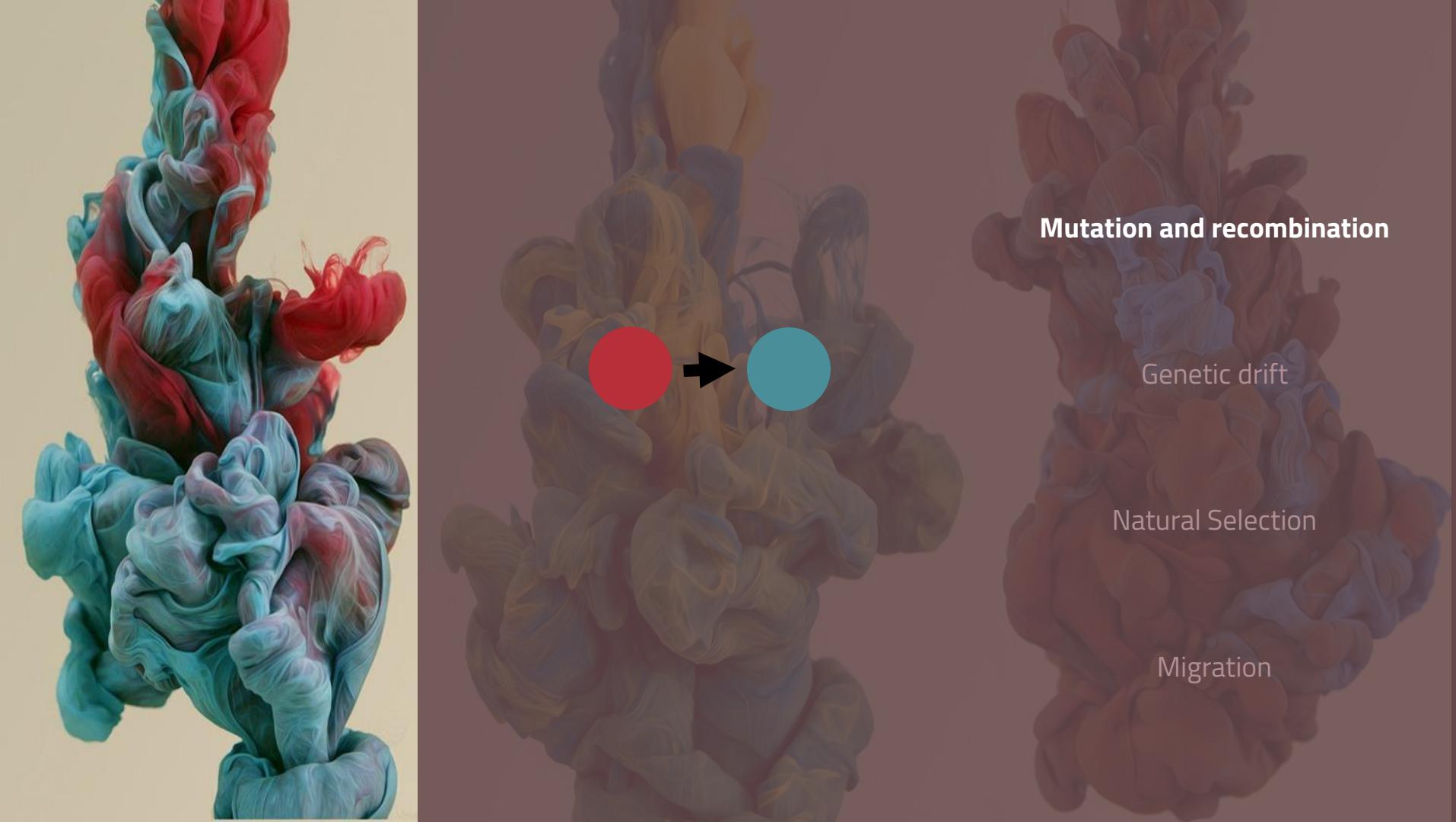
Evolutionary forces that modulate the genetic diversity

Mutation and recombination

Genetic drift

Natural Selection

Migration

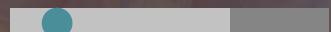
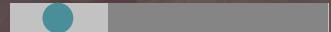
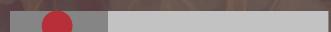
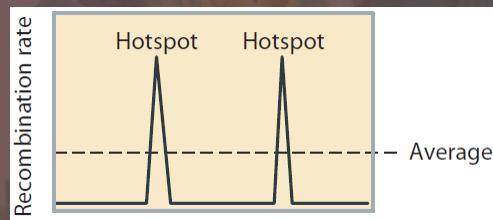
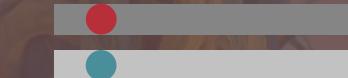
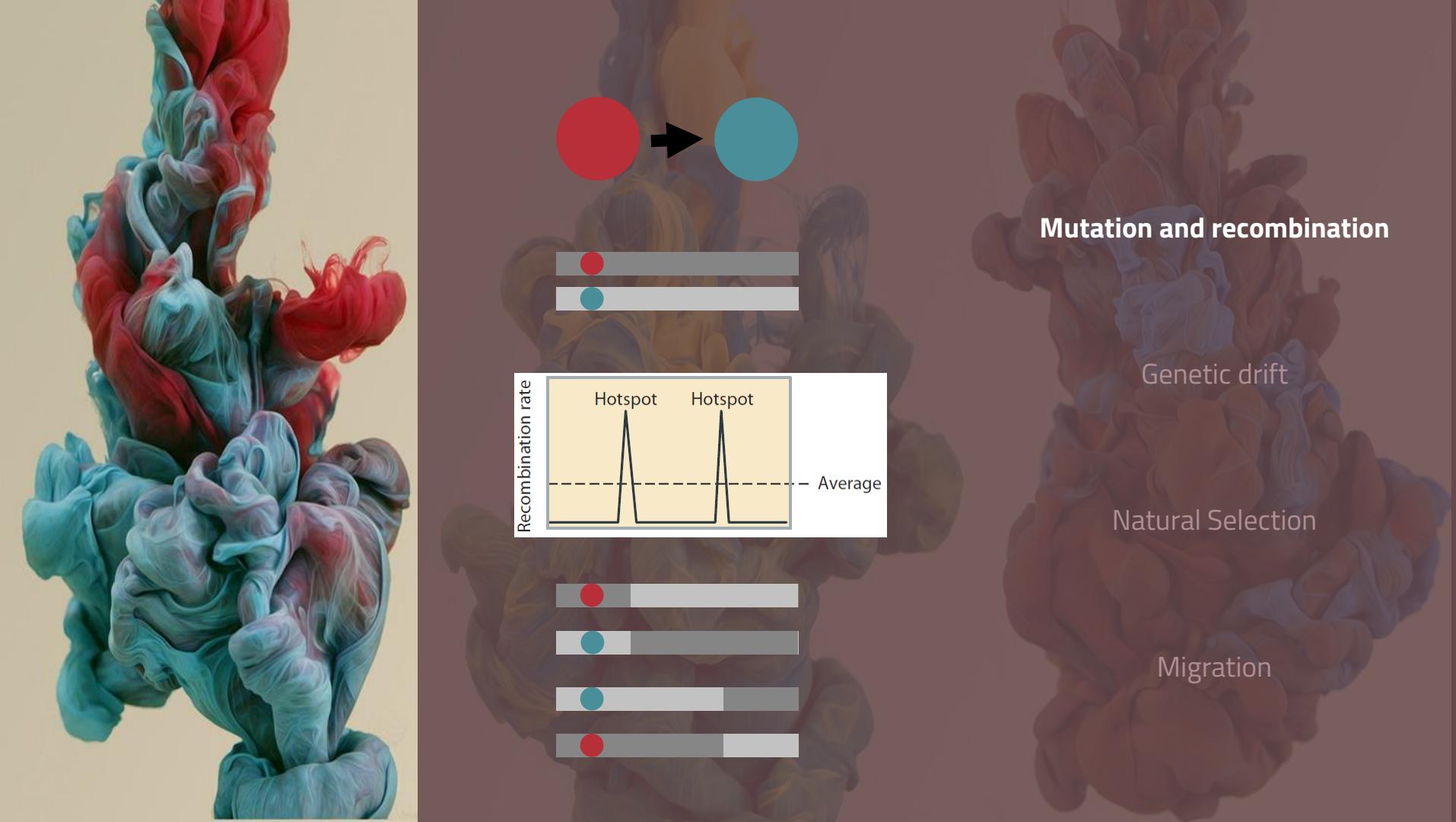


Mutation and recombination

Genetic drift

Natural Selection

Migration

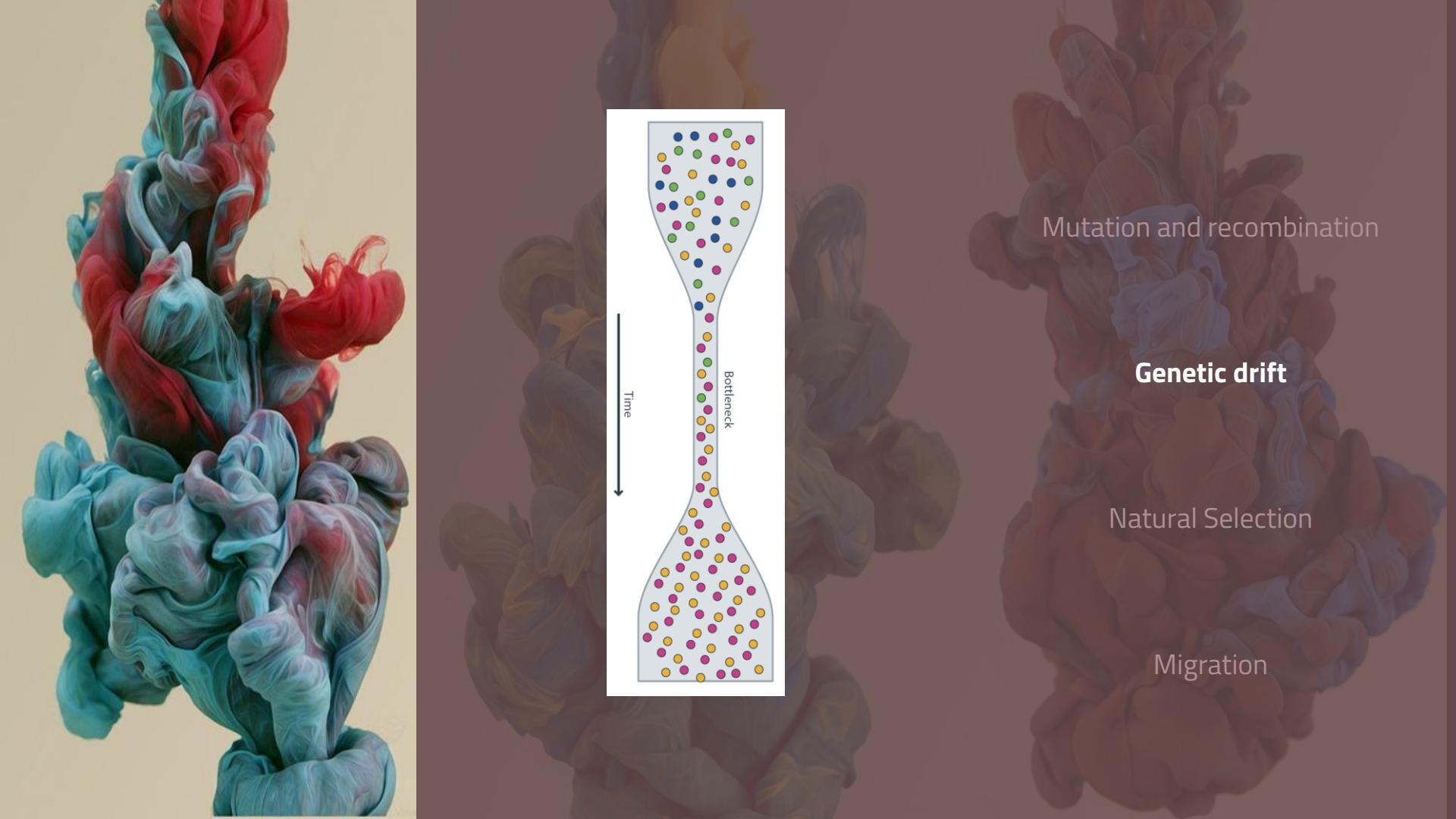


Mutation and recombination

Genetic drift

Natural Selection

Migration

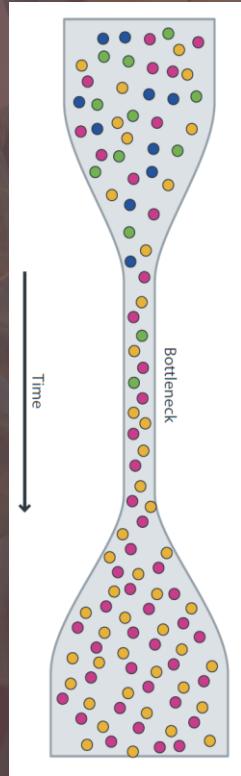


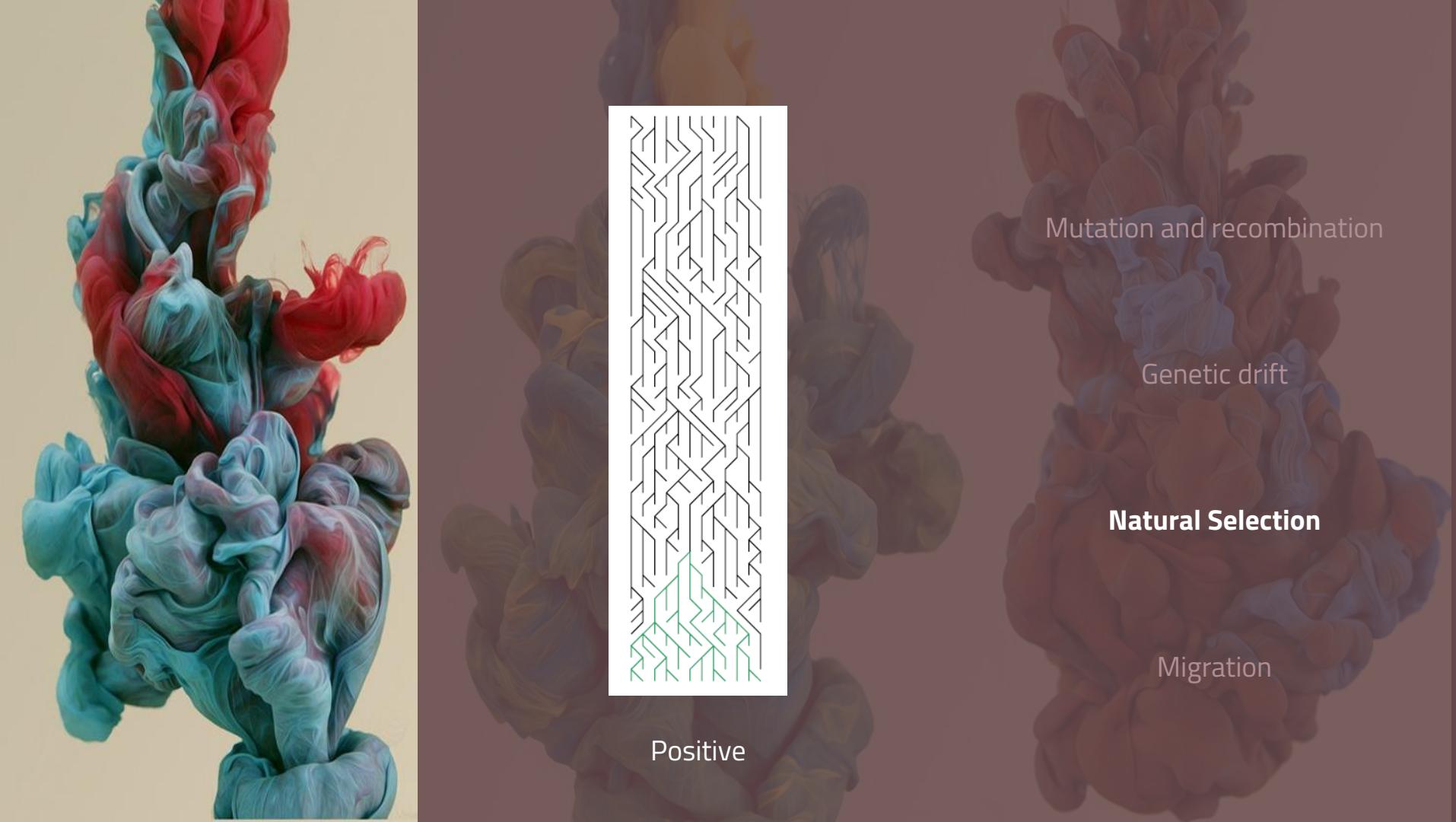
Mutation and recombination

Genetic drift

Natural Selection

Migration





Positive

Mutation and recombination

Genetic drift

Natural Selection

Migration



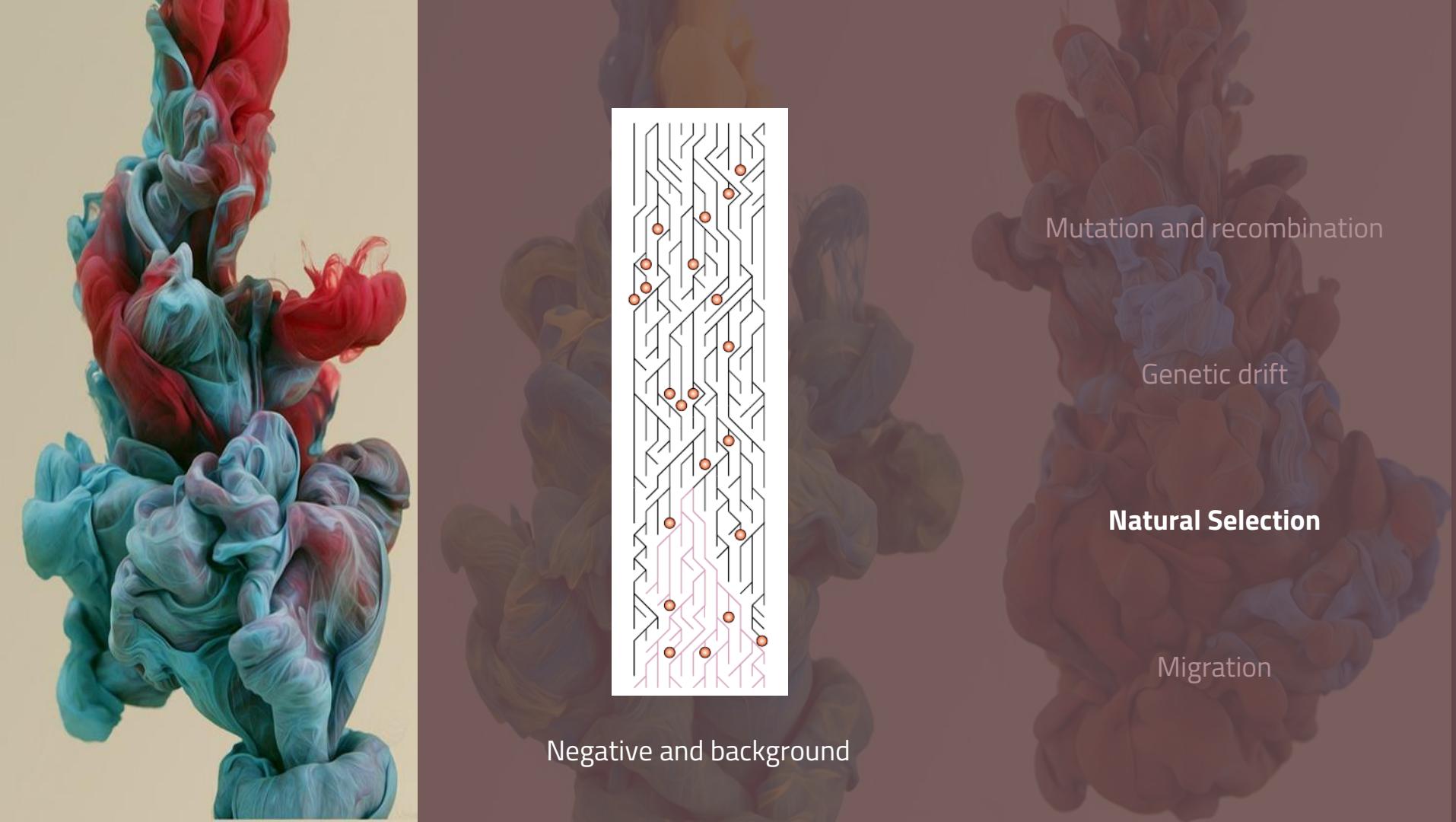
Balancing

Mutation and recombination

Genetic drift

Natural Selection

Migration



Negative and background

Mutation and recombination

Genetic drift

Natural Selection

Migration



Mutation and recombination

Genetic drift

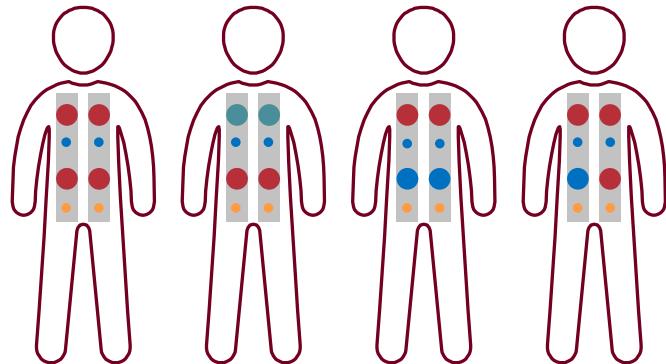
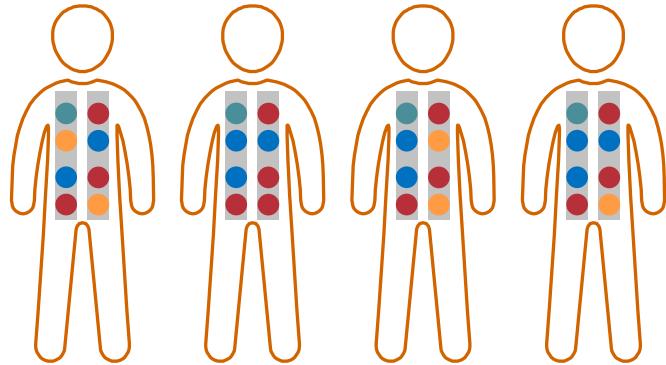
Natural Selection

Migration

Human genetic diversity

Studying the human genetic diversity

Summarizing the genetic diversity within a population



Summarizing the genetic diversity within a population

- **Watterson estimator**

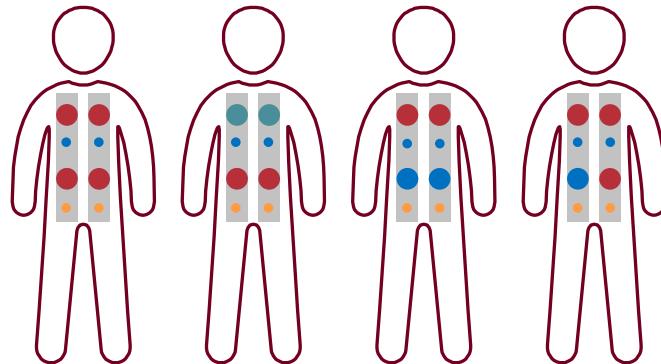
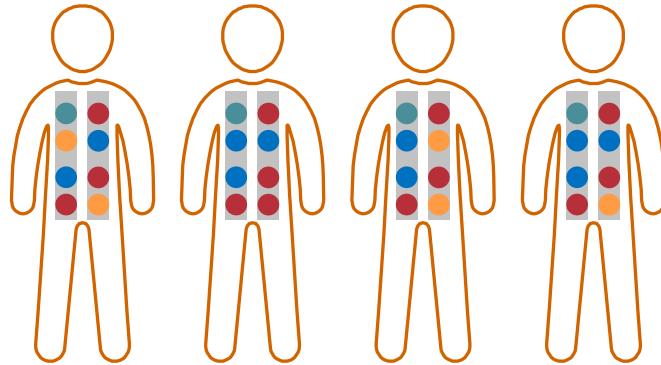
Number of segregating sites

$$\hat{\theta}_W = \frac{S}{\sum_{k=1}^{n-1} \frac{1}{k}}$$

- **Tajima's estimator**

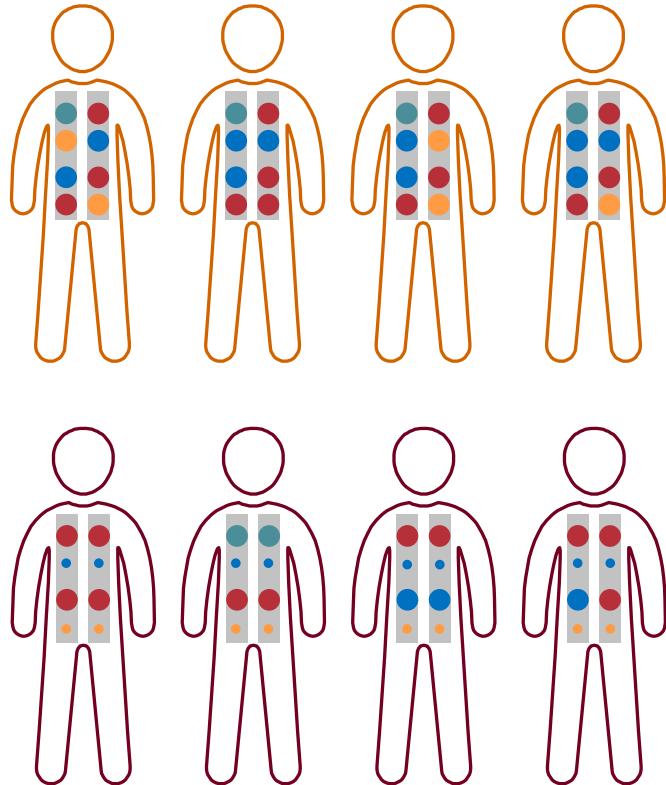
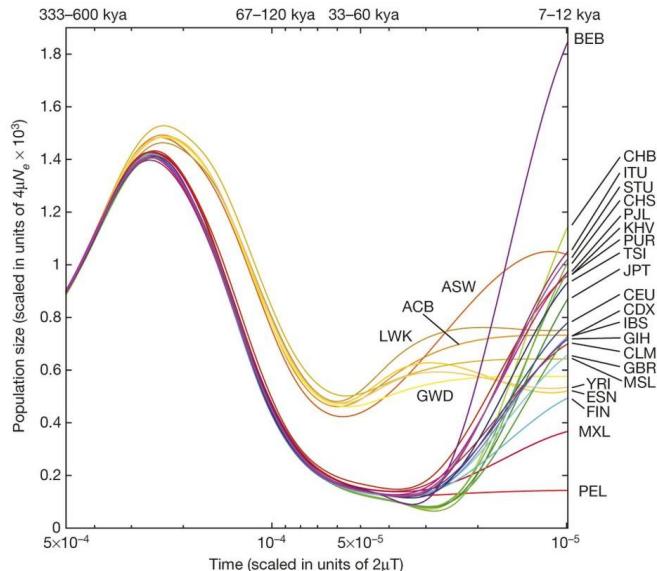
Nucleotide pairwise differences

$$\pi = \frac{\sum_{i < j} d_{i,j}}{n(n - 1)/2}$$

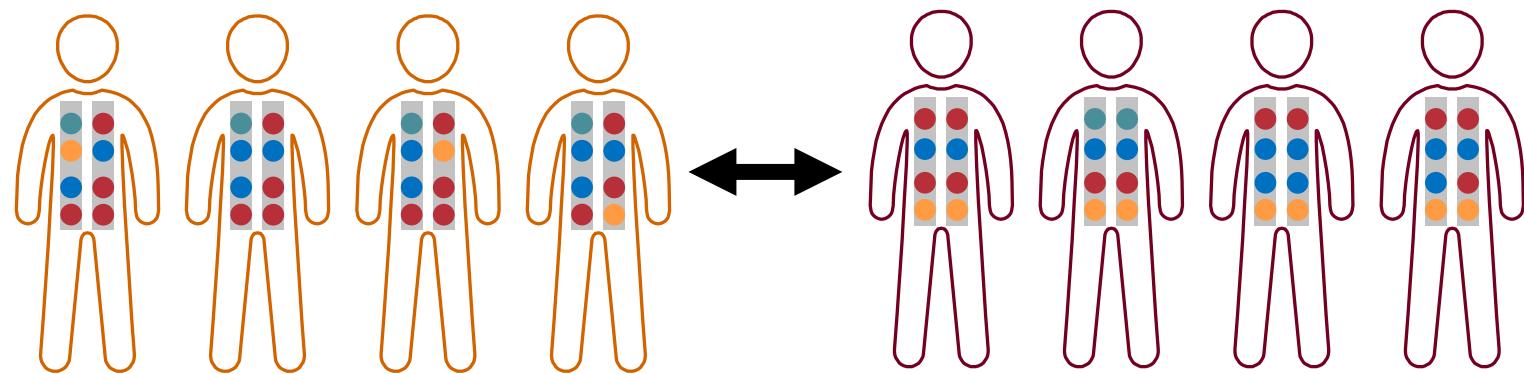


Summarizing the genetic diversity within a population

- Effective population size (N_e)



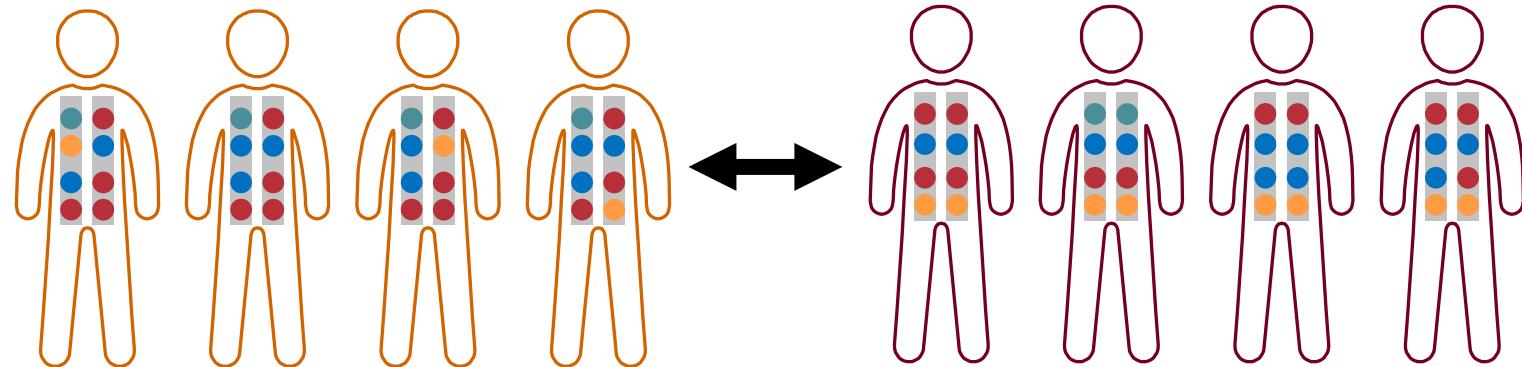
Genetic distances between populations



Genetic distances between populations

Allele frequency methods

- **Nei's D** $D = -\ln\left(\frac{J_{12}}{\sqrt{J_{11}J_{22}}}\right)$
- **F_{ST}** $F_{ST} = \frac{\pi_{\text{Between}} - \pi_{\text{Within}}}{\pi_{\text{Between}}}$

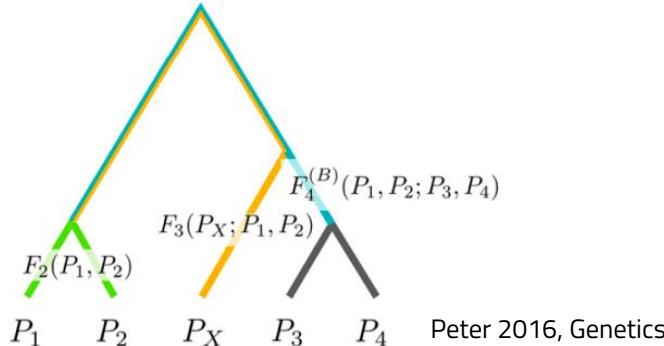


Genetic distances between populations

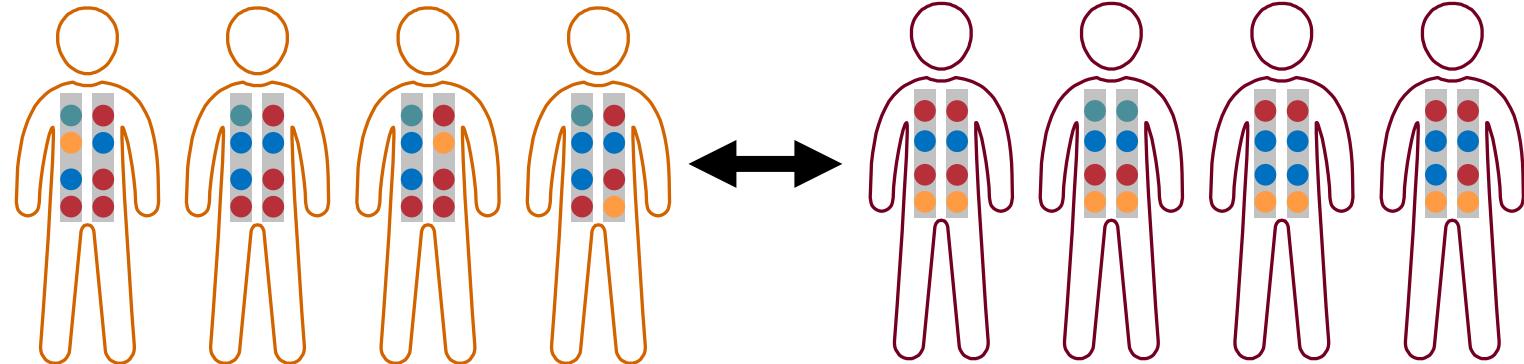
Allele frequency methods

F-statistics (Reich et al. 2009, Nature)

- F_2
- F_3
- F_4

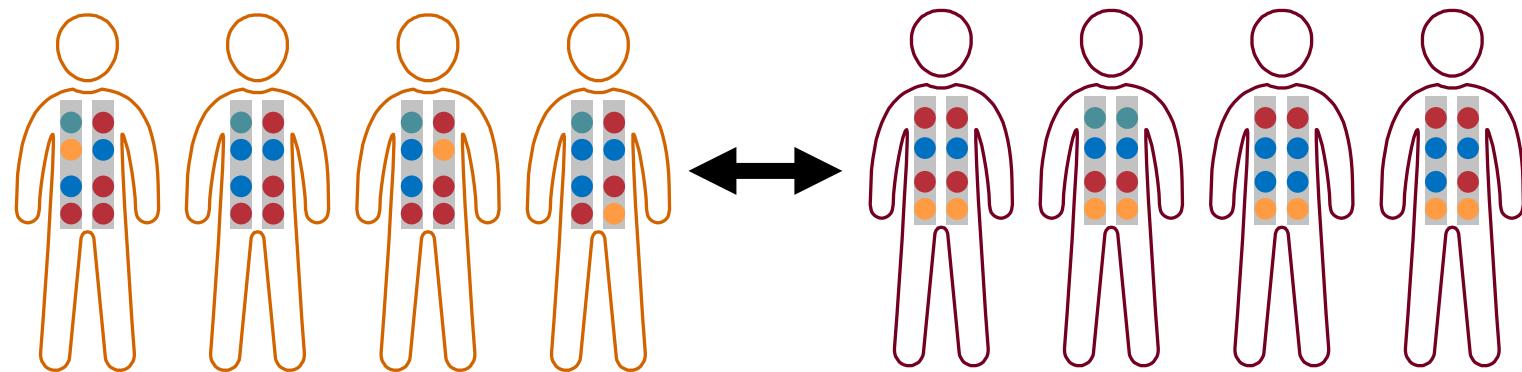


Peter 2016, Genetics



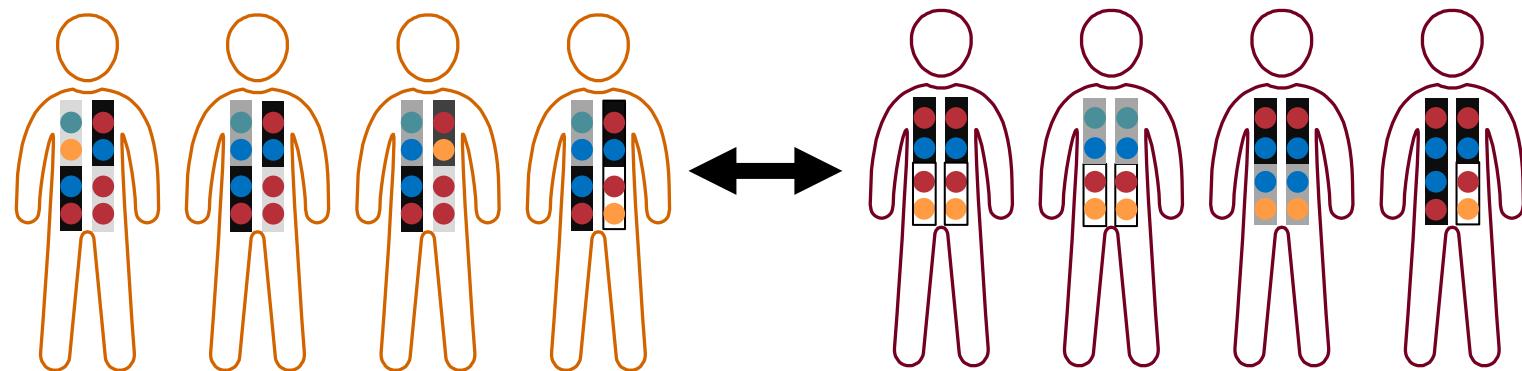
Genetic distances between populations

Haplotype-based methods



Genetic distances between populations

Haplotype-based methods

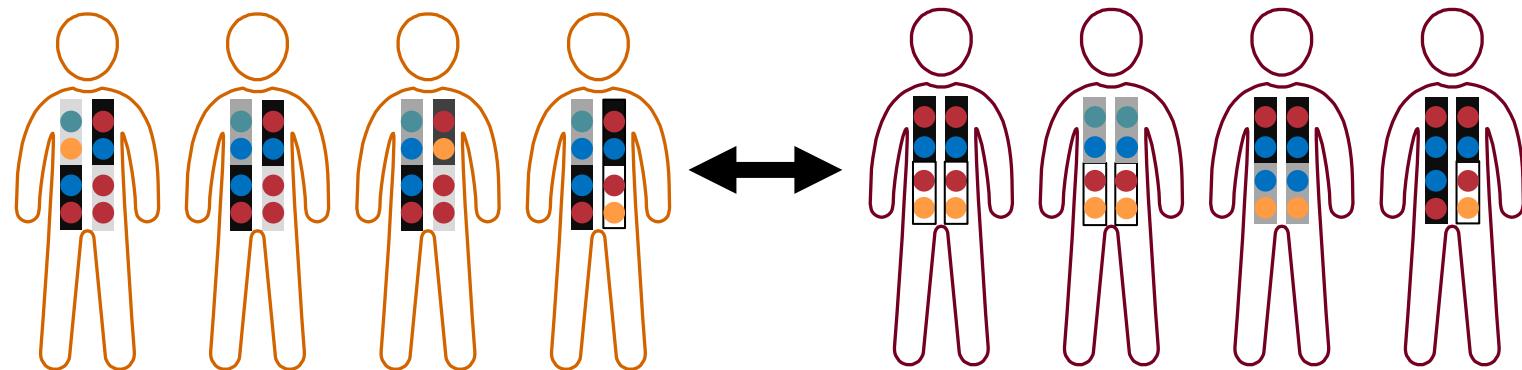


Genetic distances between populations

Haplotype-based methods

- ChromoPainter

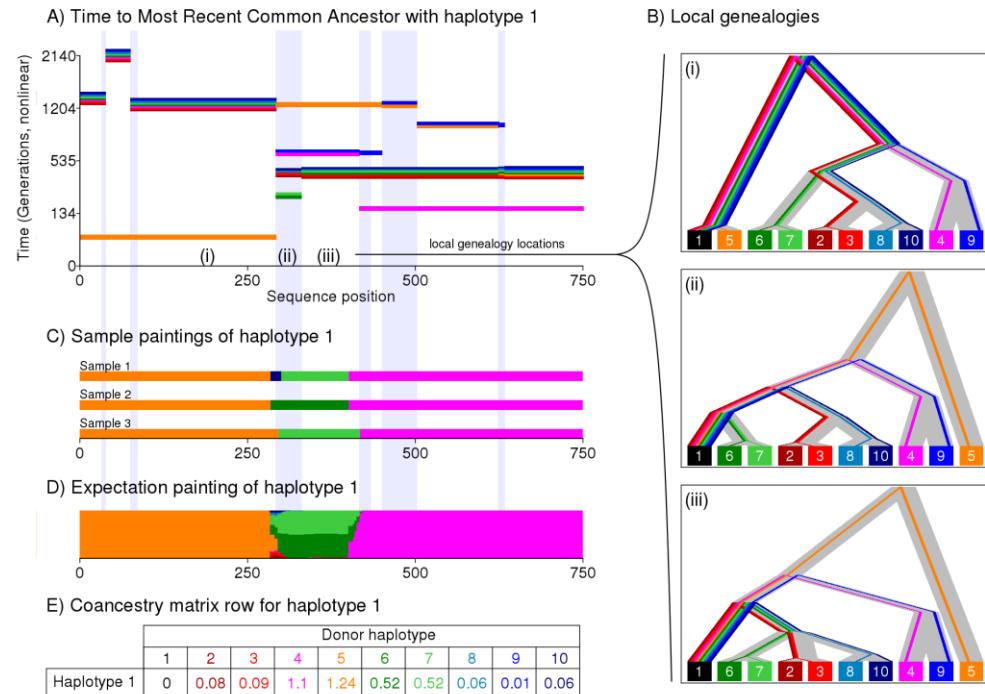
Lawson et al. 2012, PLoS Genet



Genetic distances between populations

Haplotype-based methods

- ChromoPainter
Lawson et al. 2012, PLoS Genet
- Search for the most common recent ancestor of each individual haplotype within the haplotypes of the other individuals of the dataset

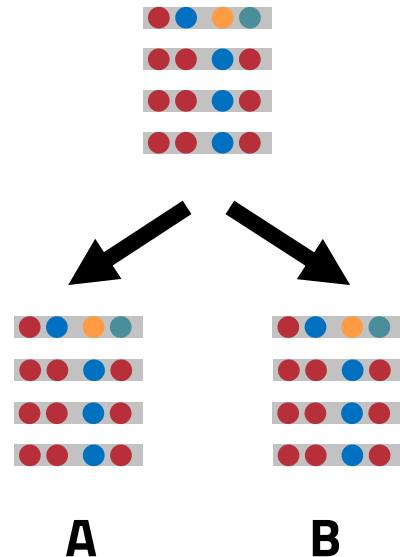


Genetic distances between populations

Haplotype-based methods

- ChromoPainter

Lawson et al. 2012, PLoS Genet

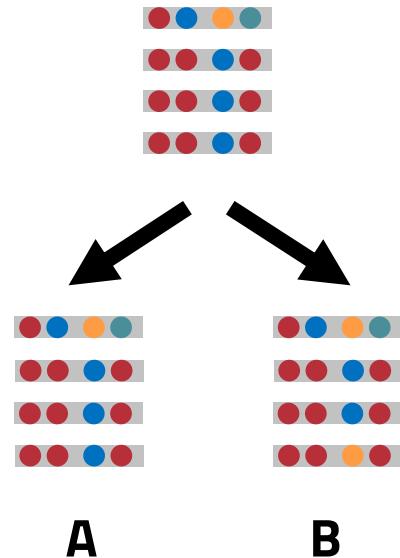


Genetic distances between populations

Haplotype-based methods

- ChromoPainter

Lawson et al. 2012, PLoS Genet

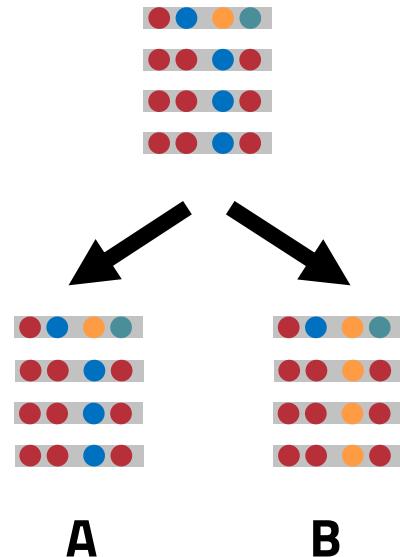


Genetic distances between populations

Haplotype-based methods

- ChromoPainter

Lawson et al. 2012, PLoS Genet

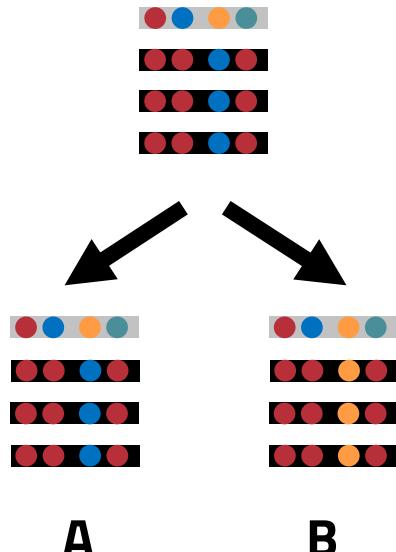


Genetic distances between populations

Haplotype-based methods

- ChromoPainter

Lawson et al. 2012, PLoS Genet



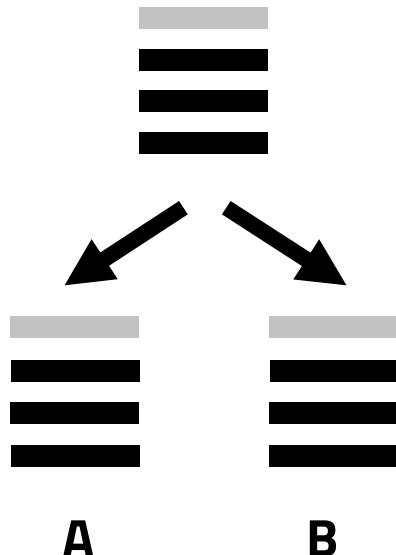
Analyzing the context of the snps, **the haplotypes**, we can smooth the weight of increased allele frequencies after genetic drift and relate the populations trough shared haplotypes

Genetic distances between populations

Haplotype-based methods

- ChromoPainter

Lawson et al. 2012, PLoS Genet



Analyzing the context of the snps, **the haplotypes**, we can smooth the weight of increased allele frequencies after genetic drift and relate the populations through shared haplotypes

Genetic distances between populations

Population structure through clustering methods

Genetic distances between populations

Population structure through clustering methods

From allele frequencies

Genetic distances between populations

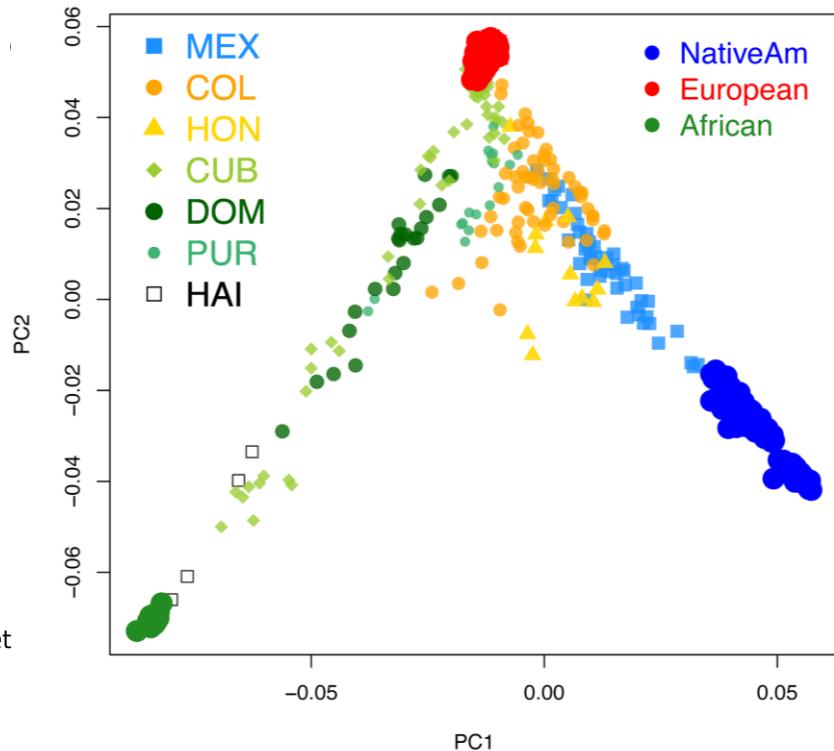
Population structure through clustering methods

From allele frequencies

- **Principal Component Analysis**

- Transforms allele frequencies to a set of linearly uncorrelated variables called principal components.
- The visualization of the individuals as points of two principal component coordinates clusters them based on their genetic distances.

Moreno-Estrada et al. 2013, PLoS Genet



Genetic distances between populations

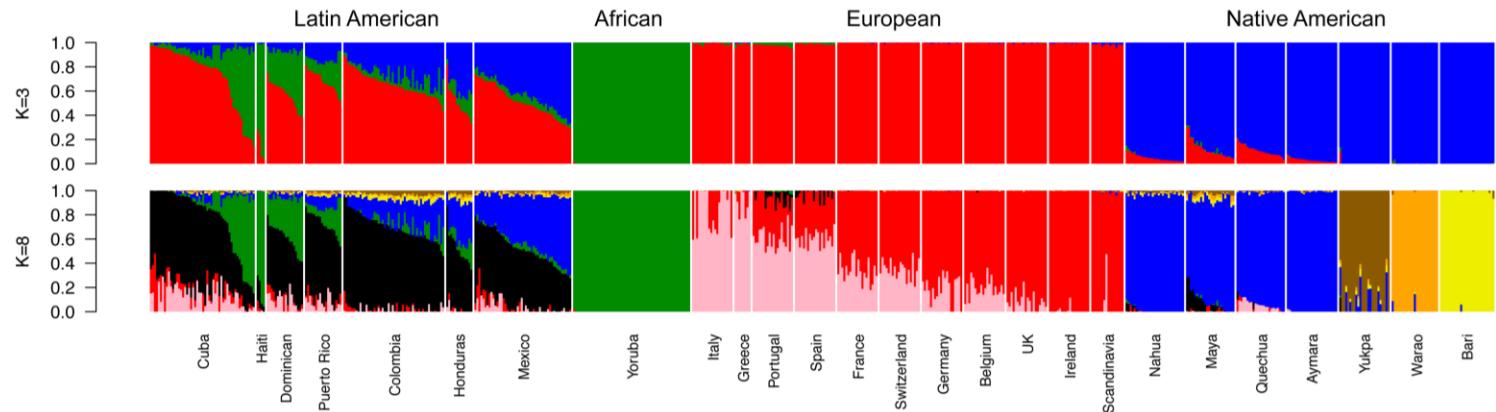
Population structure through clustering methods

From allele frequencies

- **Admixture**

Alexander et al. 2019, Genome Res

Moreno et al. 2013, PLoS Genet



- analyses differences in the distribution of allele frequencies amongst individuals with a Bayesian iterative algorithm by placing samples into groups whose members share similar patterns of variation

Genetic distances between populations

Population structure through clustering methods

From haplotype-based methods

Genetic distances between populations

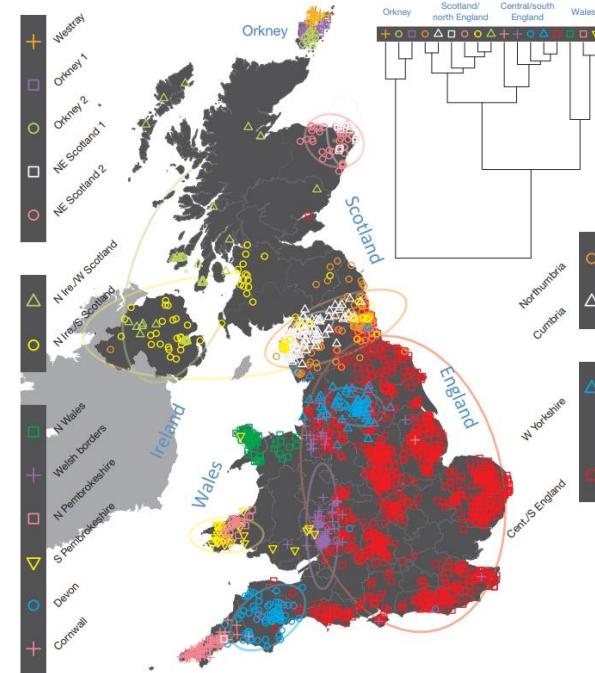
Population structure through clustering methods

From haplotype-based methods

- **FineStructure**

Lawson et al. 2012, PLoS Genet

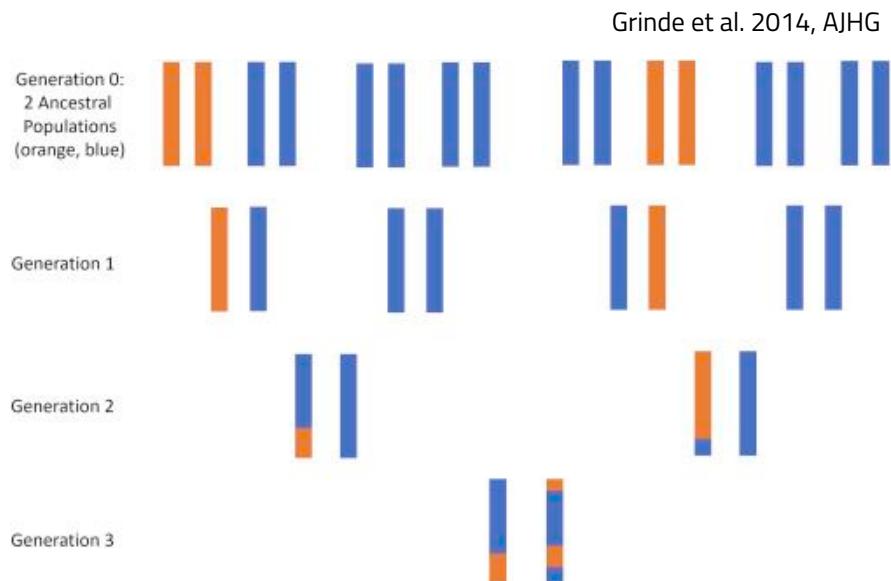
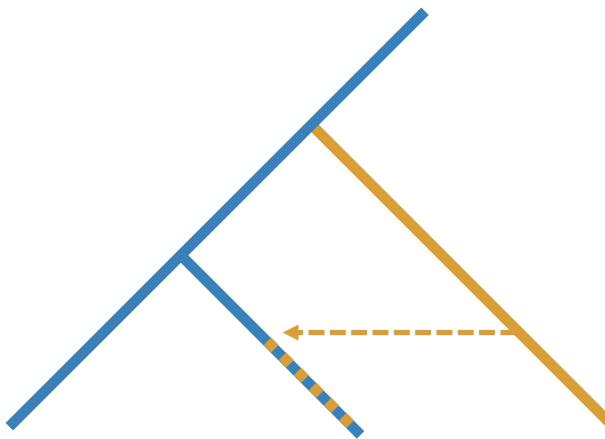
- Clusters the individuals based on their **haplotypic similatiries** computed in the ChromoPainnter coancestry matrix



Leslie et al. 2015, Nature

Inference of admixture between populations

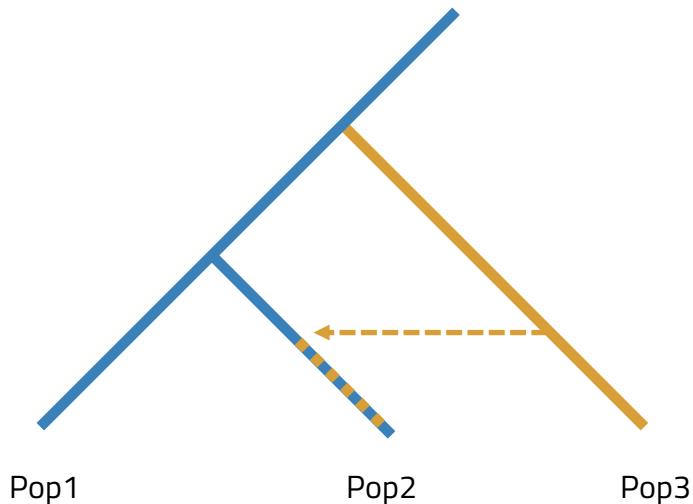
Inference of admixture between populations



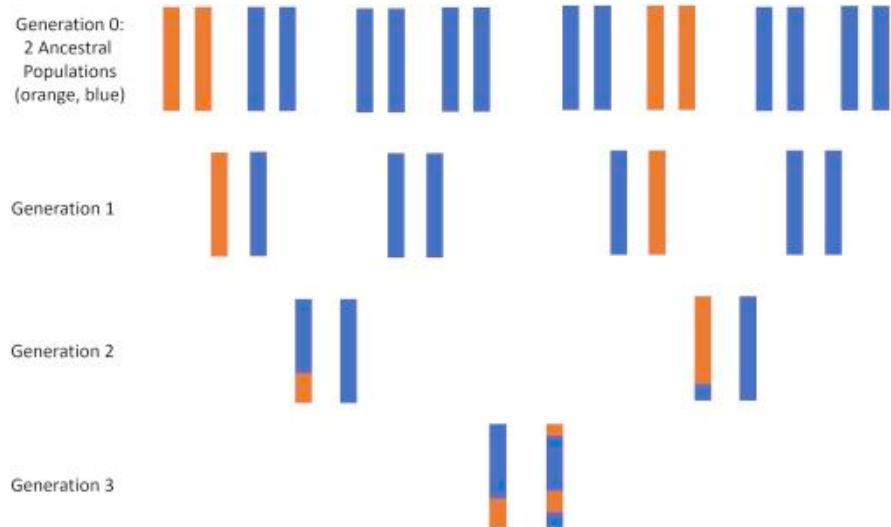
Inference of admixture between populations

From allele frequencies

- F_3



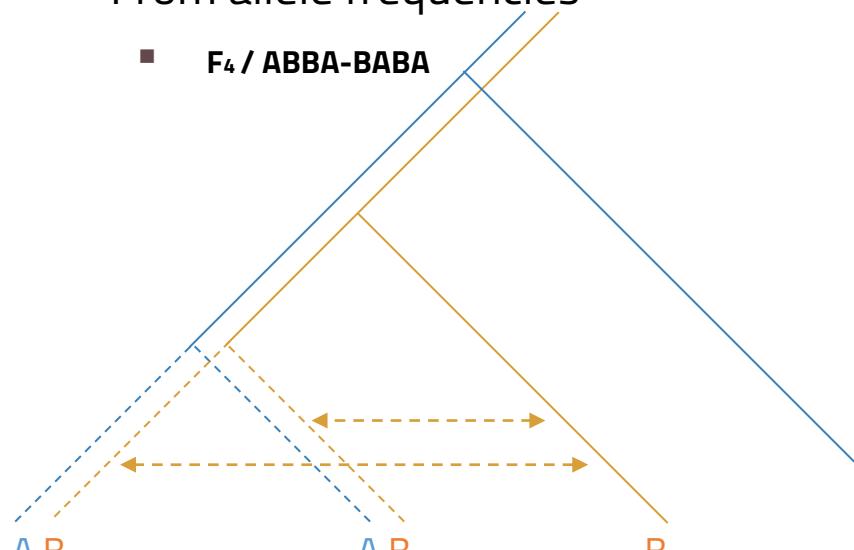
$$F_3(\text{Pop2}; \text{Pop1}, \text{Pop3}) < 0$$



Inference of admixture between populations

From allele frequencies

- $F_4 / \text{ABBA-BABA}$



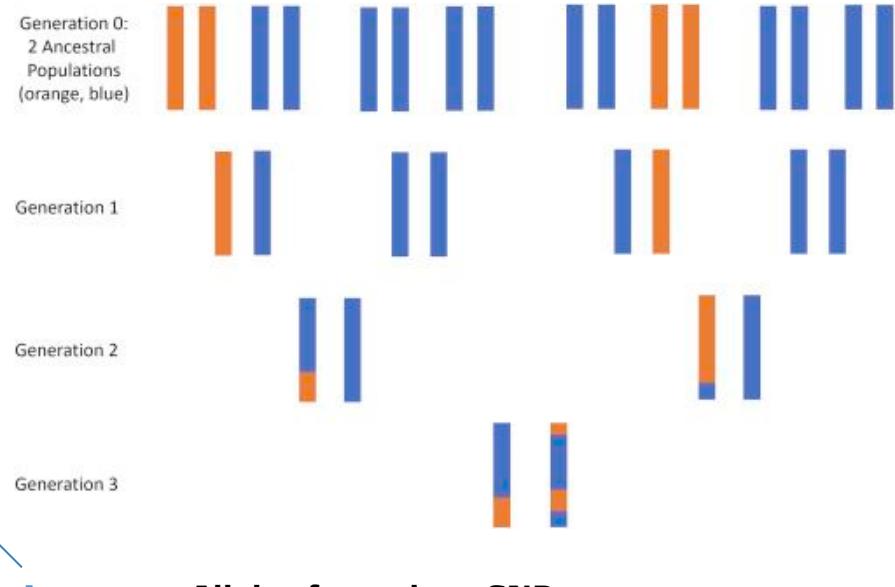
Pop1

Pop2

Test

Outgroup

$F_4 > 0$: Admixture in Pop2
 $F_4 < 0$: Admixture in Pop1

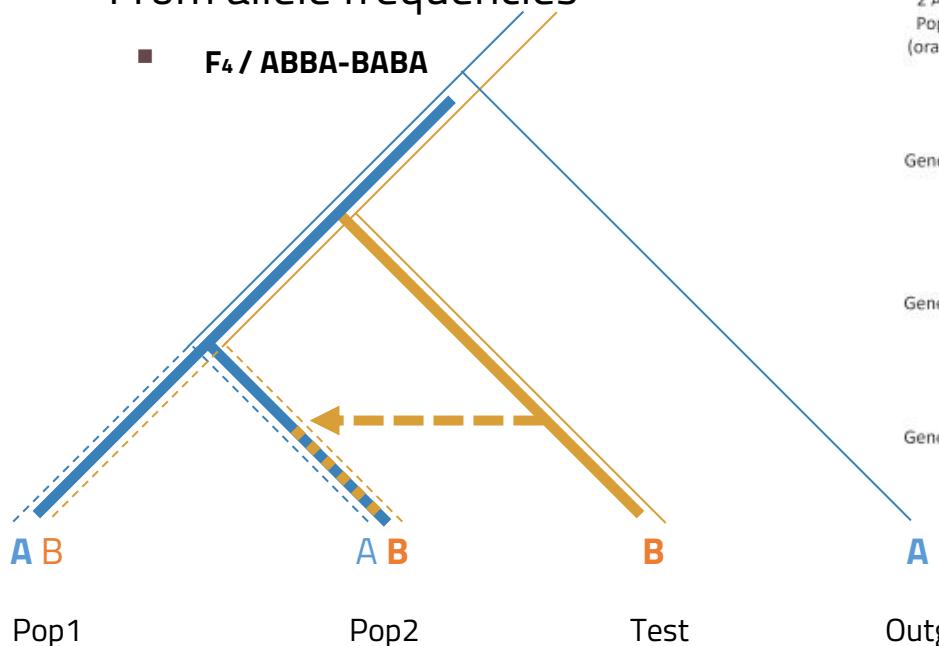


Population

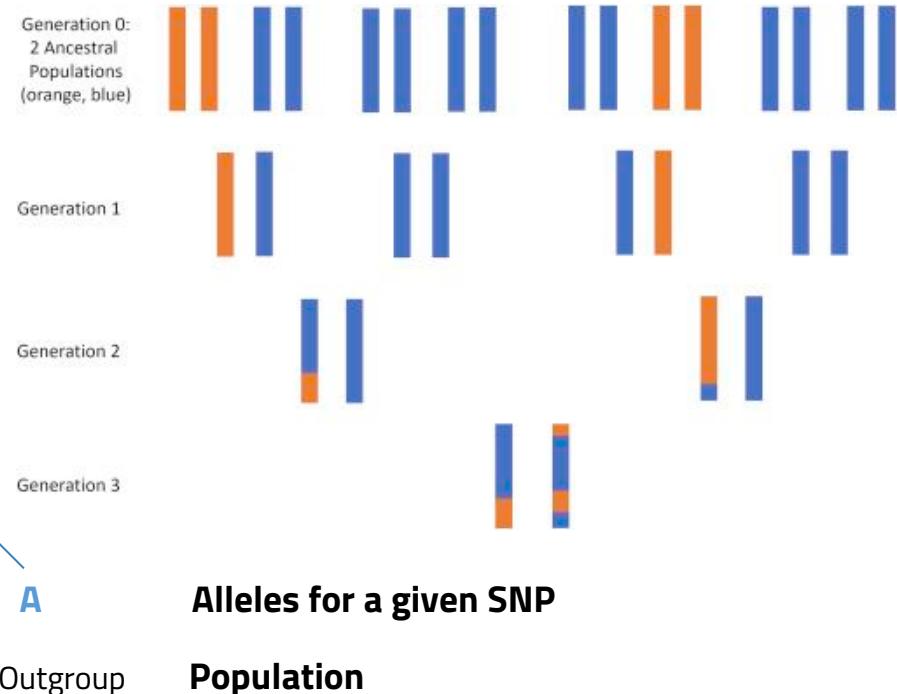
Inference of admixture between populations

From allele frequencies

- $F_4 / \text{ABBA-BABA}$



$F_4 > 0$: Admixture in Pop2
 $F_4 < 0$: Admixture in Pop1

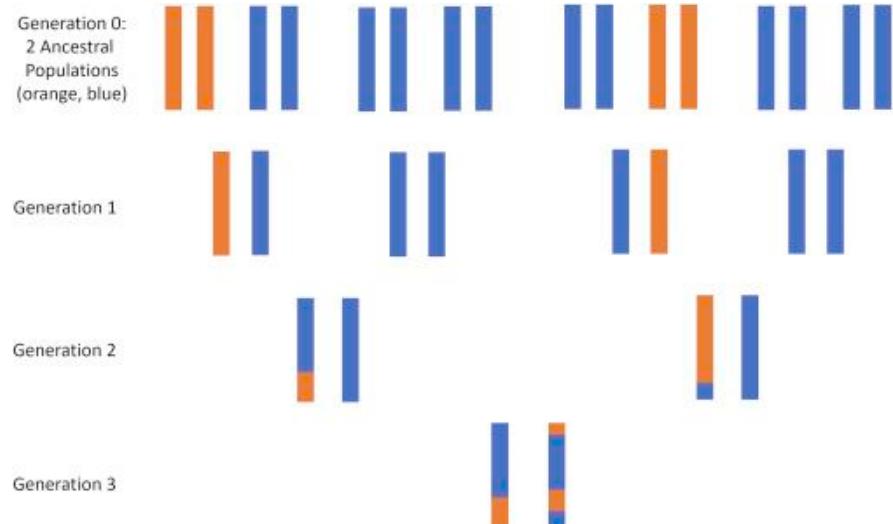
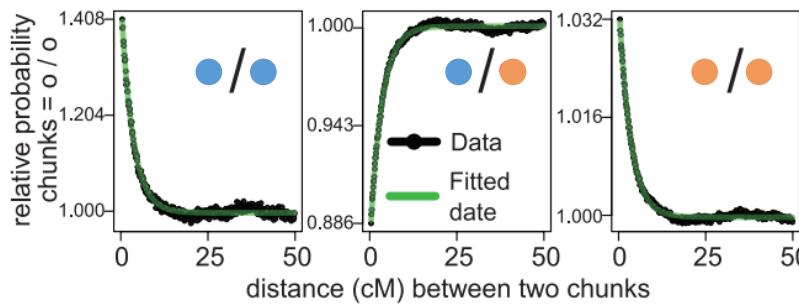


Inference of admixture between populations

From haplotype-based methods

- **Globetrotter**

Hellenthal et al. 2014, Science



Generation 4 Longer fragments, longer distance between fragments



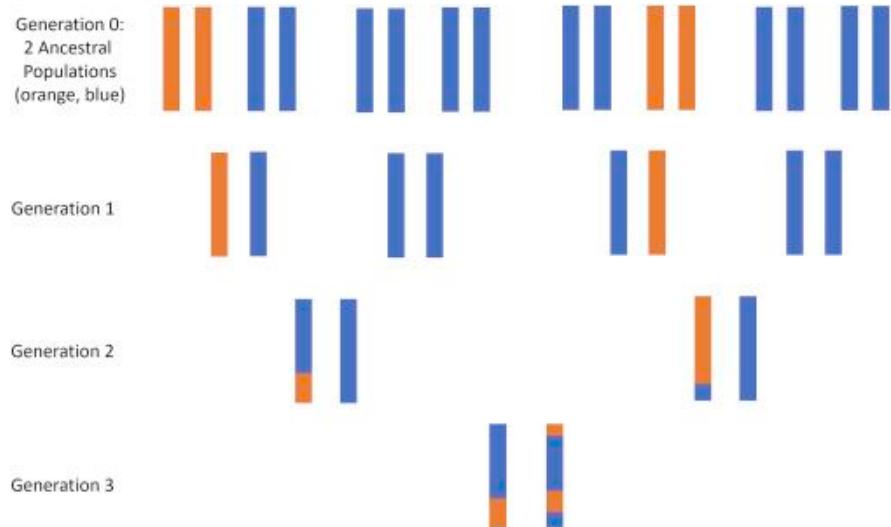
Generation 8 Shorter fragments, shorter distance between fragments



Inference of admixture between populations

- Other methods using similar approaches

- Tracts
 - ▶ Gravel et al. 2012, Genetics
- ALDER
 - ▶ Loh et al. 2013, Genetics



Generation 4 Longer fragments, longer distance between fragments



Generation 8 Shorter fragments, shorter distance between fragments



Human genetic diversity

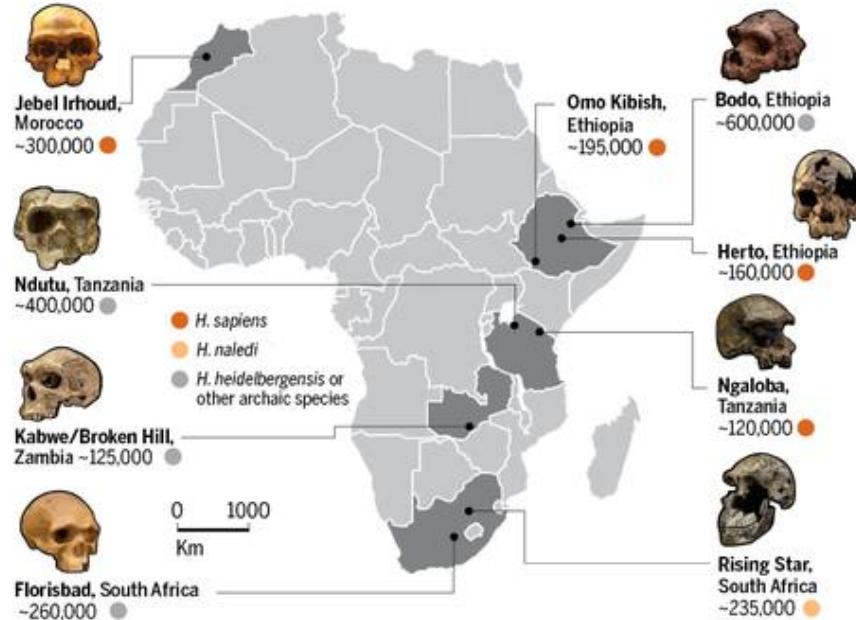
The human genetic history

Human genetic diversity

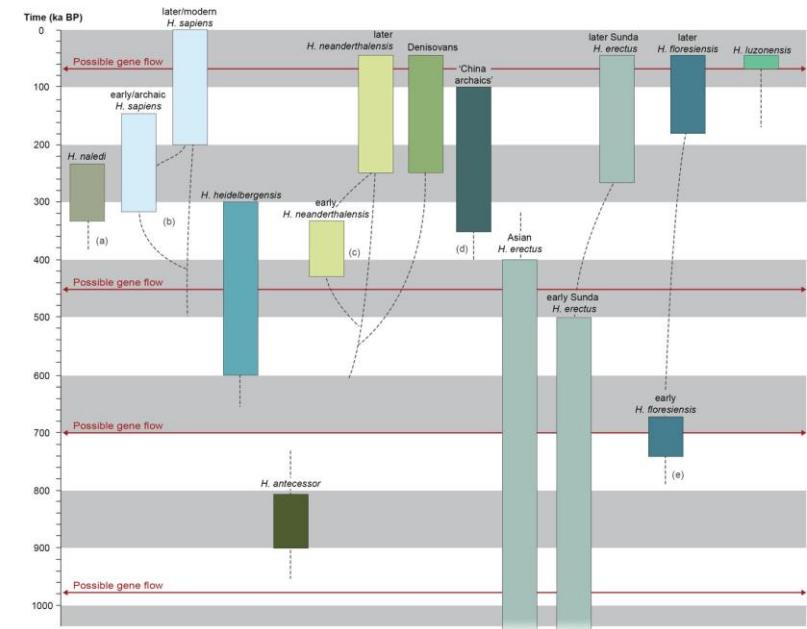
The human genetic history

The African Cradle

The earliest Homo sapiens evidences



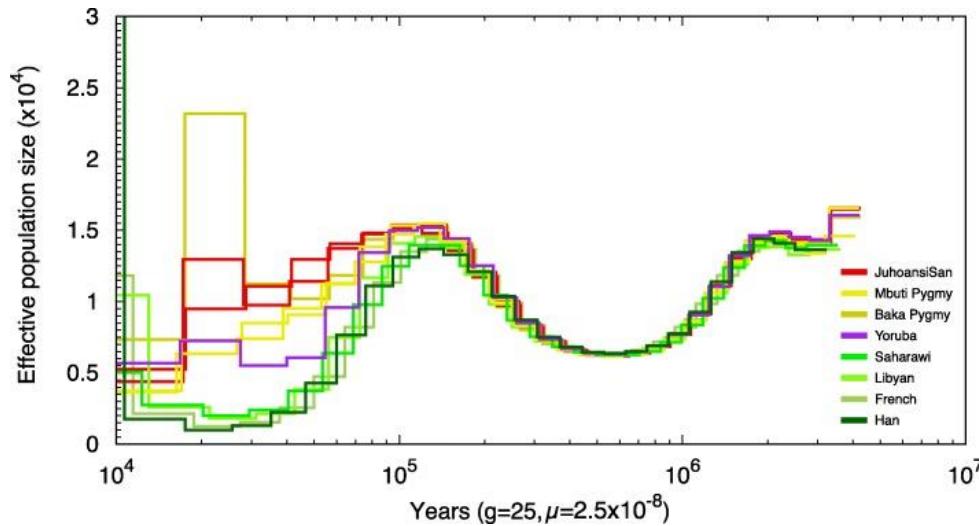
Science, 2017



Galway-Witham et al. 2019, JQS

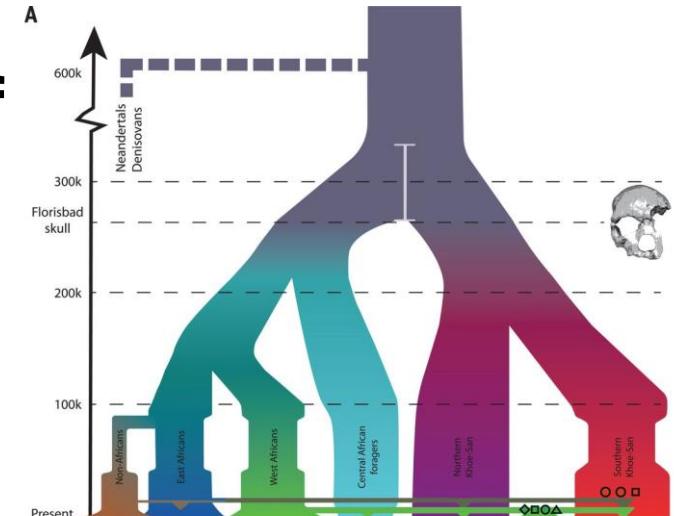
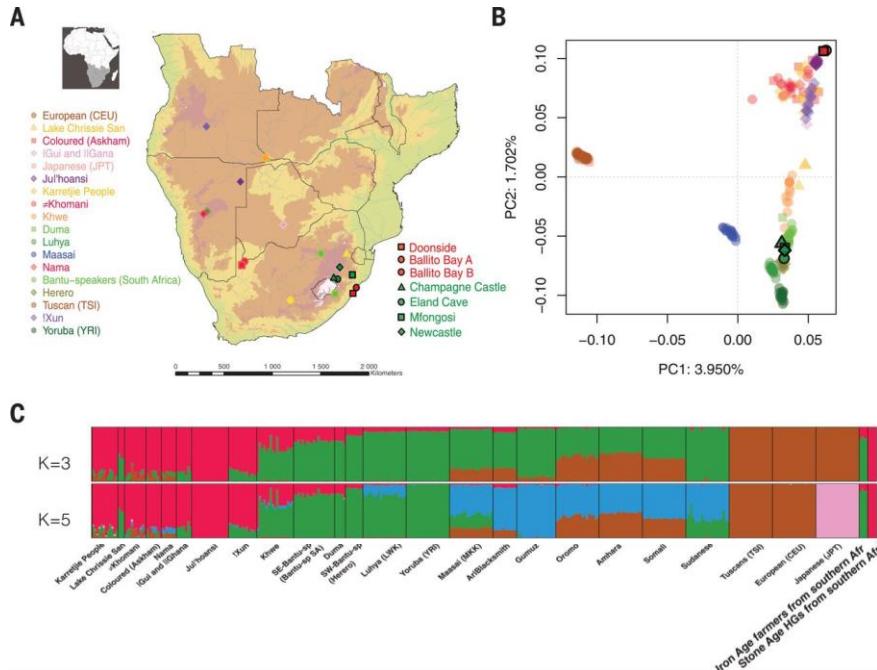
The oldest divergence time of Modern Humans

- Coalescence time between Khoe San and other human populations dates back to **~200.000 years ago**



The oldest divergence time of Modern Humans

- Ancient San-related genomes without Bantu admixture push back divergence to 350 to 260 kya



	Human-Neandertal (Neon-BBAYA)	Human-Neandertal (Near-San)	Human-Neandertal (Near-Dinka)	Deep Human (Bela-BBAYA)	Deep Human (Bela-San)	Deep Human (Masaai-BBAYA)	Deep Human (Masaai-San)	NKSP-SKSP (San-BBAYA)	Out of AFR (Oimka-Sardinian)
G-PhoCS	545 ± 9	534 ± 8	535 ± 9	336 ± 7	282 ± 7	356 ± 7	298 ± 7	185 ± 6	115 ± 6
TT-method	660 ± 33	639 ± 26	632 ± 28	265 ± 5	255 ± 5	256 ± 6	261 ± 5	156 ± 5	76 ± 6

REPORT

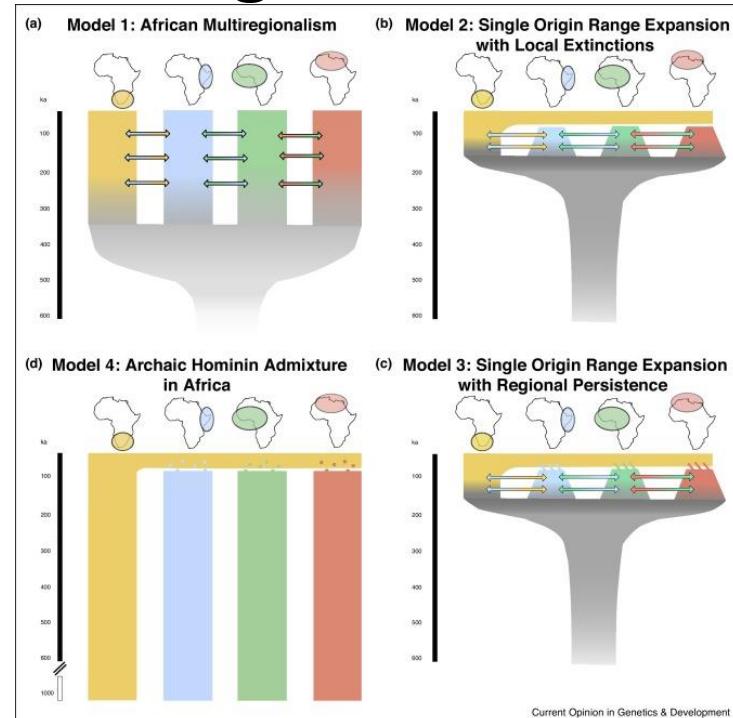
Southern African ancient genomes estimate modern human divergence to 350,000 to 260,000 years ago

Carina M. Schlebusch^{1,4,*}, Helena Malmström^{1,4,*}, Torsten Günther¹, Per Sjödin¹, Alexandra Coutinho¹, Hanna Edlund¹, Ariel...

* See all authors and affiliations

The multiregionalism hypothesis for Modern Human origins

- Most recent research points to a multiple population origin of Modern Homo Sapiens.
- Gene flow from other archaic Homo sapiens populations and other Homo populations

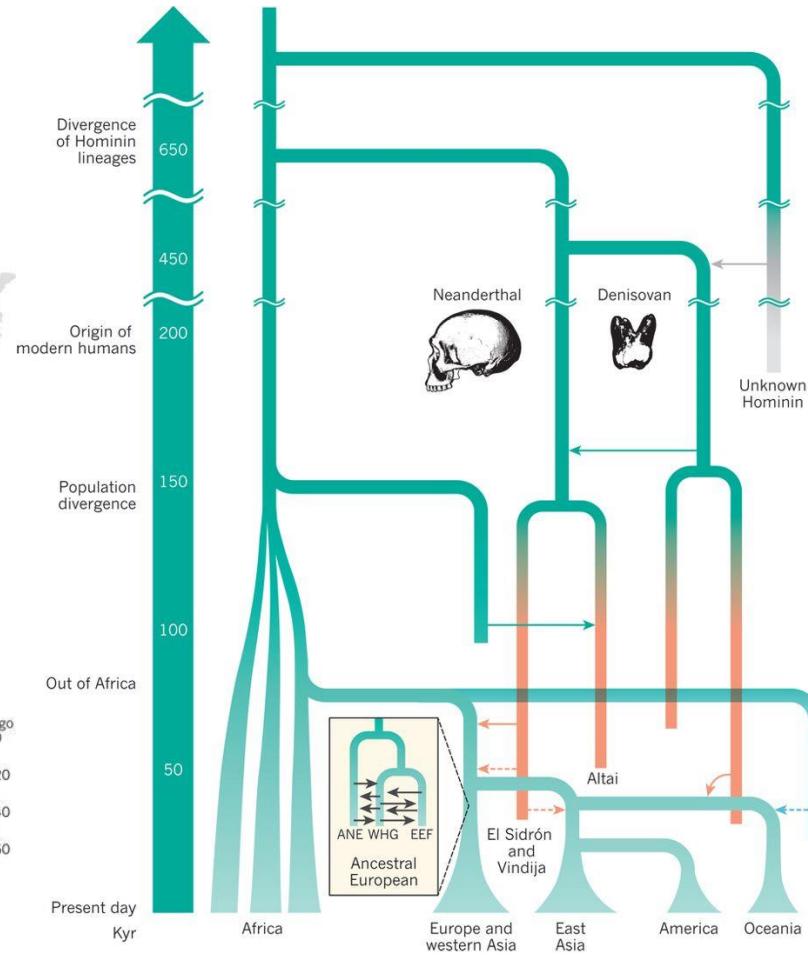
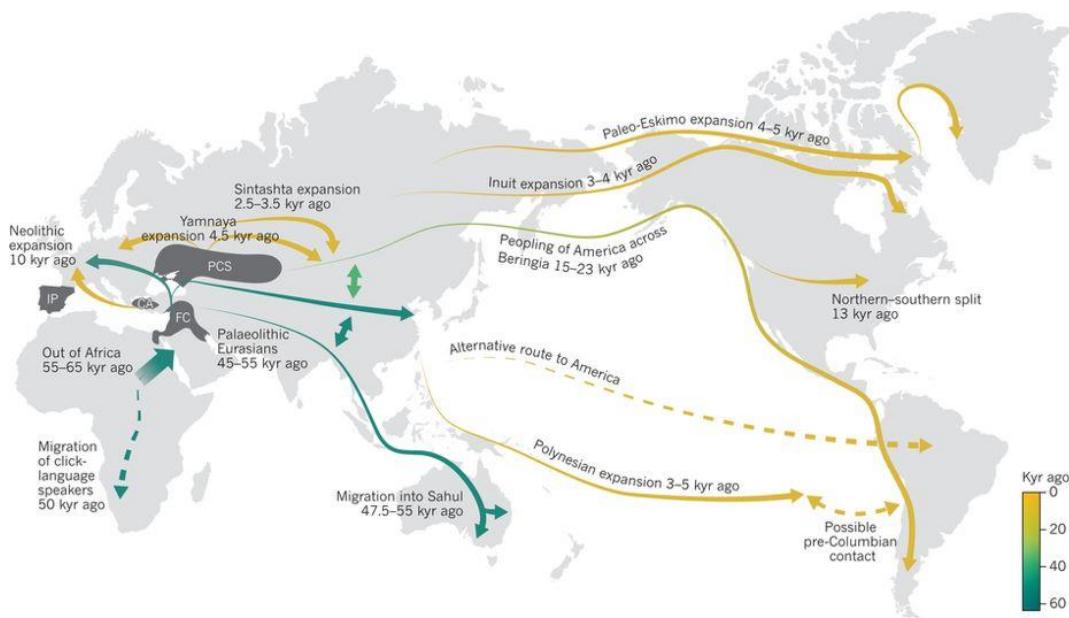


Human genetic diversity

The human genetic history

The Out of Africa and the main human migrations

Out of Africa and main migrations

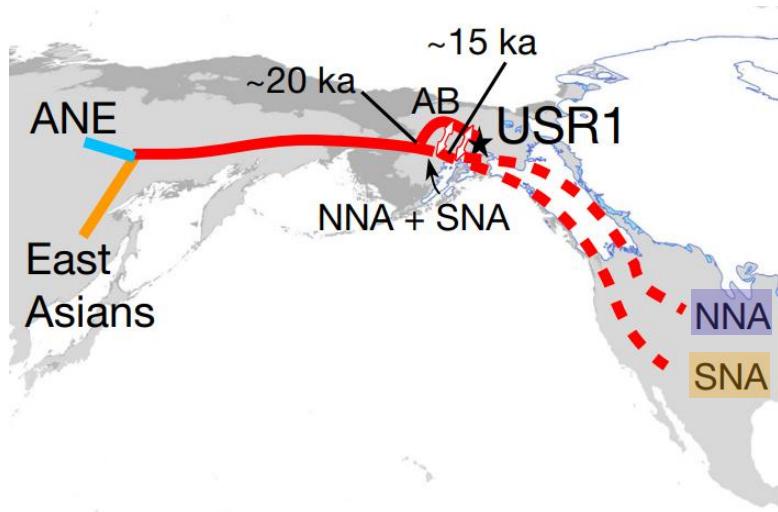


Human genetic diversity

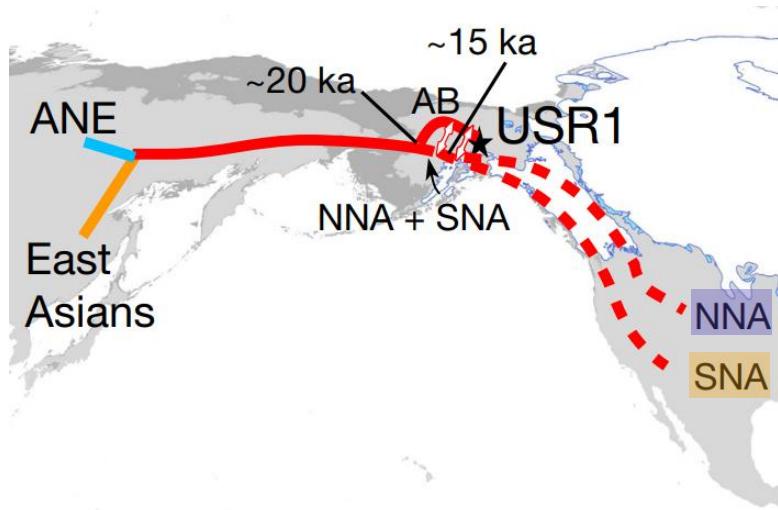
The human genetic history

The peopling of America

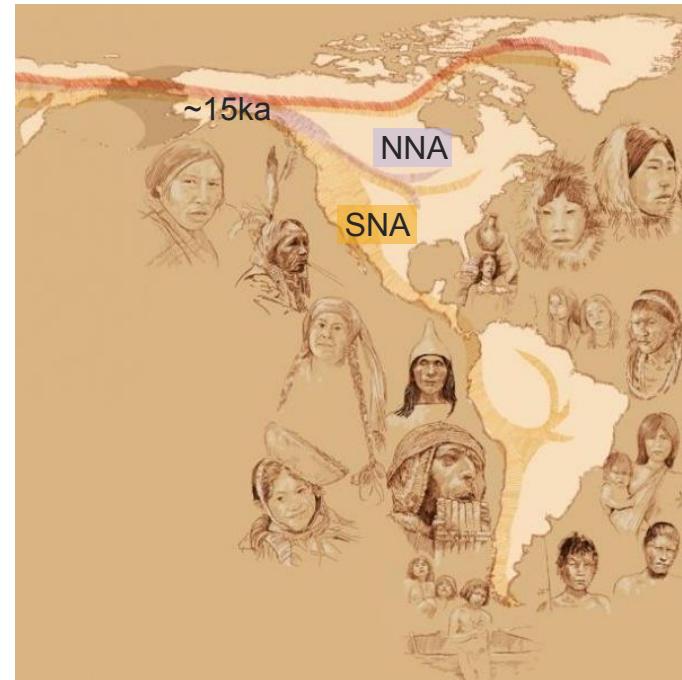
The peopling of America



The peopling of America

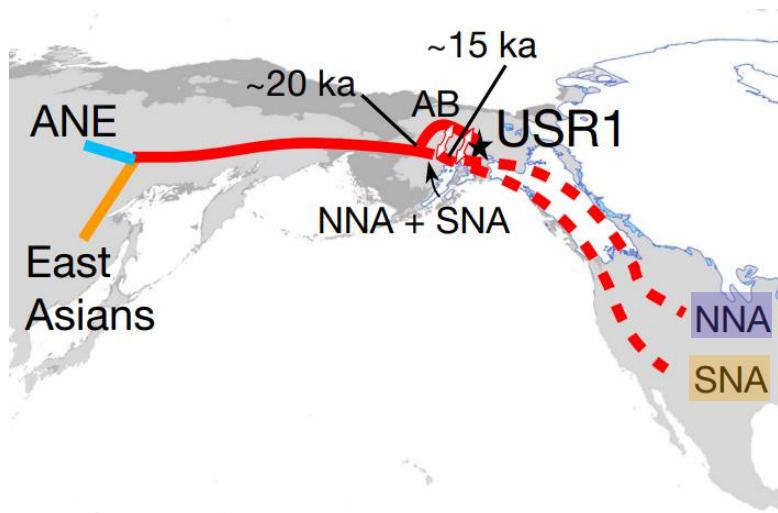


Moreno-Mayar et al. 2018, Nature

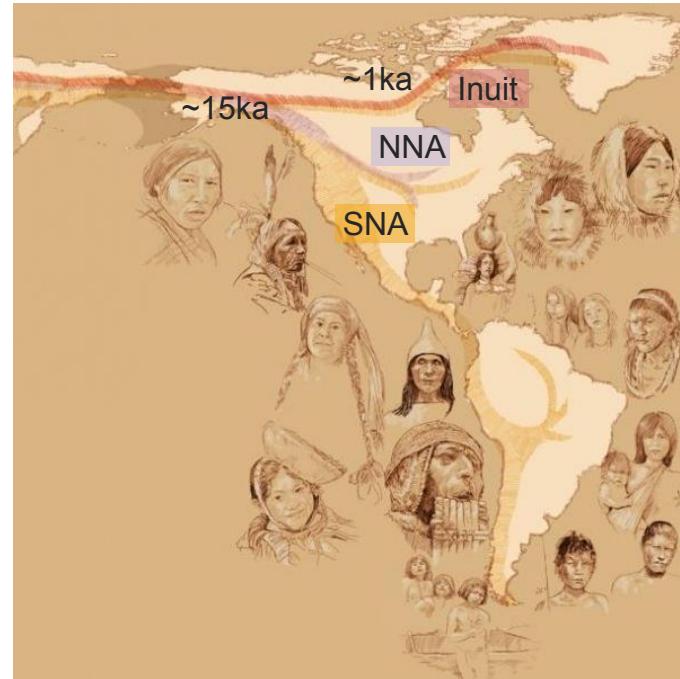


Emiliano Bellini after Reich et al. 2012, Nature

The peopling of America

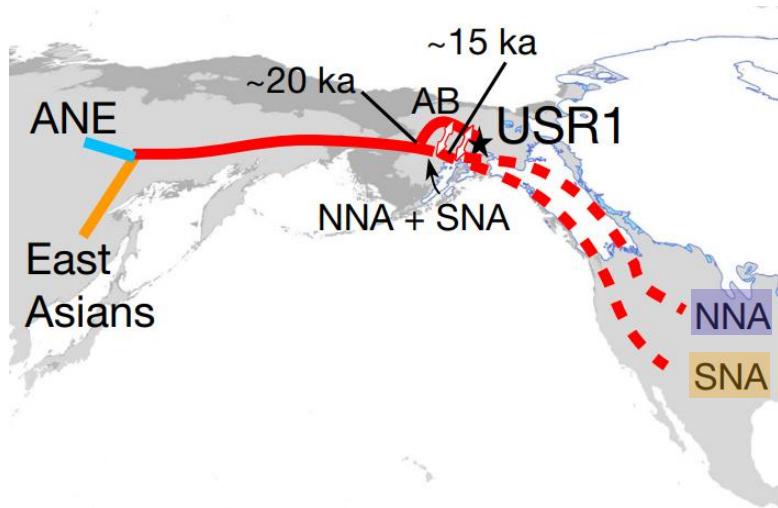


Moreno-Mayar et al. 2018, Nature

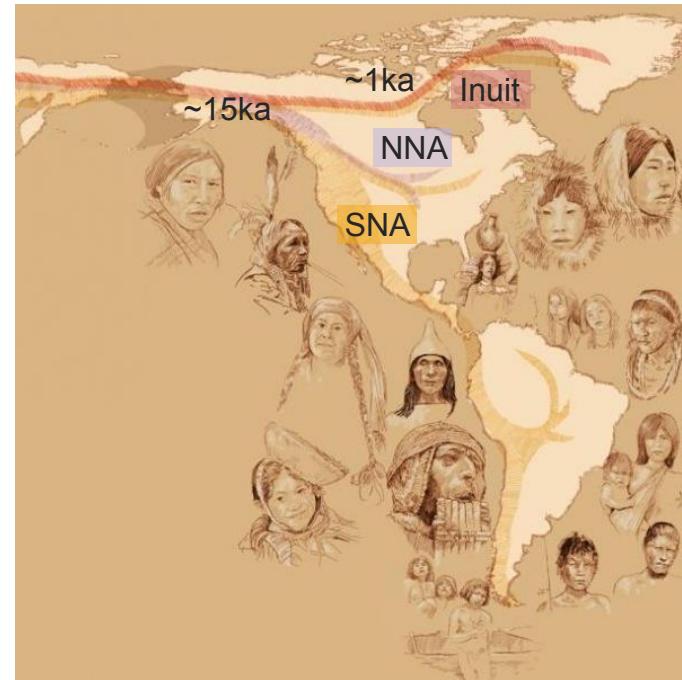


Emiliano Bellini after Reich et al. 2012, Nature

The peopling of America

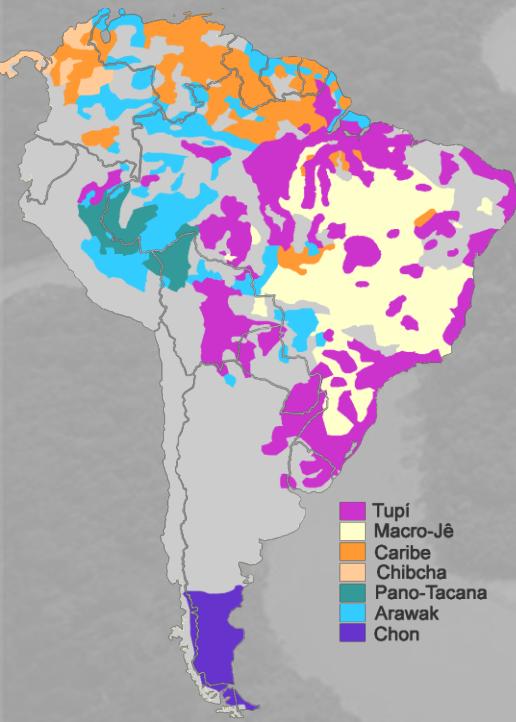


Moreno-Mayar et al. 2018, Nature



Emiliano Bellini after Reich et al. 2012, Nature

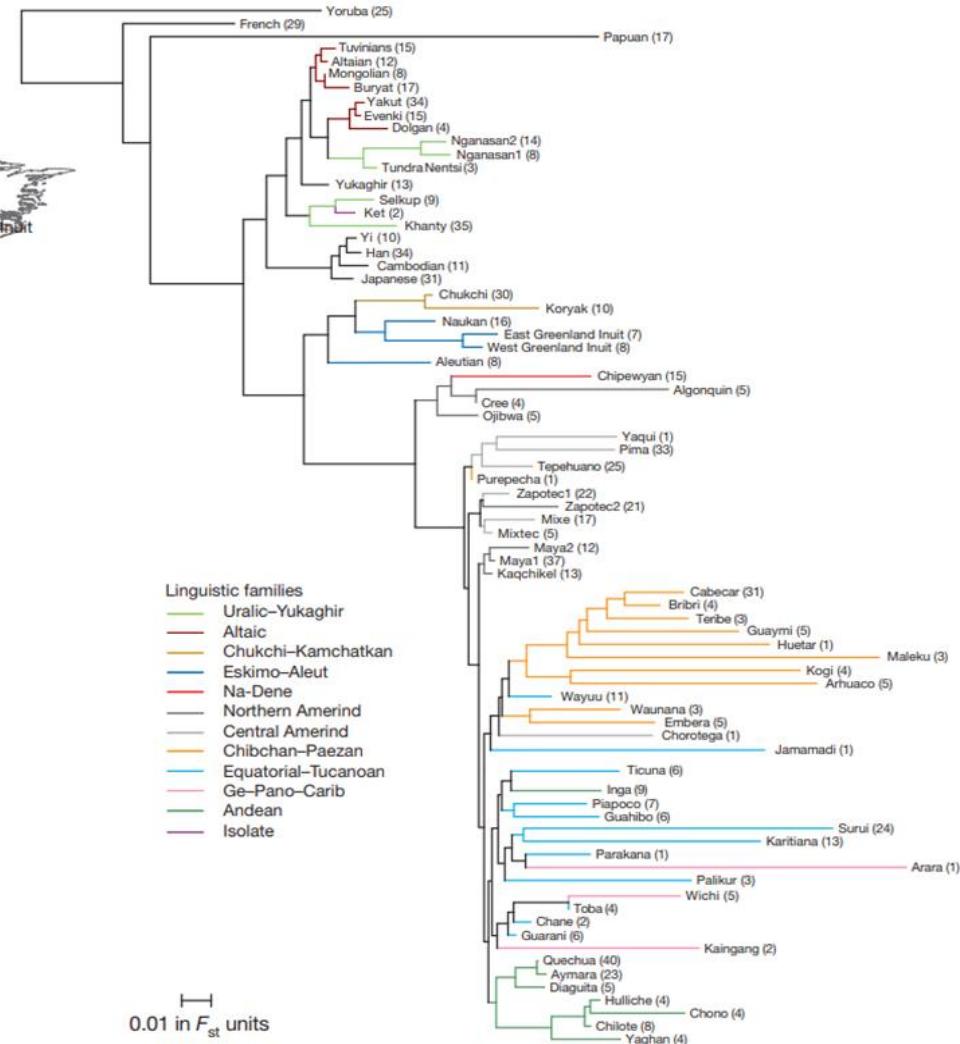
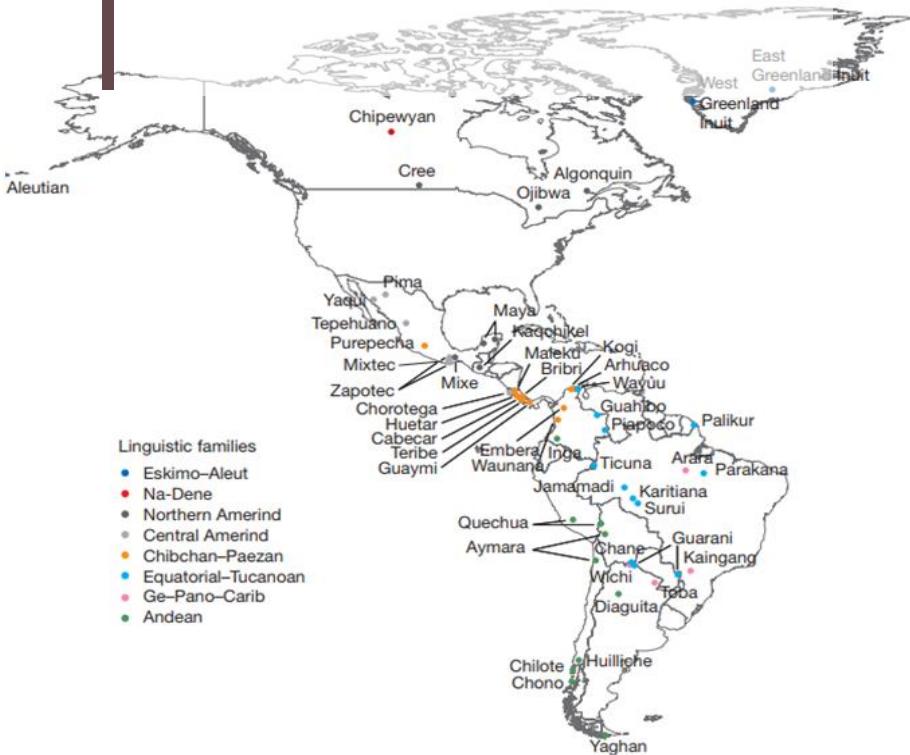
Languages and peoples



~420 languages

~108 families
from which 55 isolate languages

Genetics



The human genetic history

**The European colonization, the Slave Trade
and the admixture history of the Americas**

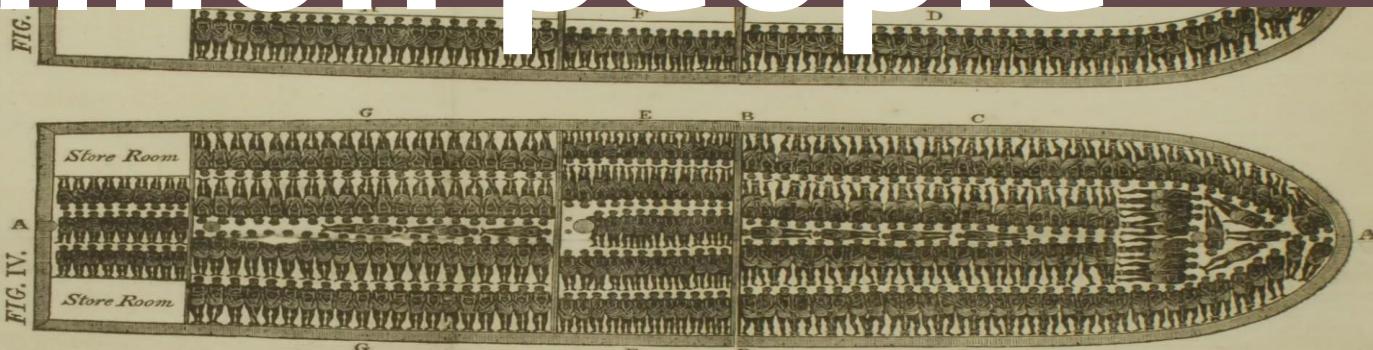
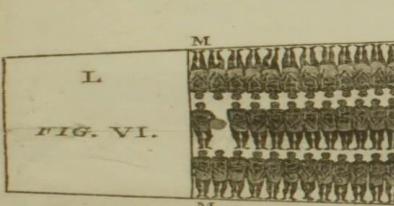
The European Colonization



The Transatlantic slave trade

1500-1850 from sub-Saharan Africa to America

10 million people



The PLAN and SECTIONS annexed exhibit a slave ship with the slaves bowed.* In order to give a representation of the trade against which no country or nation can be brought by any means, the first vessel, the *Brooks*, is here described as that very known in the trade, and the first mentioned in the report delivered to the House of Commons last year by Captain Parker, who sent ten men by Government to take the dimensions of the ships employed in the African slave trade from that port. The plans and sections are on a scale of the 8th of an inch to a foot.

DIMENSIONS OF THE SHIP.
Length of the Lower Deck, gratings and bulk-heads included
Feet Inches
58 0
Width A.A. 15 0
Width B.B. 15 0
Width C.C. 15 0
Width D.D. 15 0
Width E.E. 15 0
Width F.F. 15 0
Width G.G. 15 0
Width H.H. 15 0
Width I.I. 15 0
Width J.J. 15 0
Width K.K. 15 0
Width L.L. 15 0
Width M.M. 15 0
Width N.N. 15 0

With this allowance of room the utmost number that can be stowed in a vessel of the dimension of the *Brooks*, is as follows, (being the number exhibited in the plan) and is $\frac{1}{2}$ to a ton, viz. †

	On the Plants	Abruptly carried.
Men—on the lower deck, at CC	124	190
Ditto—on the platform of ditto, CC DD	66	351
Men—lower deck, EE	58	82
Ditto—ditto, FF	52	90
Women—lower deck, GG	83	
Ditto—platform, HH	40	
Women Hall, II, MM	36	
Platform ditto, NN	24	127

It may be expected, from this mode of packing a number of our fellow-creatures, used in their own country to a life of ease, and from the confinement and misery their situation must necessarily create, that many of them fall sick and die. Infants, especially, are not hardy, and the decks were so covered with the blood and mucus which had proceeded from those who had been unable to bear the heat, that the young ones perished. The average is not less than 1-5th, or 20 per cent. The half deck is sometimes appropriated for a sick-birth; but the men slaves are seldom indulged the privilege of lying down there, unless they are dead. The slaves are never allowed the least bedding, either tick or well; but are floated on the floor, and on the deck, the floor being bound up, from the friction of which, occasioned by the motion of the ship, they were rubbed upon the deck, where numbers of them died, and some were buried in the deck itself.**

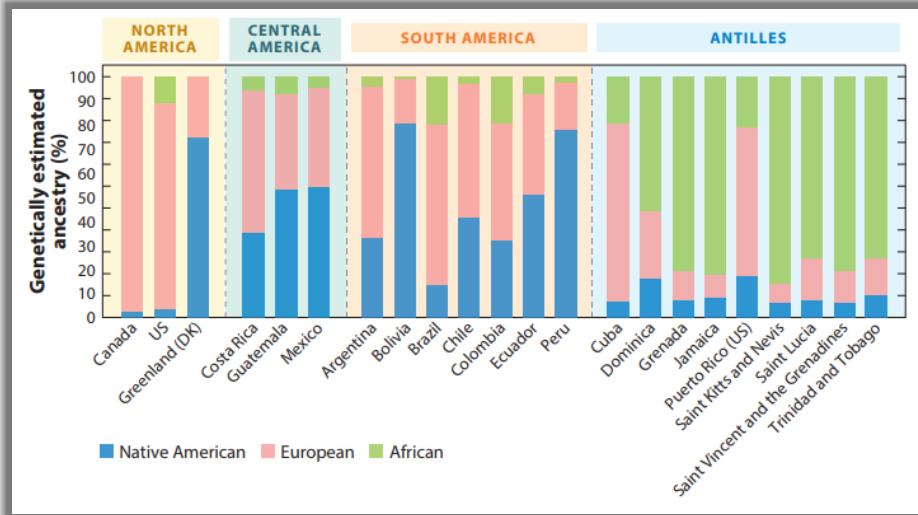
It may not be improper to add a short account of the mode of securing

apertures, because so extremely hot, as to be only sufferable for a very short time. But the excessive heat was not the only misery their masters' situation intolerable. The decks, that is, the floor of their rooms, was to be covered with the blood and mucus which had proceeded from those in confinement, the floor being rendered quite unfit to walk upon. It is not in the power of the human imagination to conceive how such a situation more dreadful or disgusting. Numbers of the slaves had, and still have, their feet bound, from the friction of which, occasioned by the motion of the ship, they were rubbed upon the deck, where several of them died, and some were buried in the deck itself.**

The objection which may be started, is, that here no room is allowed for the fakirs' hammocks. In Slave ships, where the floor

The admixture history of the Americas

Genome-wide ancestry



Adhikari et al. 2017, Annu. Rev. Genom. Hum. Genet;

The admixture history of the Americas

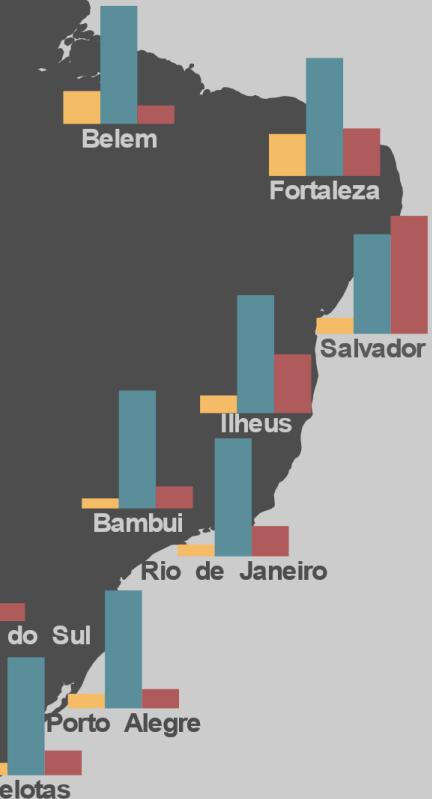
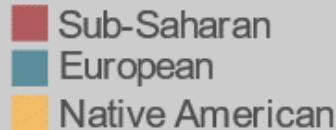
Genome-wide ancestry



Adhikari et al. 2017, Annu. Rev. Genom. Hum. Genet;

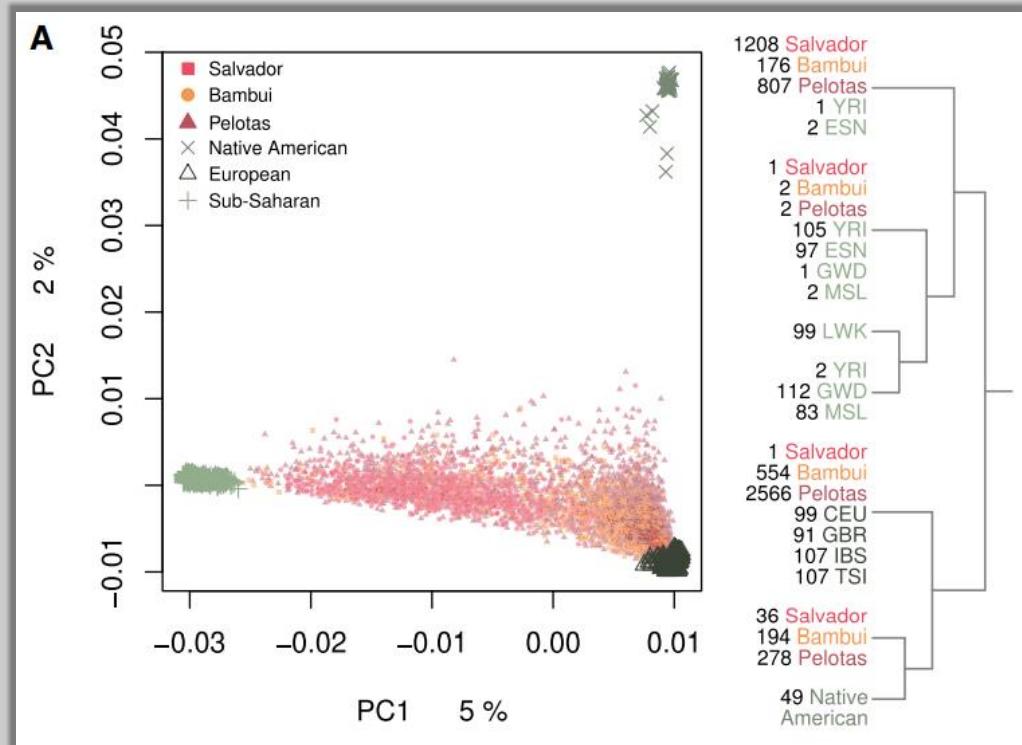
The admixture history of the Americas

Genome-wide ancestry



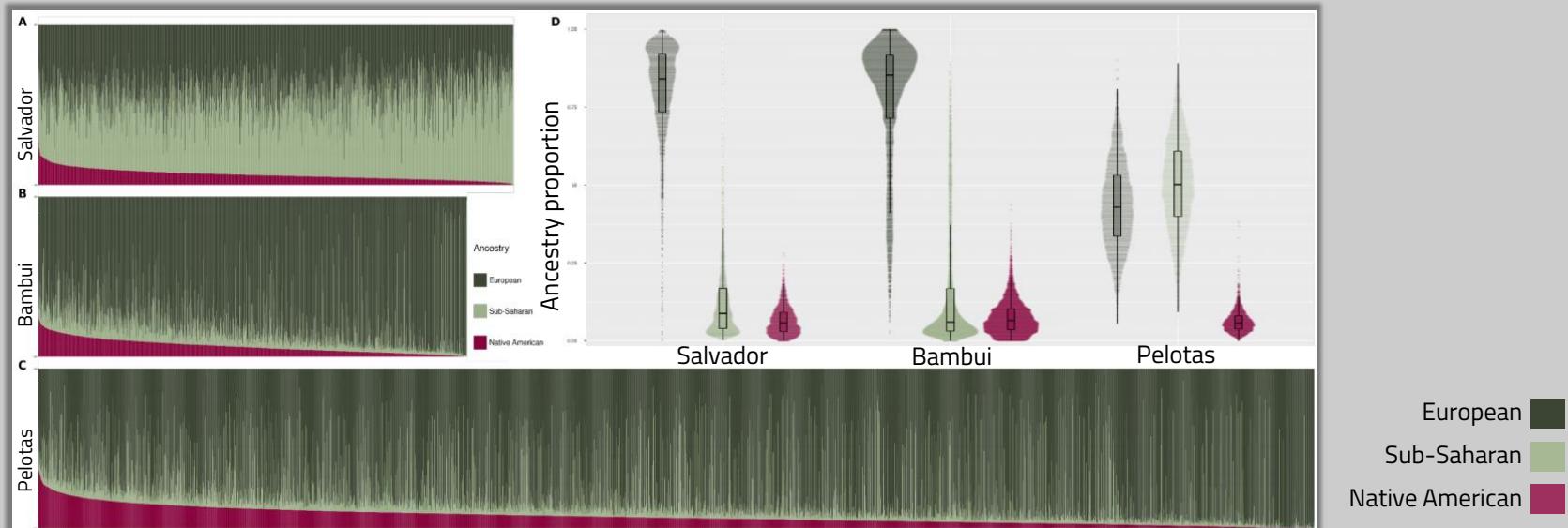
The admixture history of the Americas

Genome-wide ancestry



The admixture history of the Americas

- The distributions of ancestry proportions are very different between admixing American populations, even between cities of the same country, like in Brazil



The admixture history of the Americas

| Complex admixture process in progress shaped by social stratification

| Social stratification correlated with ancestry and influenced by gender

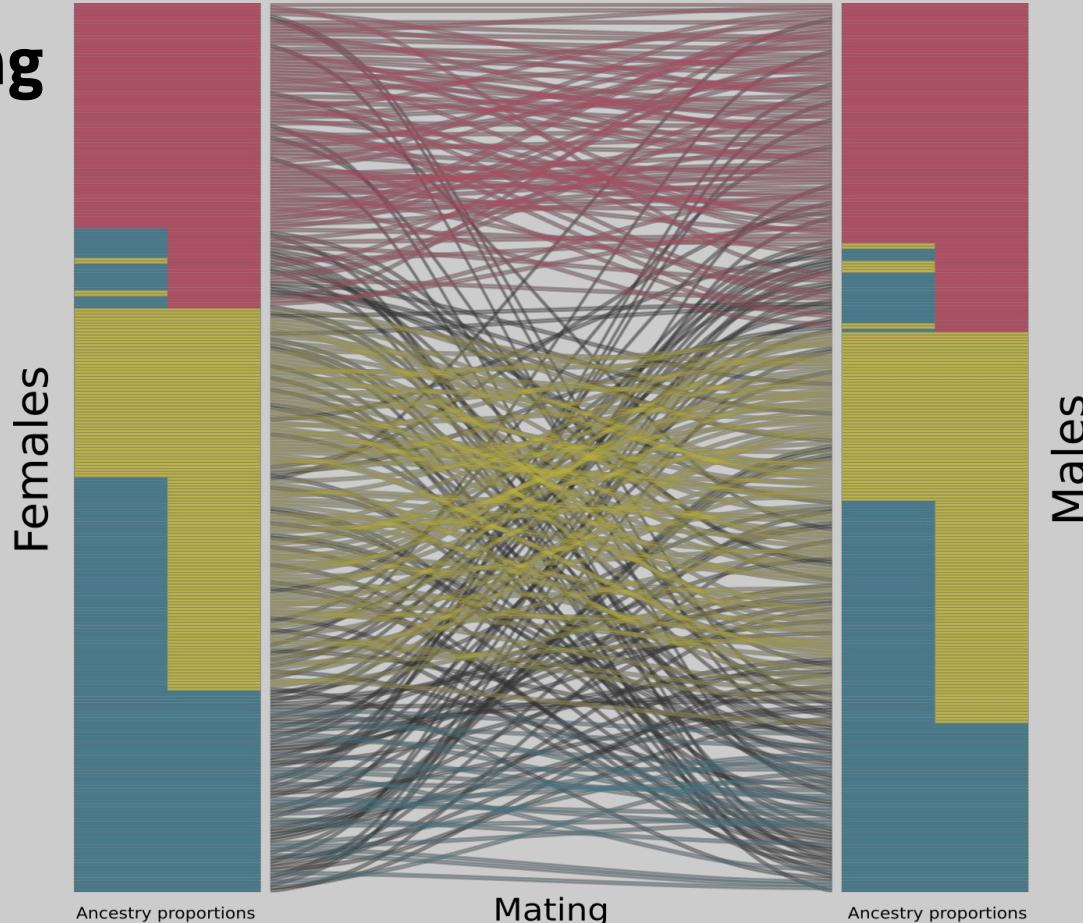
| Ancestry-related assortative mating

| Ancestry-related sex bias



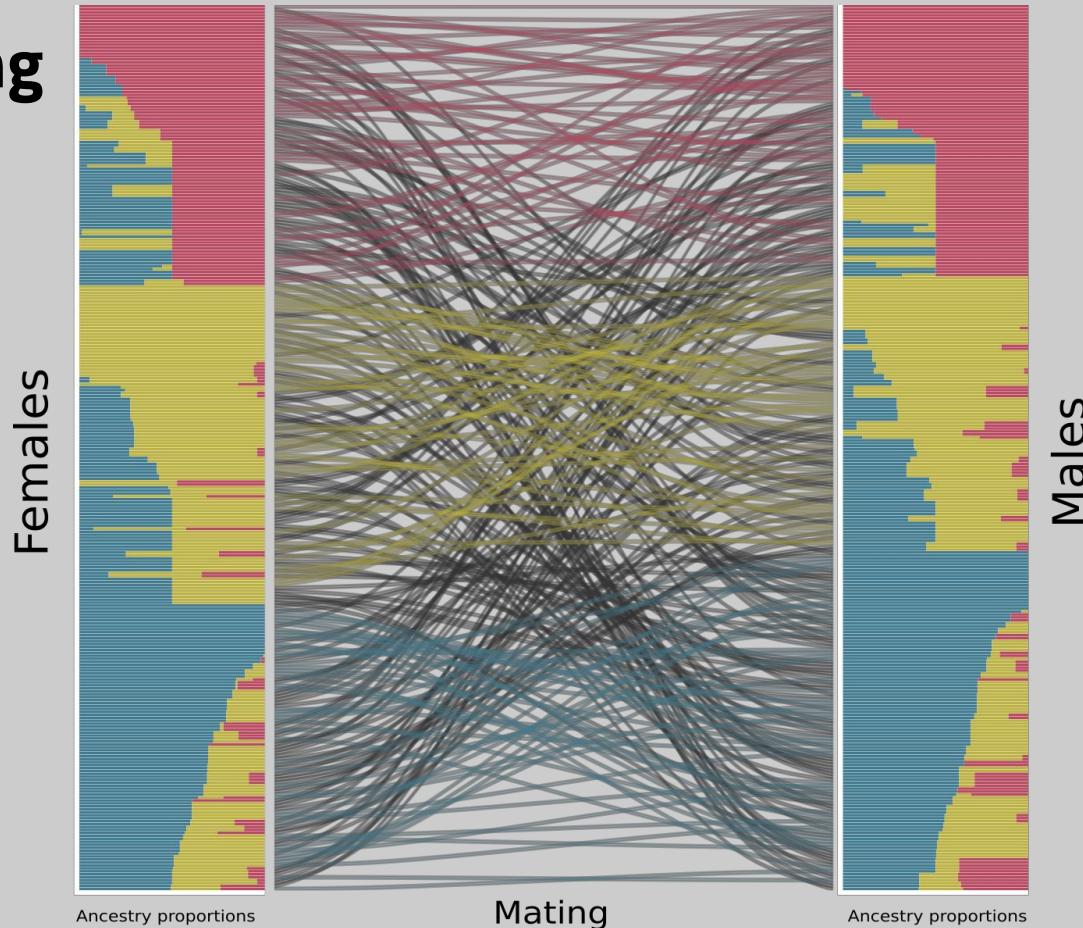
Assortative Mating

- Generation = 4



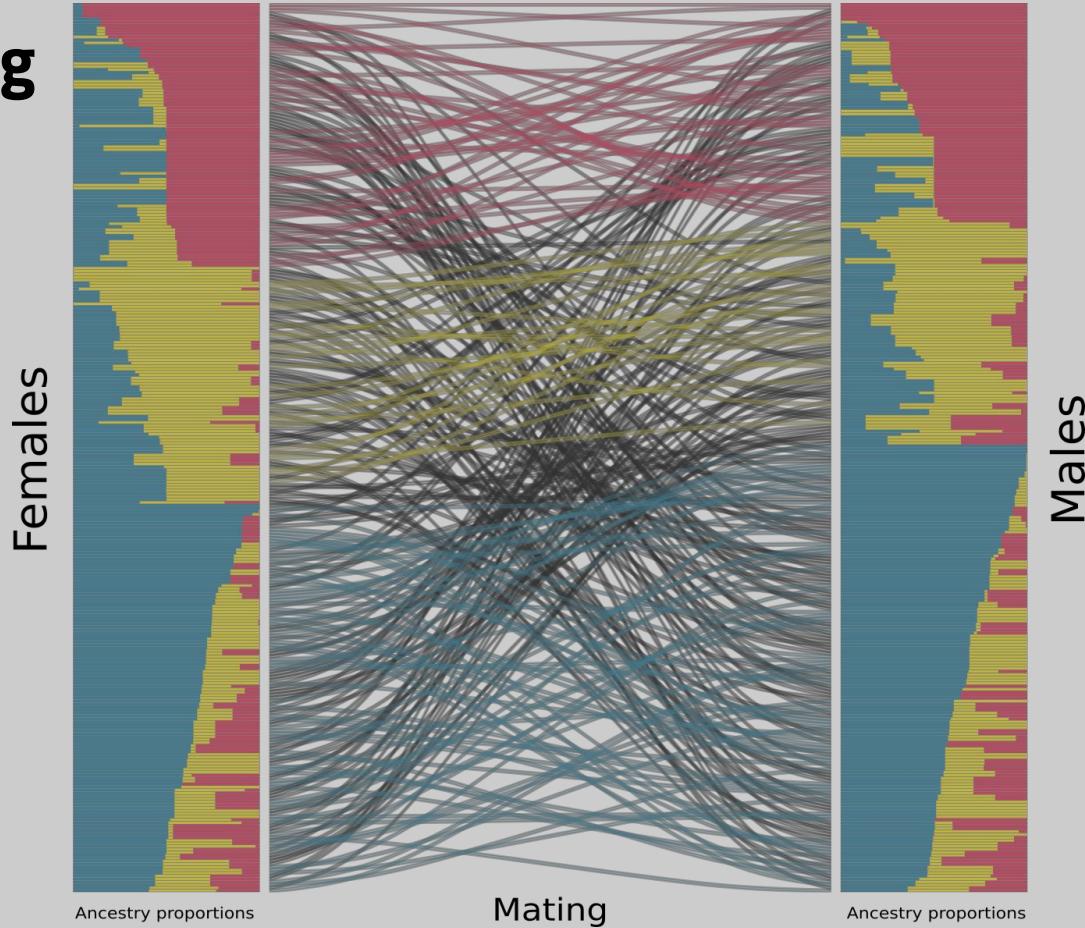
Assortative Mating

- Generation = 8



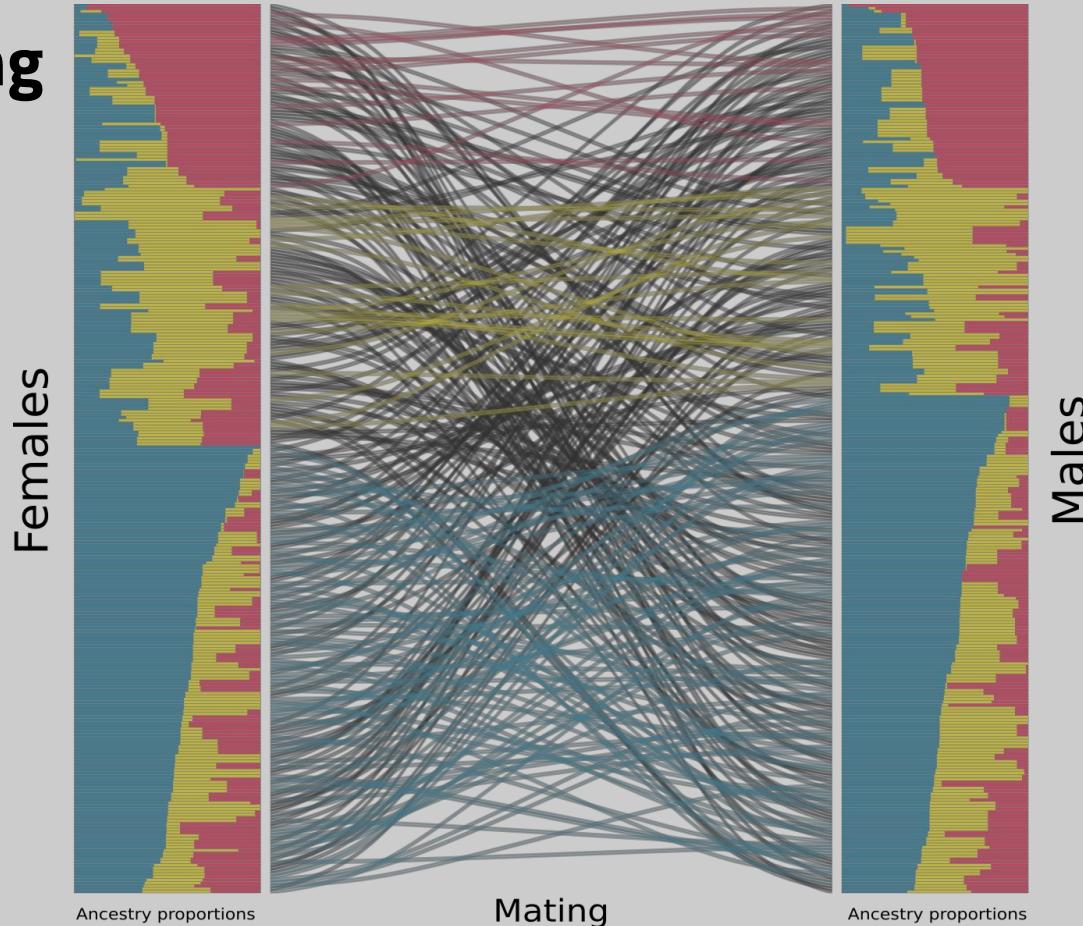
Assortative Mating

- Generation = 12



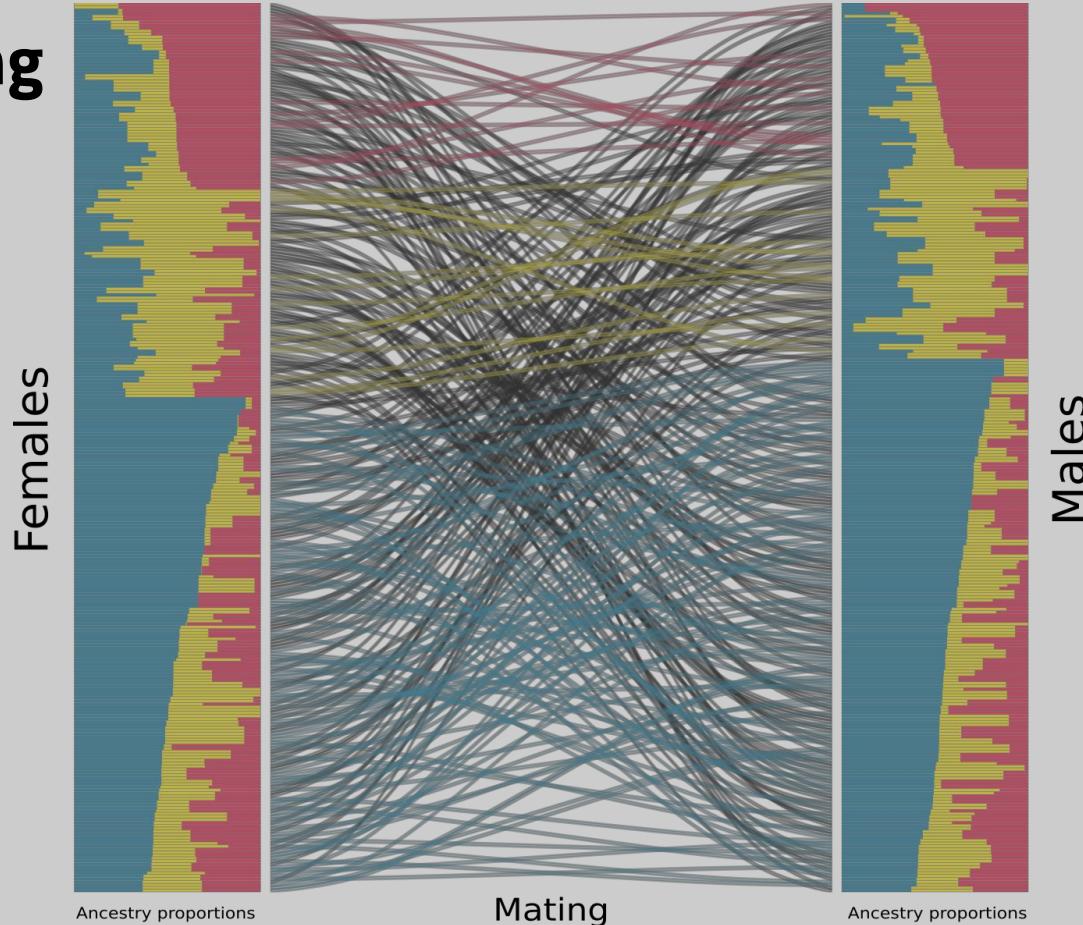
Assortative Mating

- Generation = 16



Assortative Mating

- Generation = 20



**Imperial College
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