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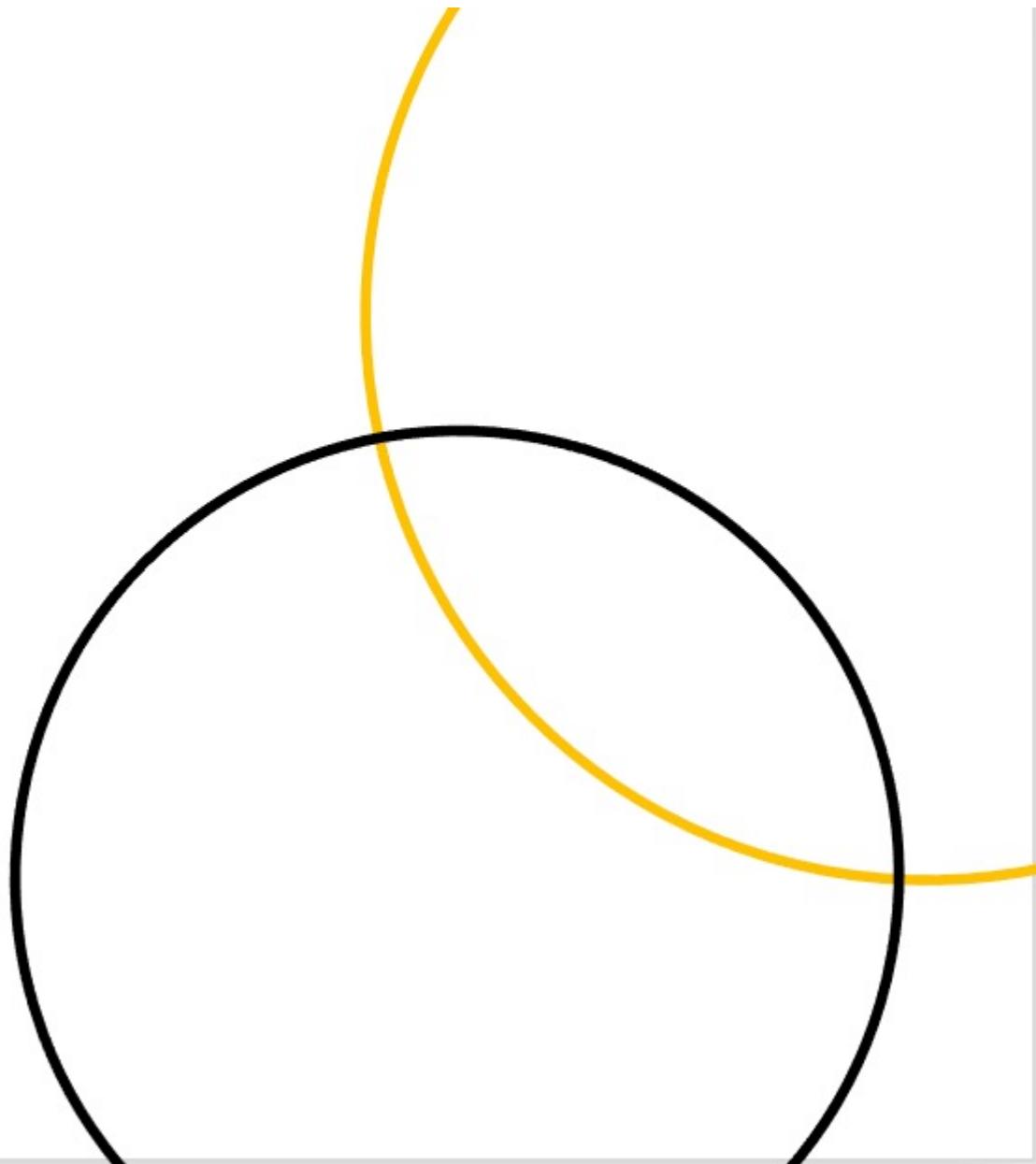
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AFRICAN
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IN BIOINFORMATICS
& DATA INTENSIVE SCIENCES

Dr Conrad Iyegbe
Instructor
Introduction to Admixture

June 2025



Lecture outline

Admixture definition

What is admixture?

Factors affecting admixture

Applications of admixture and popular tools

Preview of topic practical



Admixture

Admixture occurs when individuals from two or more isolated populations mix and produce offspring.

Recombination shuffles ancestral DNA blocks over successive generations resulting in new allele combinations.

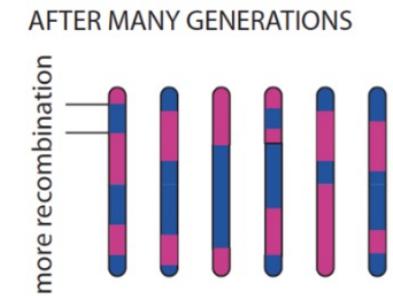
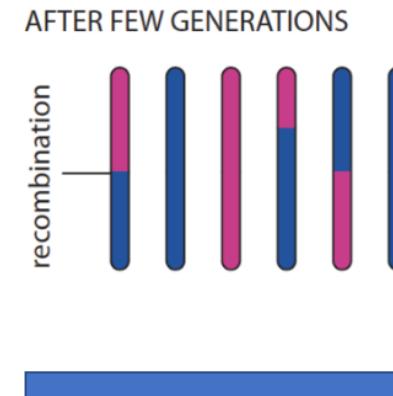
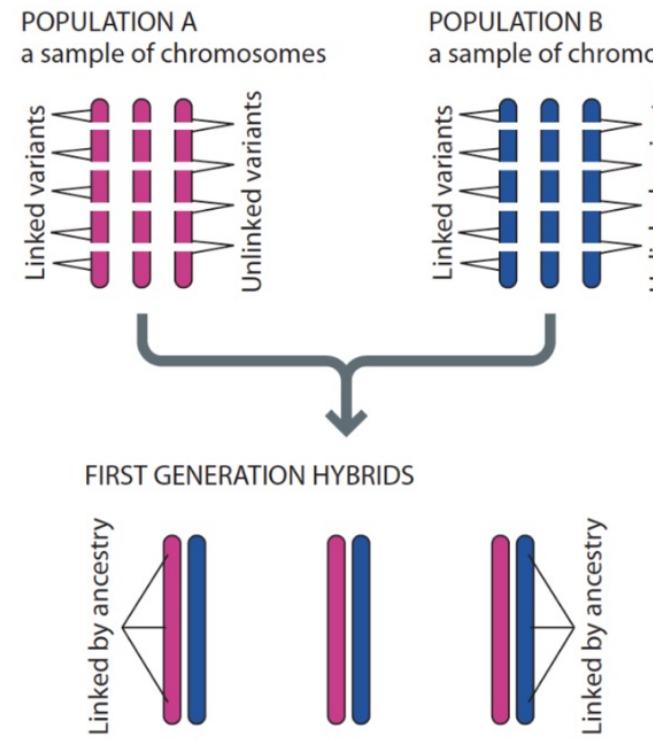
Admixture increases genetic diversity by bringing together novel combinations of variants.

Admixture definition

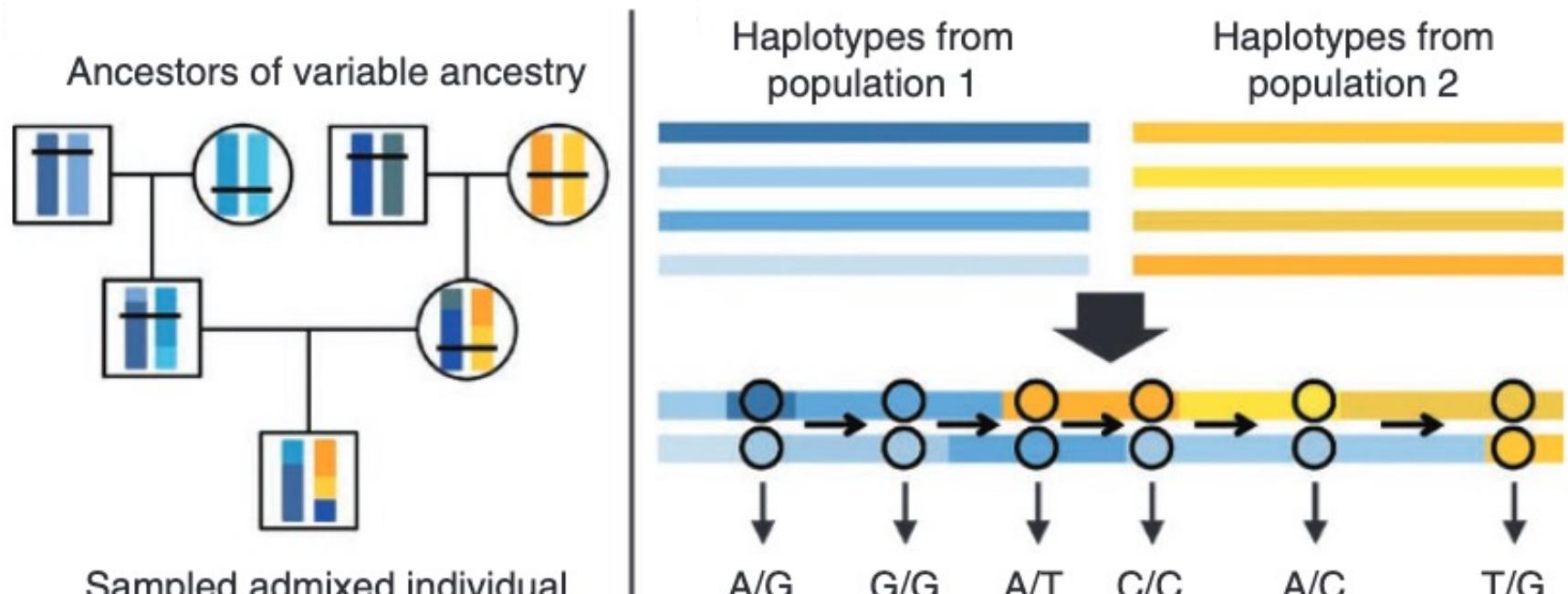
Genome-wide studies and PRS research has historically been slow to respond to the needs of this large and important global constituency.

But dedicated methodologies and frameworks are now beginning to emerge.

What is admixture? A schematic



Two-way admixture is the simplest case of admixture



Maples et al, 2013

Recombination shuffles all haplotypes over generations but only cross-ancestry events leave characteristic signatures that can be detected in descendant generations

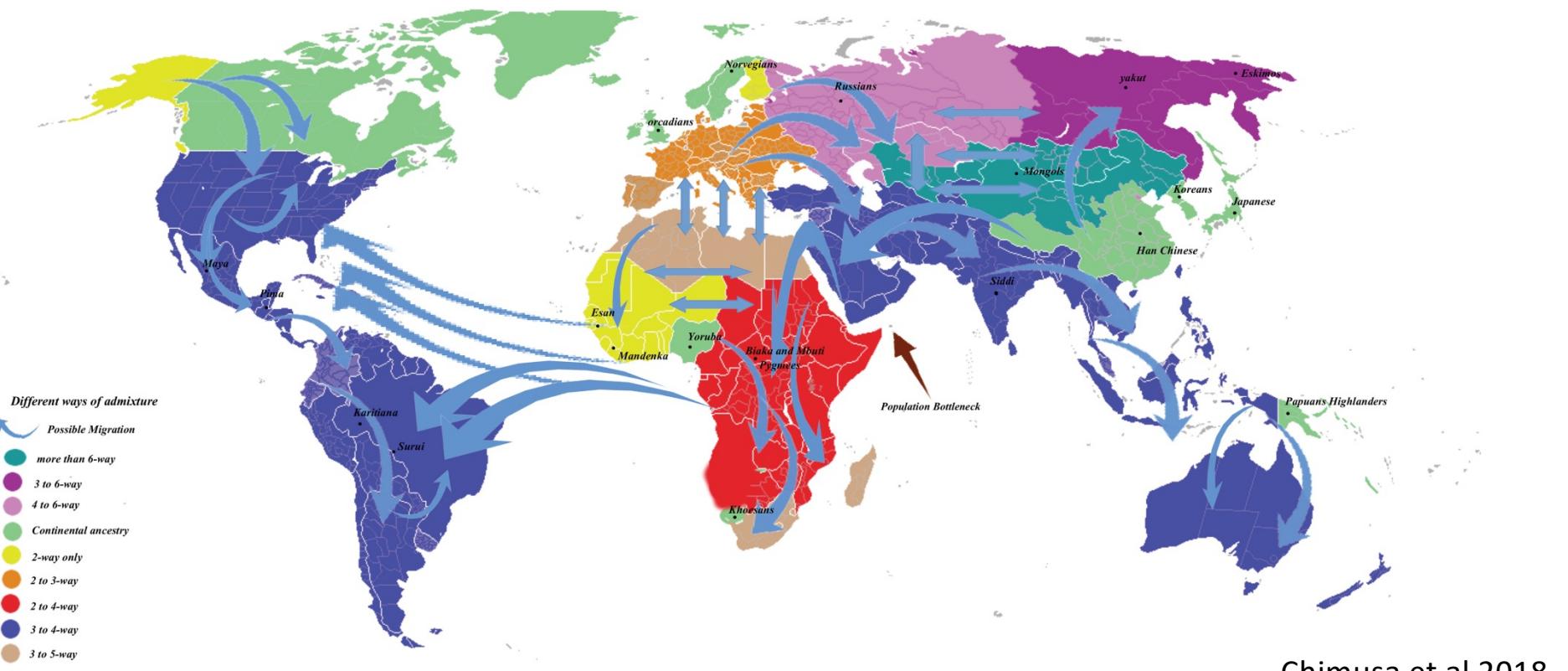
Key Consequences of Genetic Admixture

Formation of Hybrid Genomes: Offspring inherit chromosomes that are mosaics of haplotype blocks from multiple source populations.

Genetic Exchange: Meiotic recombination shuffles and swaps chromosomal segments between parental populations, mixing ancestral DNA in each gamete.

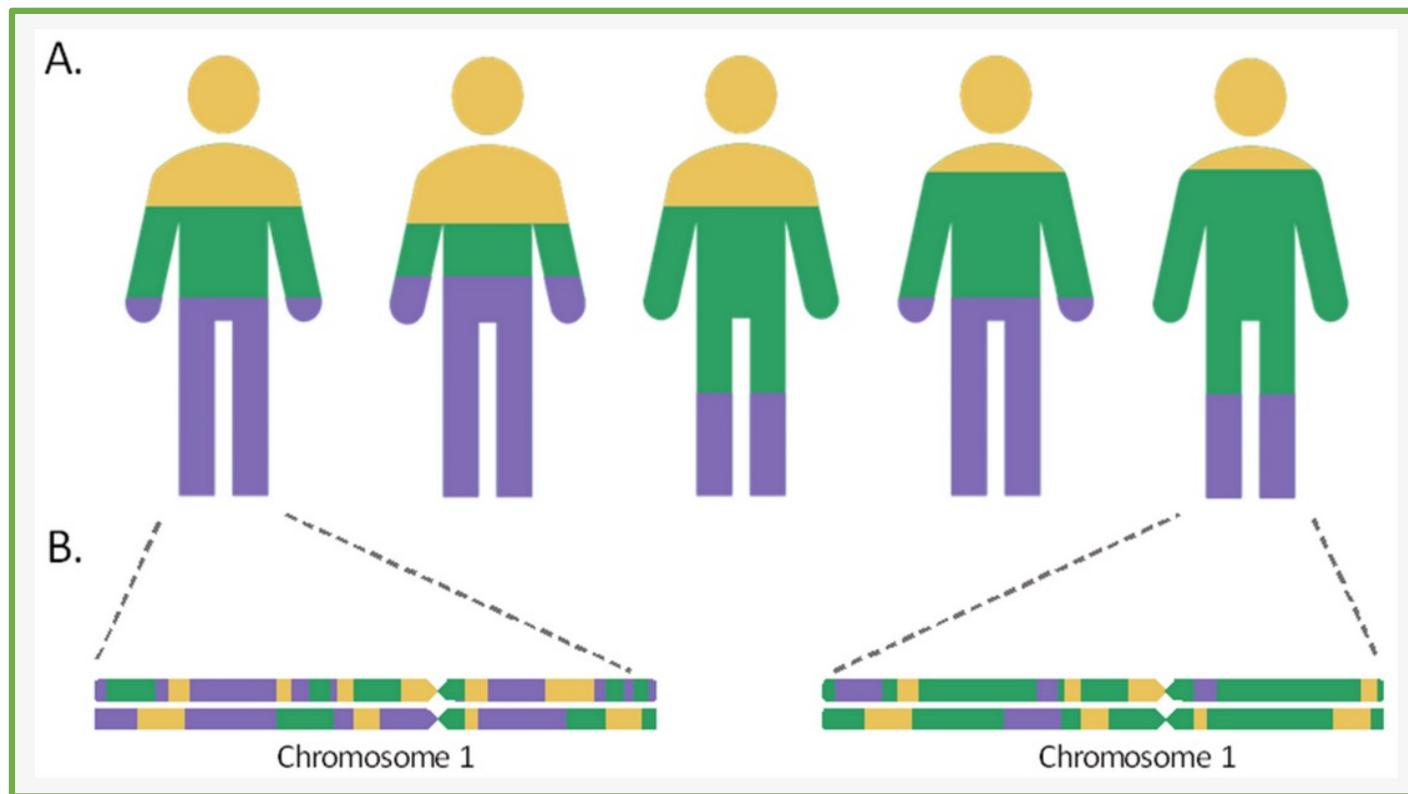
Increased Genetic Diversity: Novel combinations of alleles emerge, enhancing variation that may improve adaptation to environments or resistance to disease.

Historical Gene-Flow and Worldwide Admixture



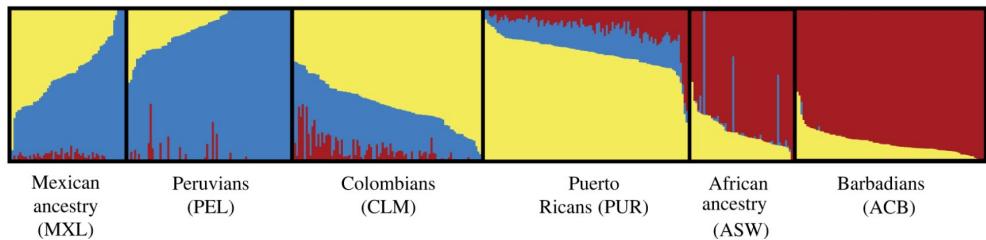
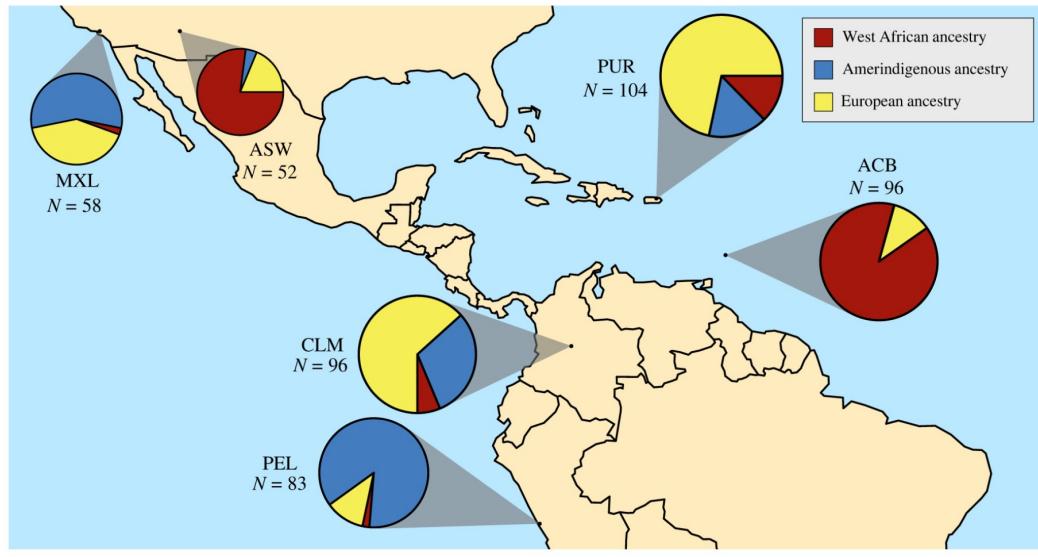
Chimusa et al 2018

Multi-way admixture increases genetic complexity

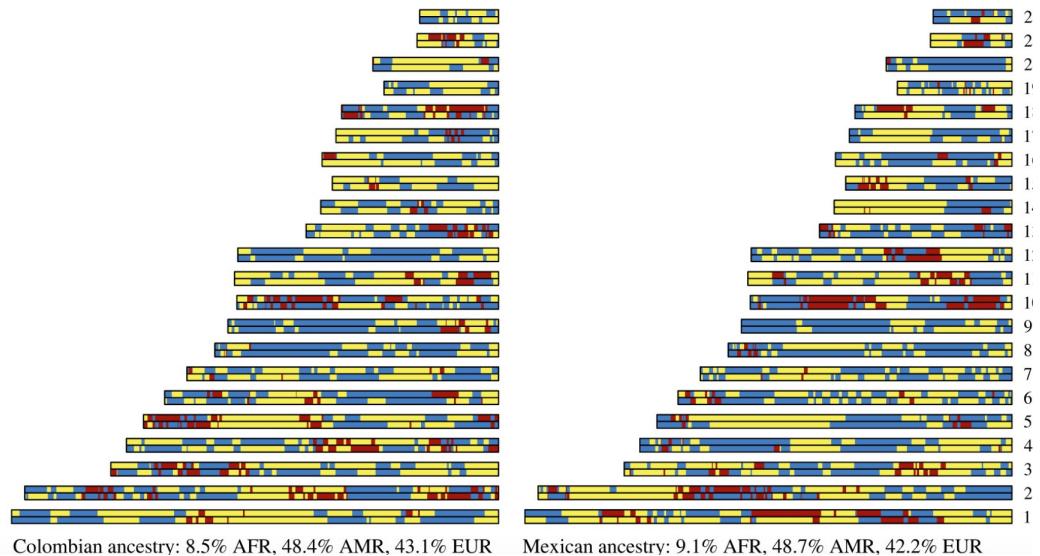


Admixture creates different levels of genetic variability

Continental - level



Locus-level



Individual-level

Auton et al. 2015

Factors influencing admixture

Time (in generations) elapsed since admixture

- Admixture LD decays more rapidly between more distant loci

Admixture model

- Number of mixing events

Effective population size and demographic history

- Bottlenecks, expansions or continuous gene flow after the initial admixture event will reshape the expected decay of ancestry LD

Source population divergence.

- The more genetically distinct your parental groups are, the easier (and more sharply) you can detect ancestry tracts.

What type of information can a standard admixture analysis provide?

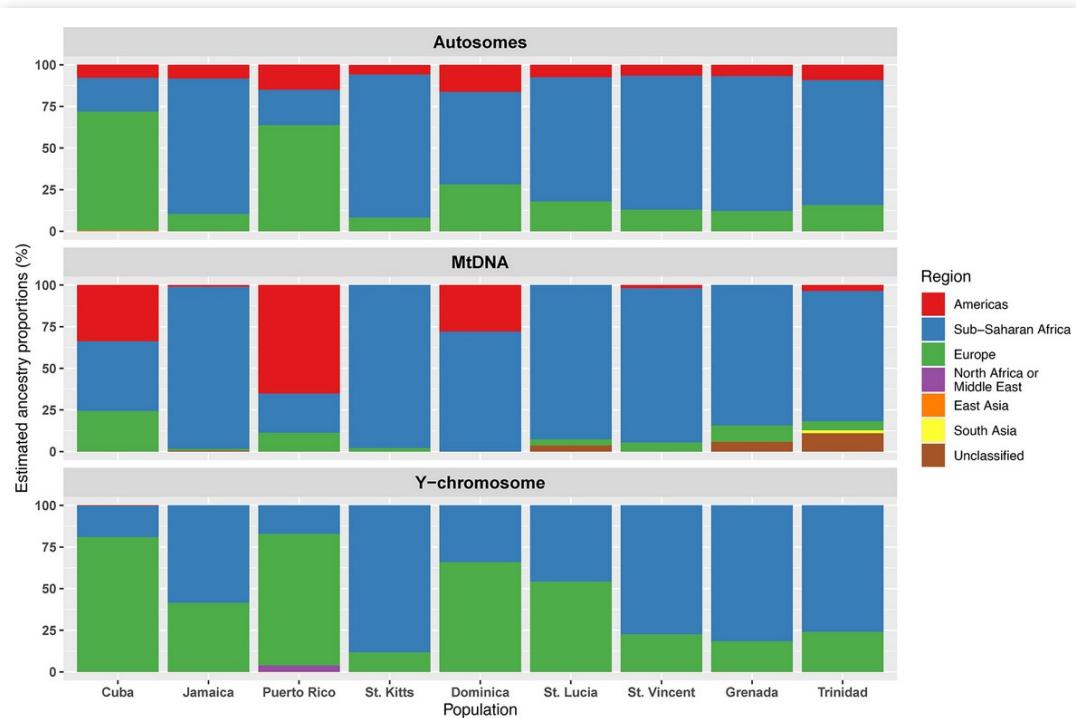
Global ancestry tests: Used to define the relative contributions of different ancestry groups to individual genomes (eg 80% AFR, 20% EUR).

Local ancestry tests: determine the ancestral origin of specific chromosomal segments.

Global tests reveal broad admixture patterns (eg. the aggregate admixture proportions of an individual) but can't infer ancestry of individual loci.

Local ancestry tests precisely identify which genomic regions' ancestry contributes to a trait or disease risk.

The population history of Caribbean islands (as told by admixture tracts)



Nieves-Colon, 2022;

Intergenerational transmission of human genomic elements

Mitochondrial DNA is passed down from the mother

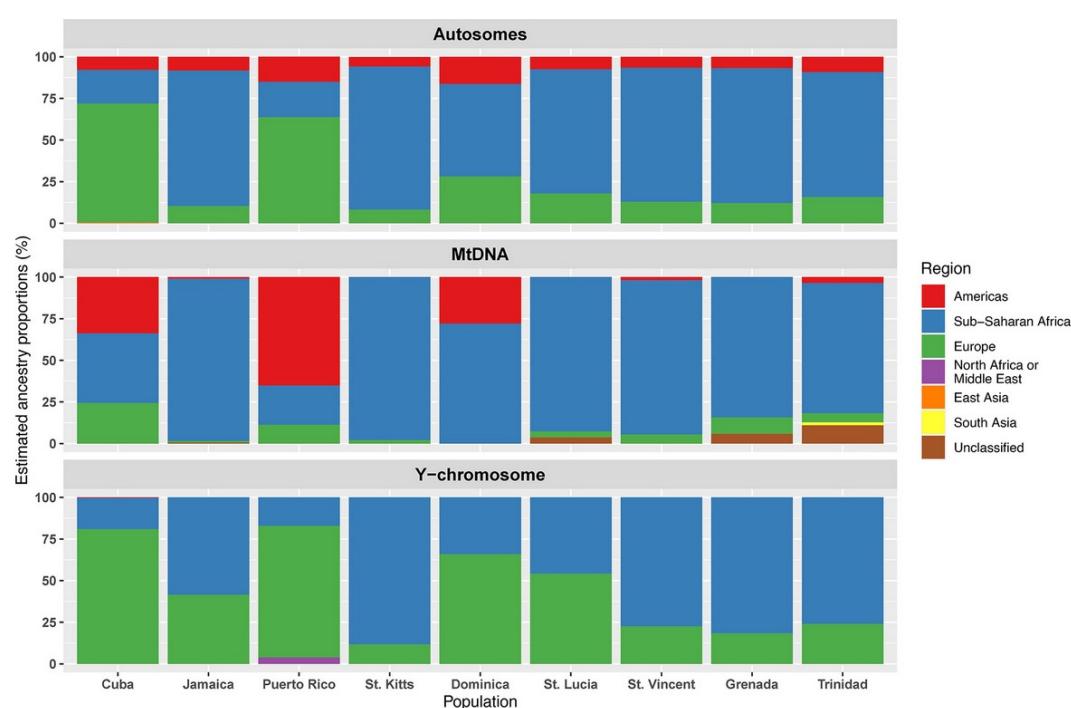
Y chromosome is inherited from fathers

Autosomal DNA: 1 copy each from both mother and father

The population history of Caribbean islands (as told by admixture tracts)

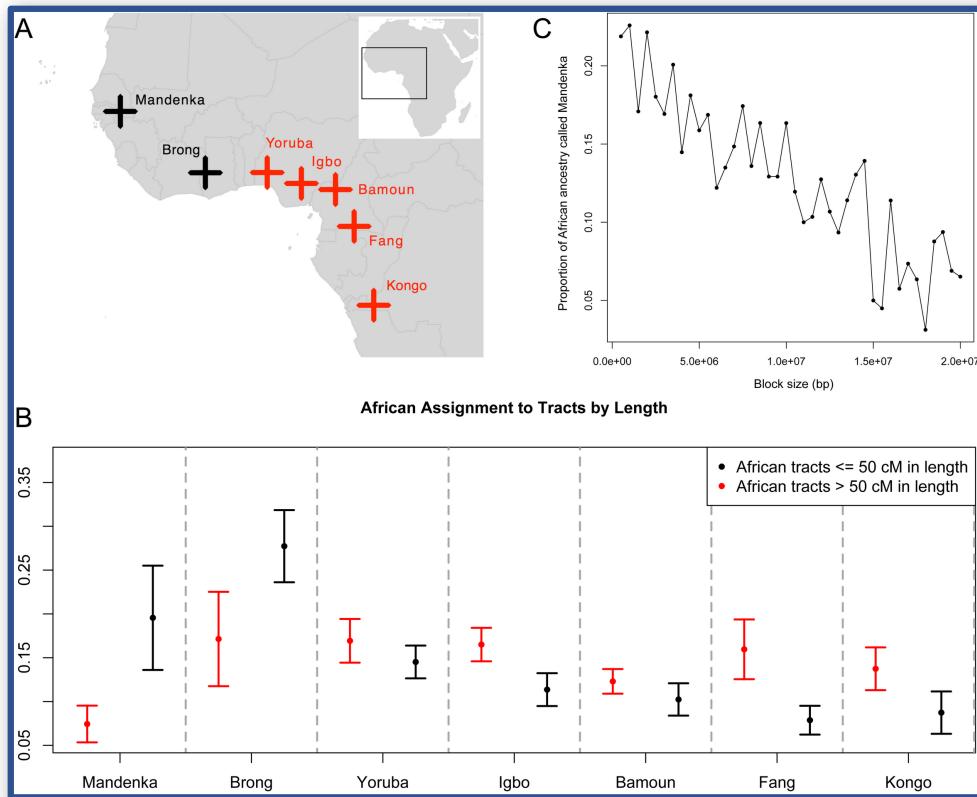
Key points

- Recent admixture in Caribbean populations has left a striking sex-biased signature on these genomes
 - Overwhelming influence of Africa and native America in maternal (mitochondrial) lineages
 - European ancestry is disproportionately represented in paternal (Y chromosome) lineages
- *These disparities highlight the deeply asymmetric social dynamics of the colonial and slave-trade era



Nieves-Colon, 2022;

Inferring the order, timing and origin of historical admixture



Key findings

- Sorted AFR ancestry tracts of caribbeans by length
- Bimodal size distribution reflective of split admixture timing.
- Dual sources: Smallest, oldest tracts mapped to far-west groups (Mandenka, Brong); larger, more recent tracts to central-west peoples (Yoruba, Igbo, Fang).
- Time-stamped gene flow: Early slave shipments came from far-west coasts, later ones from central-west—reflected in tract lengths.

Moreno-Estrada et al, 2013

Popular tools used for Admixture inference

Method	Description
ADMIXTURE	Maximum likelihood algorithm.
STRUCTURE	Bayesian clustering approach
RFMix	Use for Local ancestry inference
Haplotypic Methods	Identification of ancestry-specific chromosomal segments e.g. HAPMIX and LAMP.
Hidden Markov Models (HMMs)	Model transitions between ancestries along chromosomal segments

RFMix

ARTICLE

RFMix: A Discriminative Modeling Approach for Rapid and Robust Local-Ancestry Inference

Brian K. Maples,^{1,2} Simon Gravel,^{1,3} Eimear E. Kenny,^{1,4,5,6,7,8} and Carlos D. Bustamante^{1,8,*}

Local-ancestry inference is an important step in the genetic analysis of fully sequenced human genomes. Current methods can only detect continental-level ancestry (i.e., European versus African versus Asian) accurately even when using millions of markers. Here, we present RFMix, a powerful discriminative modeling approach that is faster (~30×) and more accurate than existing methods. We accomplish this by using a conditional random field parameterized by random forests trained on reference panels. RFMix is capable of learning from the admixed samples themselves to boost performance and autocorrect phasing errors. RFMix shows high sensitivity and specificity in simulated Hispanics/Latinos and African Americans and admixed Europeans, Africans, and Asians. Finally, we demonstrate that African Americans in HapMap contain modest (but nonzero) levels of Native American ancestry (~0.4%).

A benchmarking comparison of RFMix and ADMIXTURE

Uren *et al.* BMC Genetics (2020) 21:40
<https://doi.org/10.1186/s12863-020-00845-3>

BMC Genetics

RESEARCH ARTICLE

Open Access

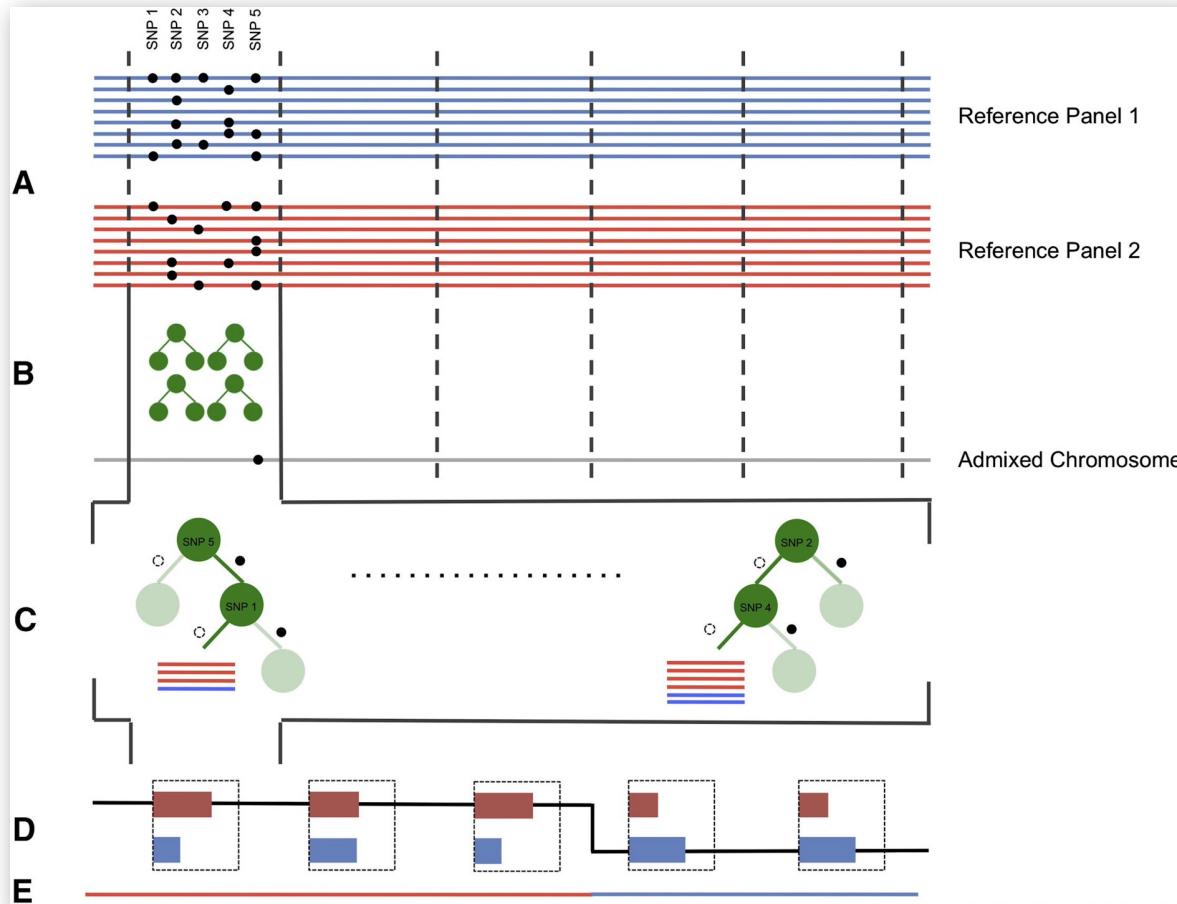
Putting RFMix and ADMIXTURE to the test in a complex admixed population



Caitlin Uren^{*} , Eileen G. Hoal and Marlo Möller

- RFMix outperforms ADMIXTURE in determining global ancestry proportions in a highly complex 5-way South African admixture scenario.
- RFMix can be used for both global and local ancestry estimation and gives robust performance in more complex admixture scenarios.

The RFMix Algorithm



Simplified Steps

- Segment the genome
- Compare against reference panels
- Random-forest classification
- Iterate and refine
- Assemble the mosaic

Maples et al, 2013

Admixture Mapping: Much like GWAS, except..

GWAS tests SNPs, admixture mapping tests ancestry:

Scans each local ancestry segment (e.g. African vs. European) instead of each SNP..

Phenotype vs. ancestry instead of allele vs. phenotype:

GWAS asks “does SNP A associate with the trait?”

Admixture mapping asks “does having more ancestry X at this region associate with the trait?”

Fewer tests, bigger signals:

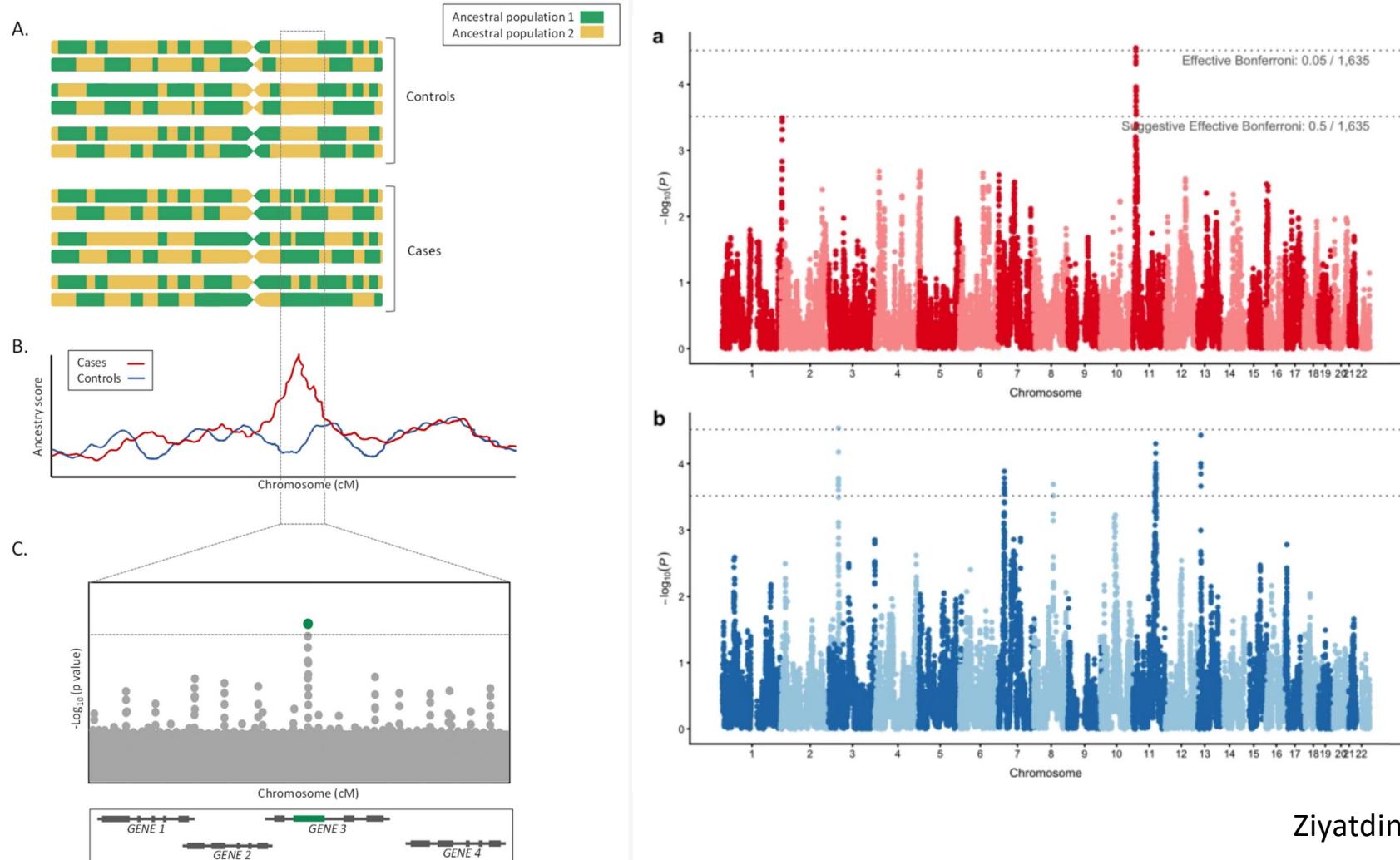
Because ancestry tracts are longer when admixture is recent, dozens of loci can be tested.

Offers greater power from fewer markers to detect regions where risk driven by ancestry.

Follow up with fine-mapping:

Once a region shows an excess of “risk ancestry,” you can zoom in with GWAS or sequencing to pinpoint the exact causal variant.

Identification of two genome-wide significant loci for Local Ancestry–smoking interaction



Ziyatdinov et al, 2020

Practical 1

Simulation and plot of Admixture LD Decay over time

Run ADMIXTURE analysis on pre-prepared data. Plot Global ancestry.

Perform local ancestry inference using RFMix. Plot results

Merge local ancestry and genotypes for PRSice analysis using custom plink file generator tool RFTransform

Evaluation of Admixture-informed PRS generated in PRSice