

Population genomics in 2023



Andrea Manica

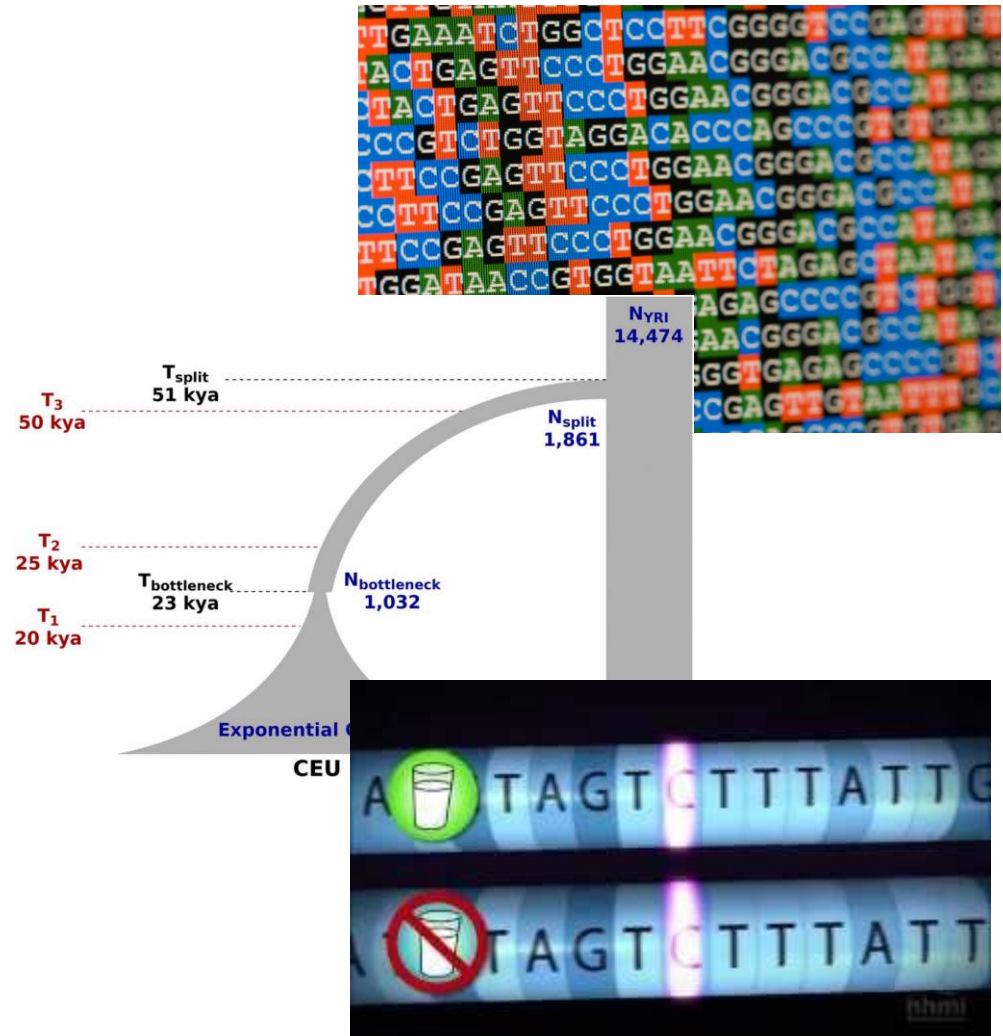


**UNIVERSITY OF
CAMBRIDGE**

Dept of Zoology

Overview

- Type of data
- Demography
- Selection

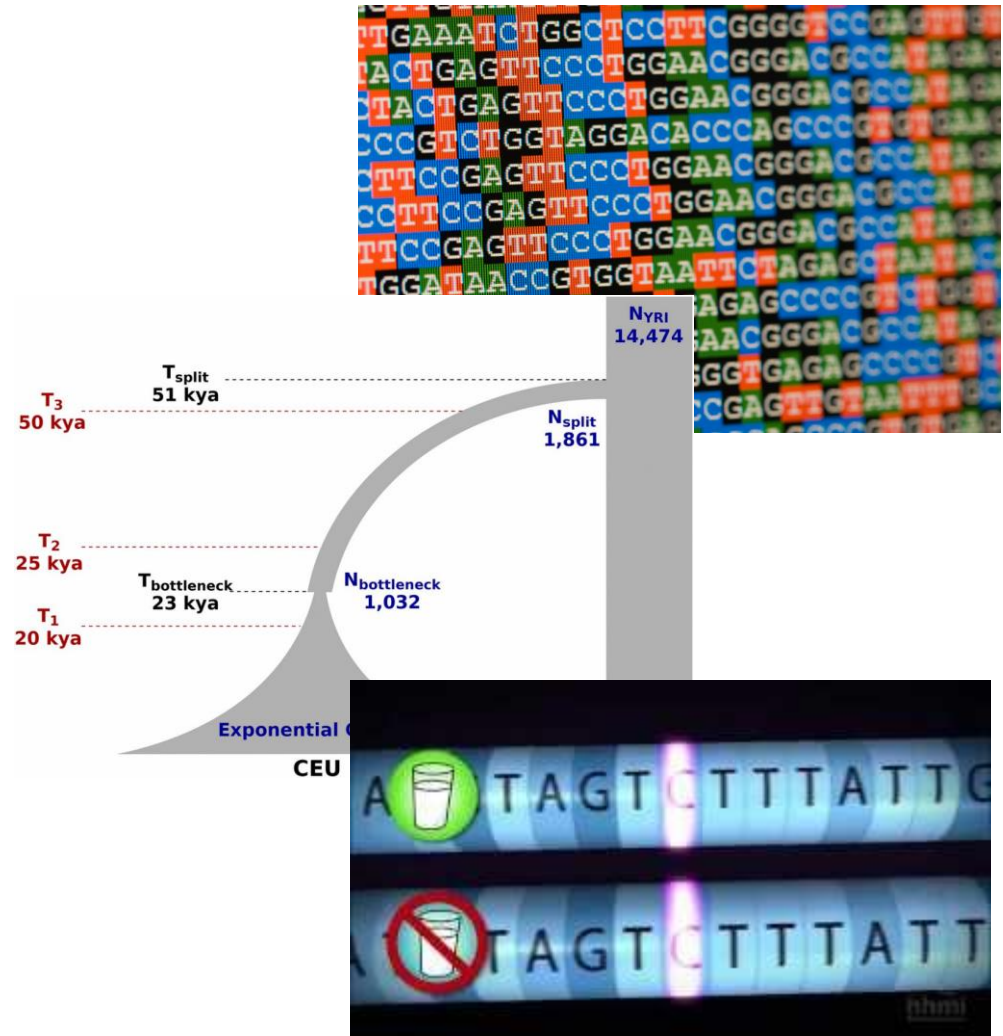


Overview

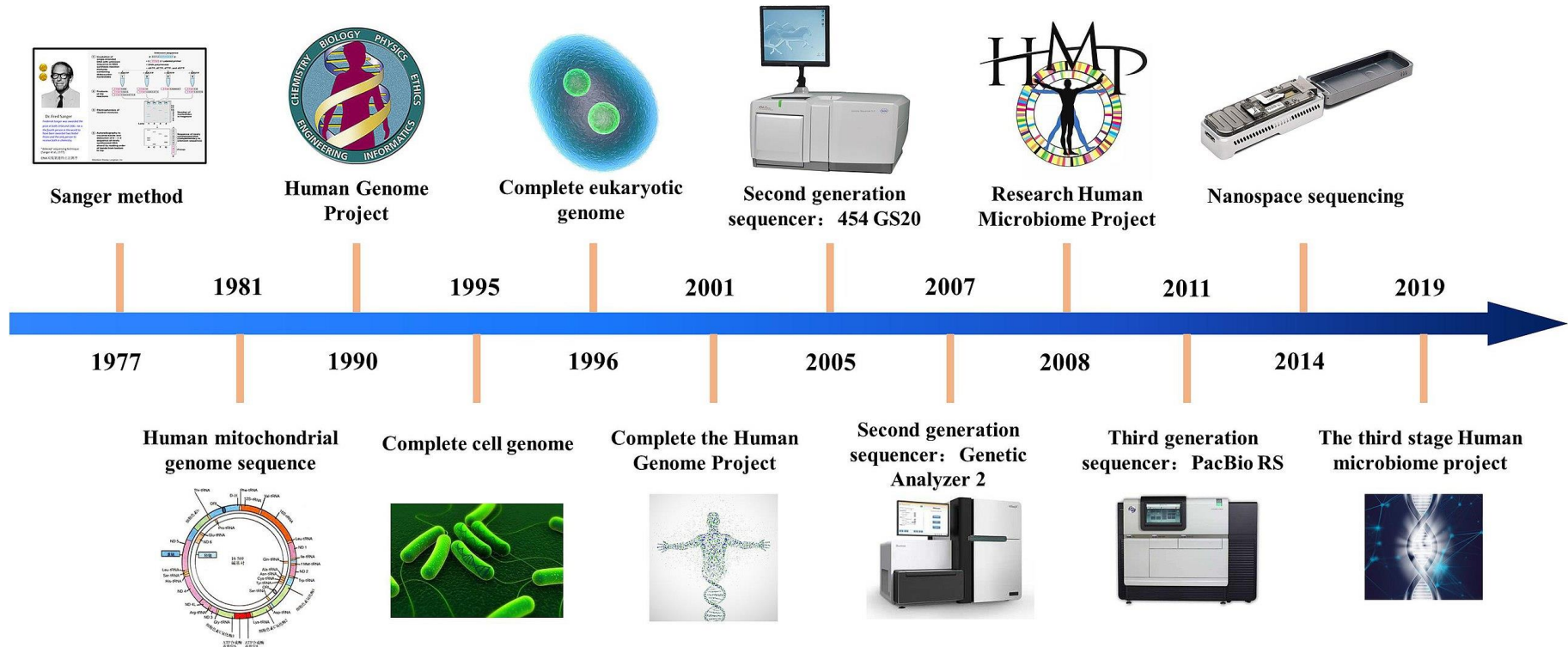
- Type of data

- Demography

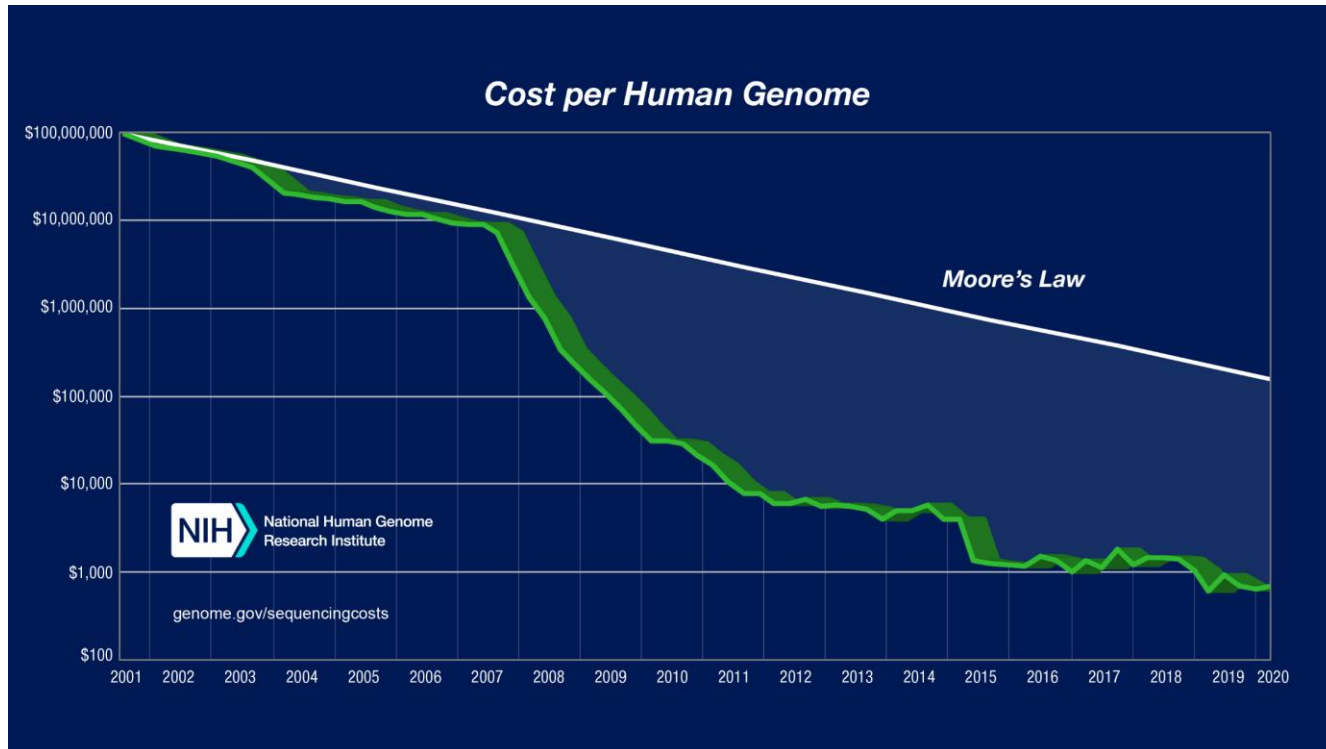
- Selection



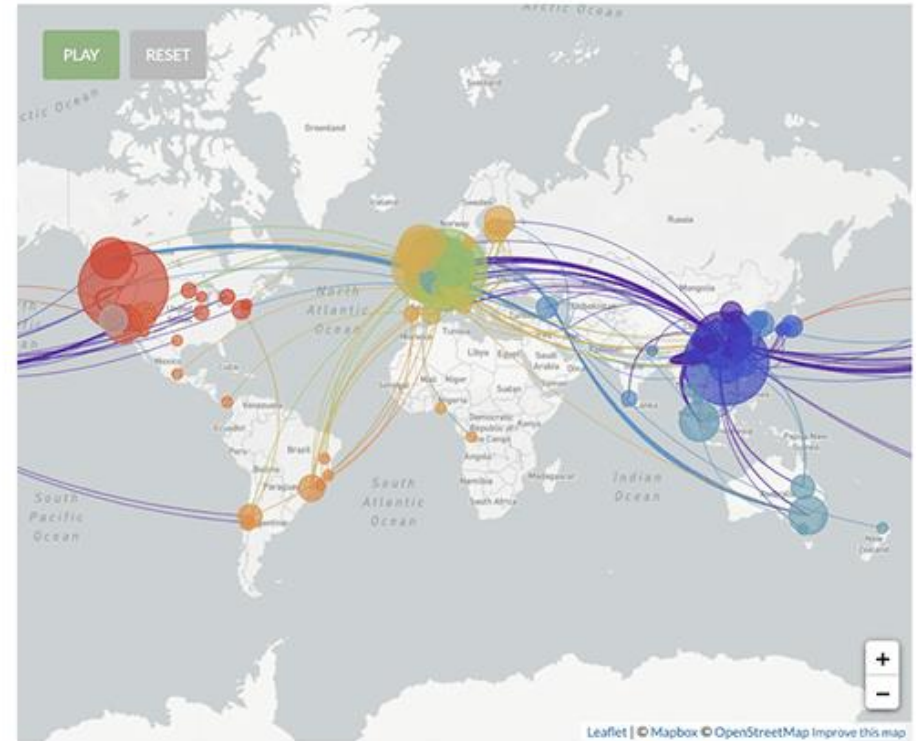
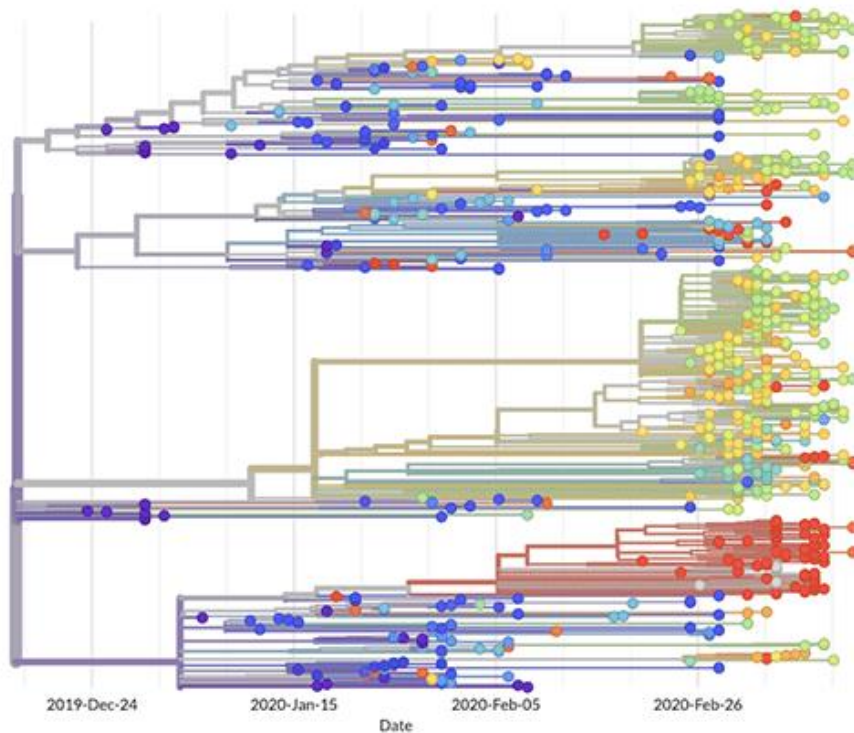
Technological advances over the years



The cost of a genome



Genomics on a big scale: an example



Tracing covid through genomics

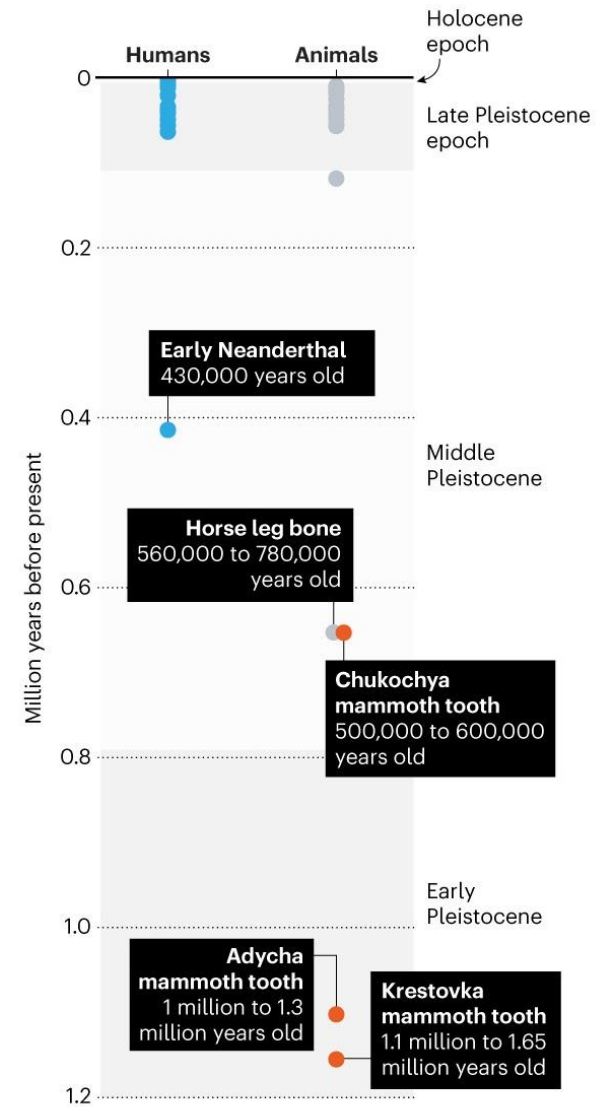
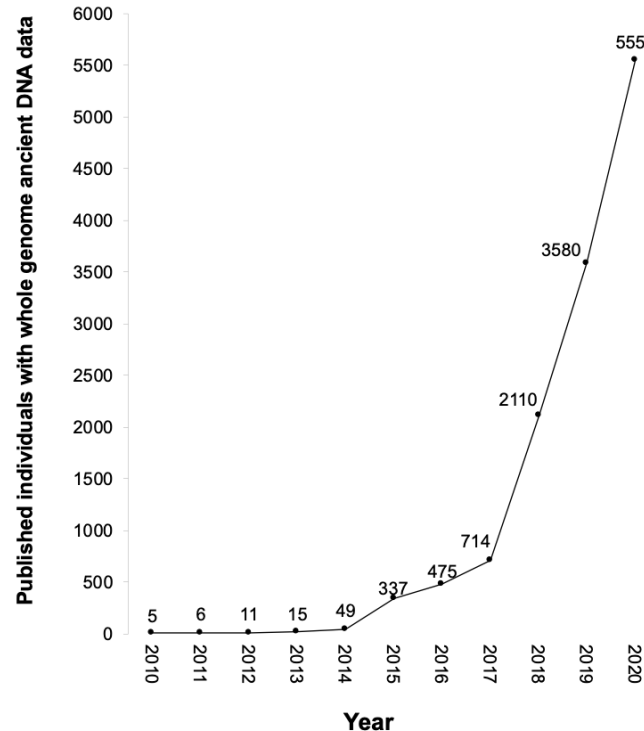
Image from UKRI

Ancient DNA

The Ancient DNA Boom



Callaway (2018) Nature



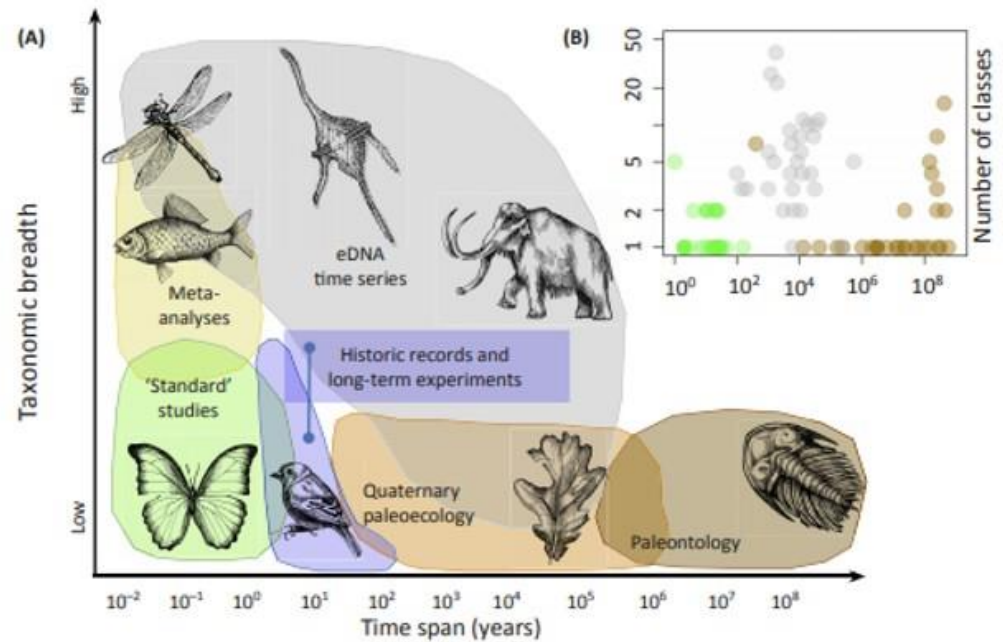
The upper age bound for the mammoth teeth is based on a genetic dating method; the lower bound is based on the age of the sediments in which the teeth were found.

©nature

But beware of the ethical issues of aDNA from human remains

Destructive sampling

Environmental DNA



But we need extensive databases for eDNA!!!

Challenges: non-model species

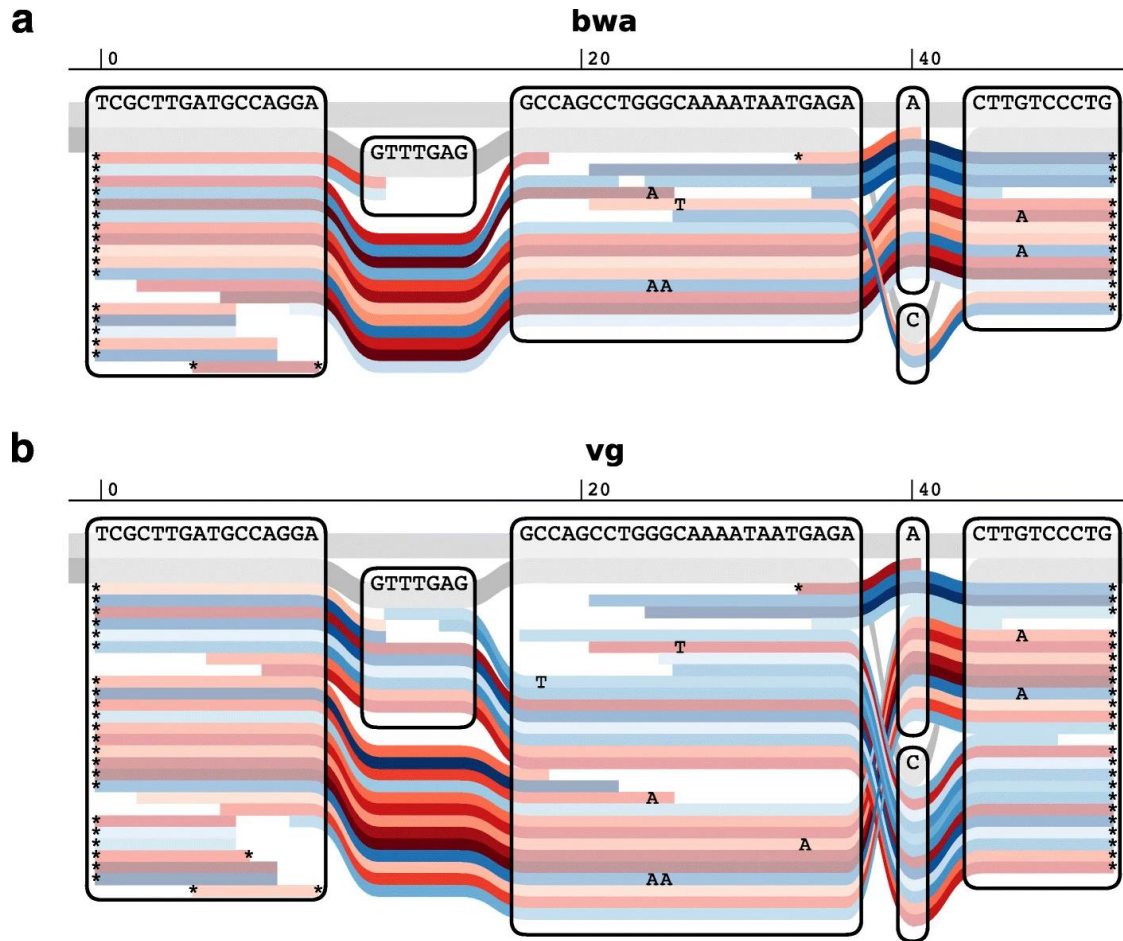


Long and linked reads have dramatically decreased the cost of new reference genomes (~US\$ 3k)

A solution for building the extensive databases needed for eDNA?

Low coverage and **genotype likelihoods**

Challenges: biases from reference



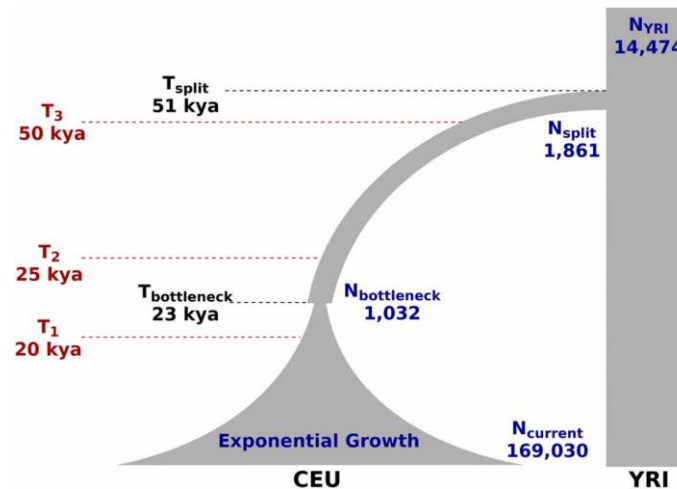
Graph based methods hold a lot of promise

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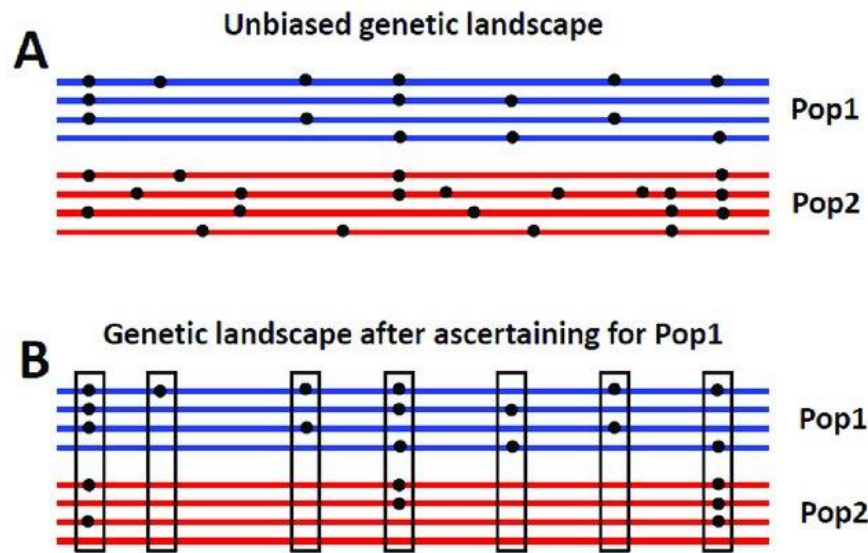
- Demography

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More of the same?

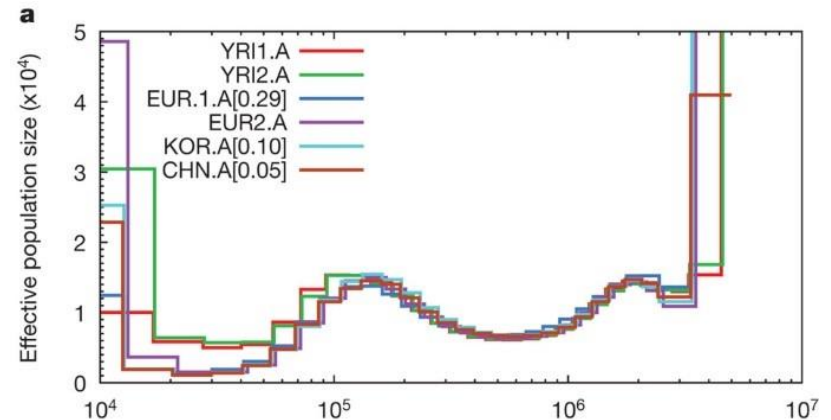
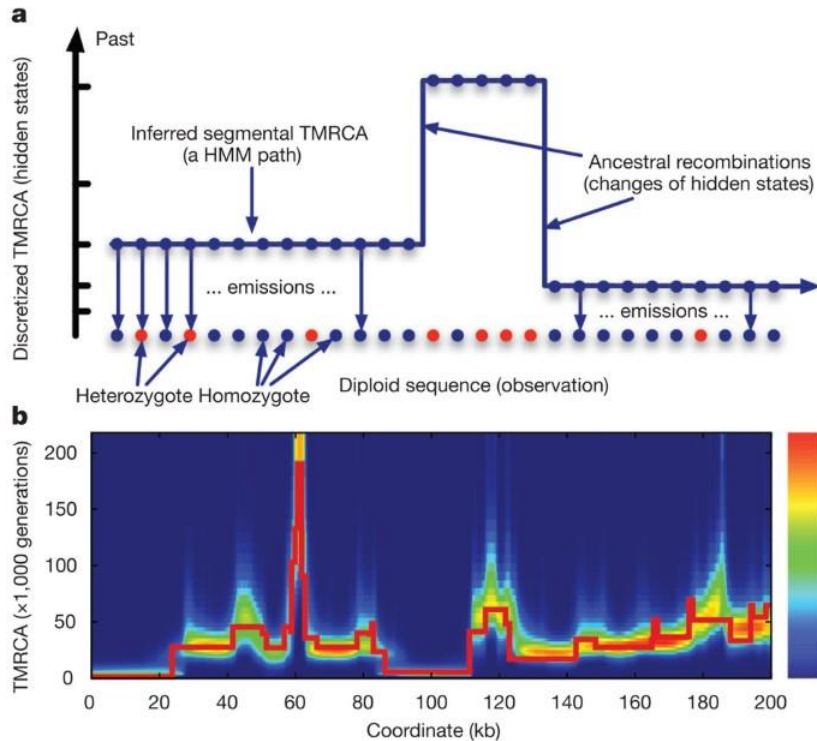
Many approaches based on metrics that describe SNP frequencies (especially the Site Frequency Spectrum)



Very challenging to model ascertained data

Whole genomes solve the problem of **ascertainment** present in SNP chips!!!

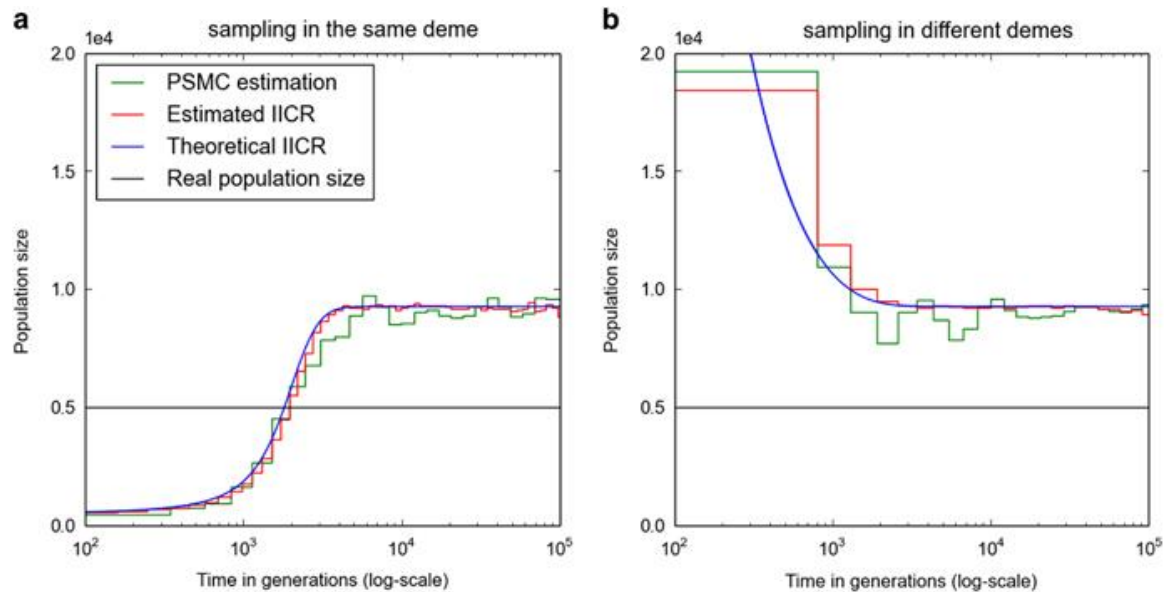
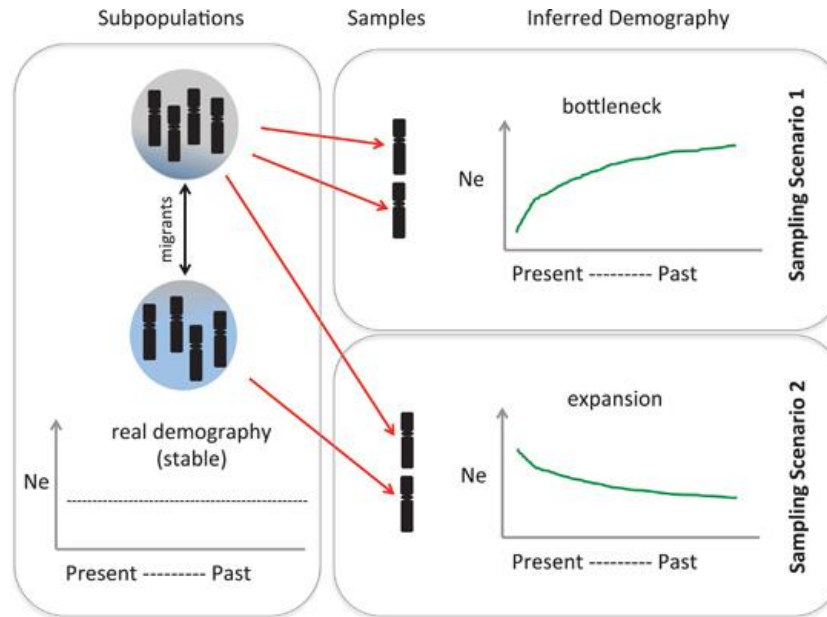
The power of whole genomes



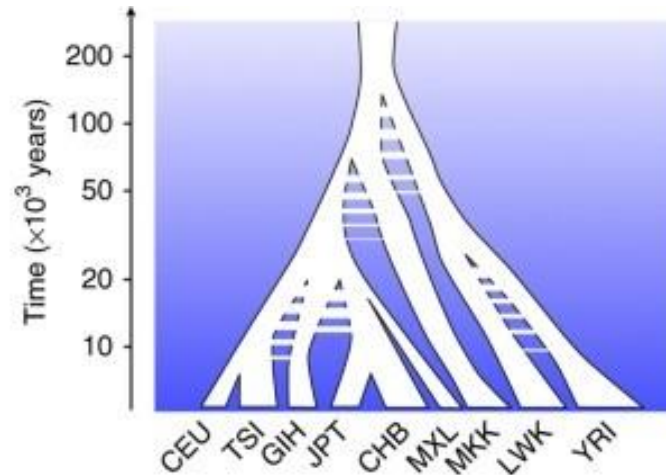
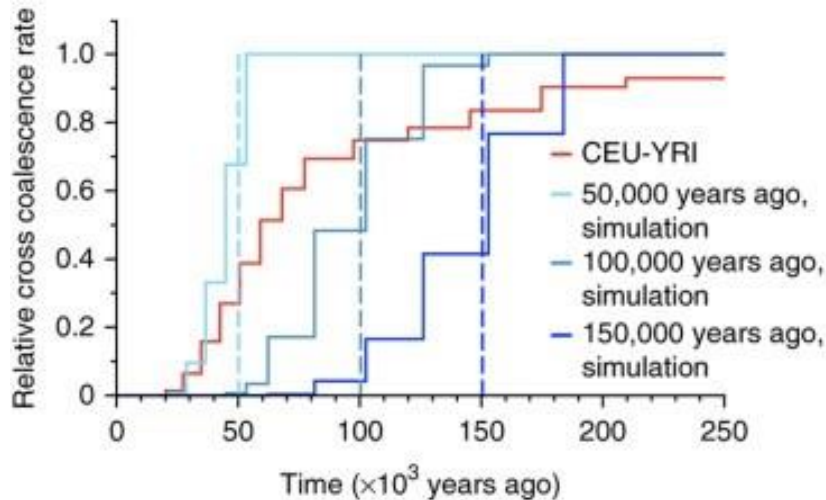
But it assumes a single panmictic population (same assumption of Bayesian Skyline Plots)

Be careful about the assumptions behind methods, they can affect your interpretation

Beware of assumptions



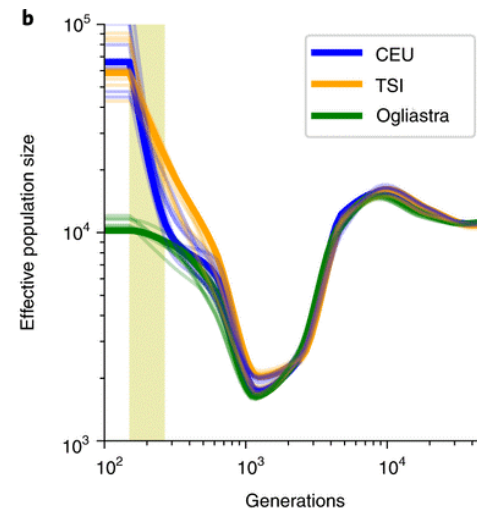
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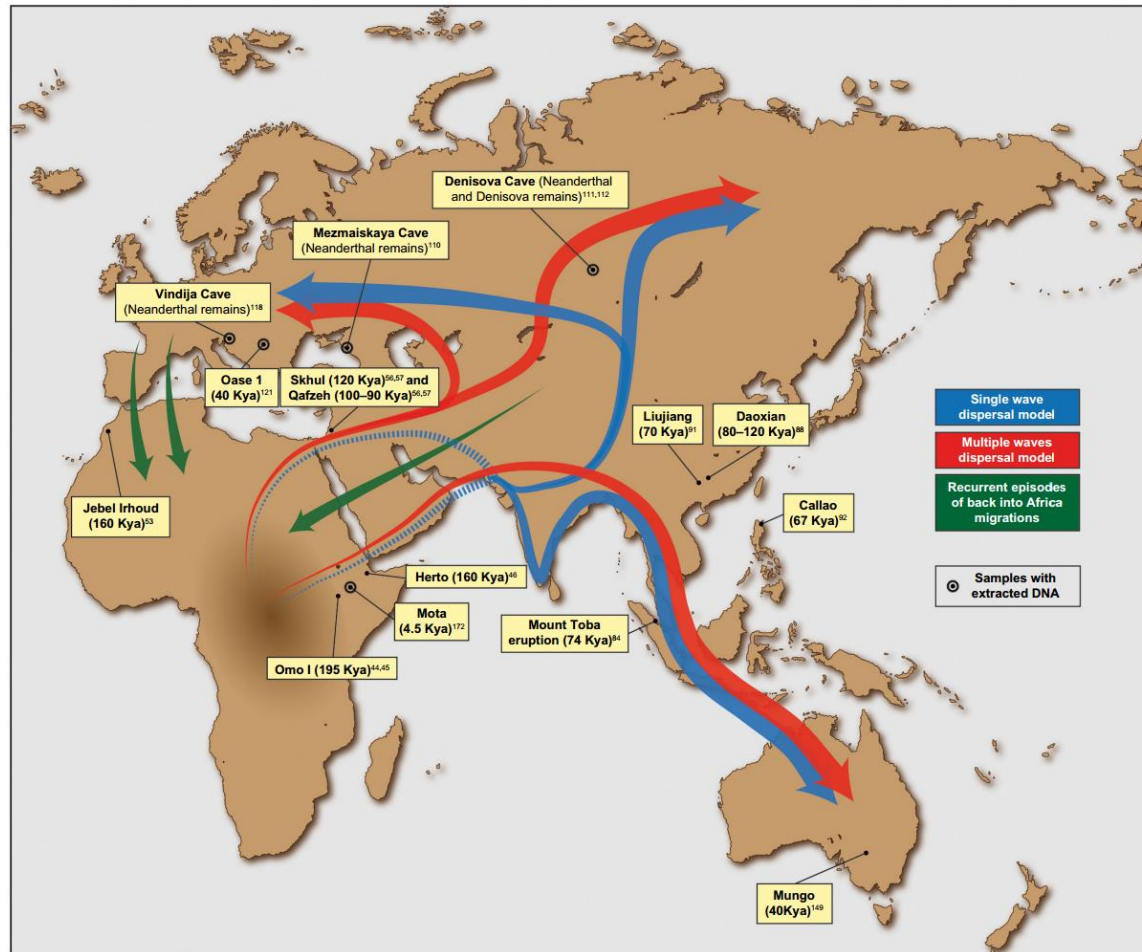
MSMC extends to multiple genomes (but only a few, and need to be phased...)

Split times assume a clean split without migrations

Methods coming out to deal with 1000s of genomes (SMC++, Relate)



But does more data mean better answers?



The story of 3 papers...

But does more data mean better answers?

ARTICLE

One wave only!

doi:10.1038/nature18299

A genomic history of Aboriginal Australia

ARTICLE

One wave (but it could have been two...)

doi:10.1038/nature18964

The Simons Genome Diversity Project:
300 genomes from 142 diverse populations

A list of authors and affiliations appears at the end of the paper.

LETTER

Two waves!

doi:10.1038/nature19792

Genomic analyses inform on migration events
during the peopling of Eurasia

A list of authors and affiliations appears at the end of the paper

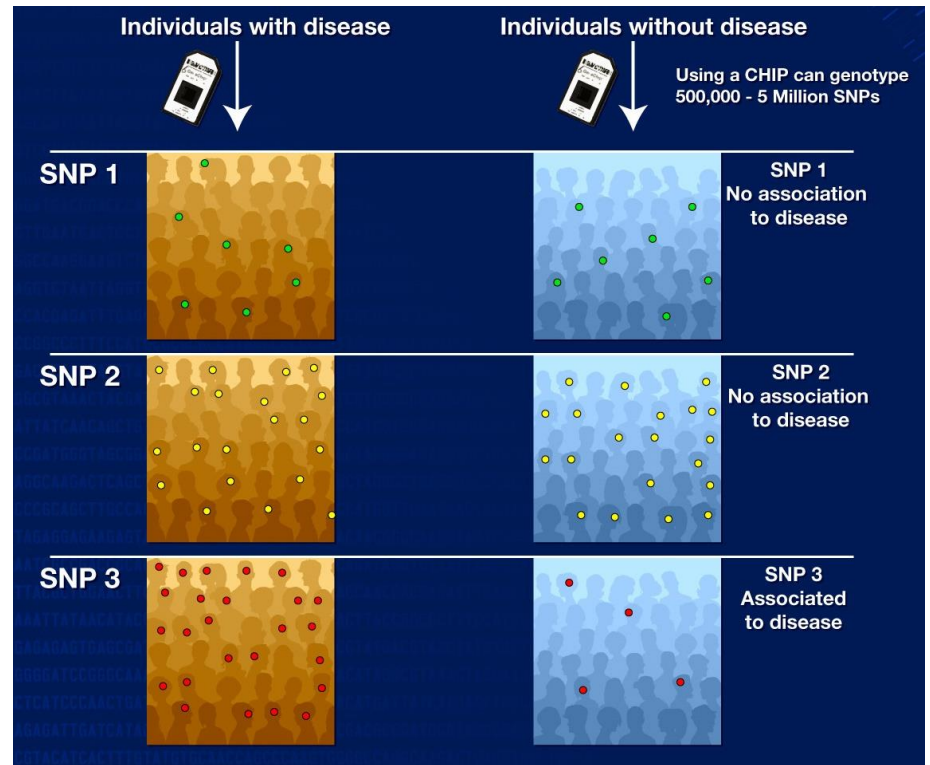
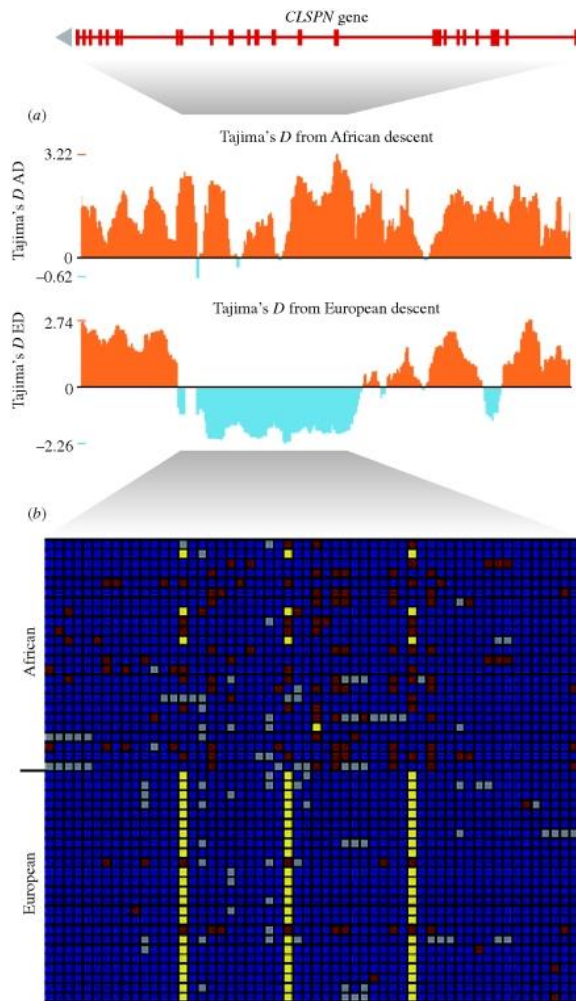
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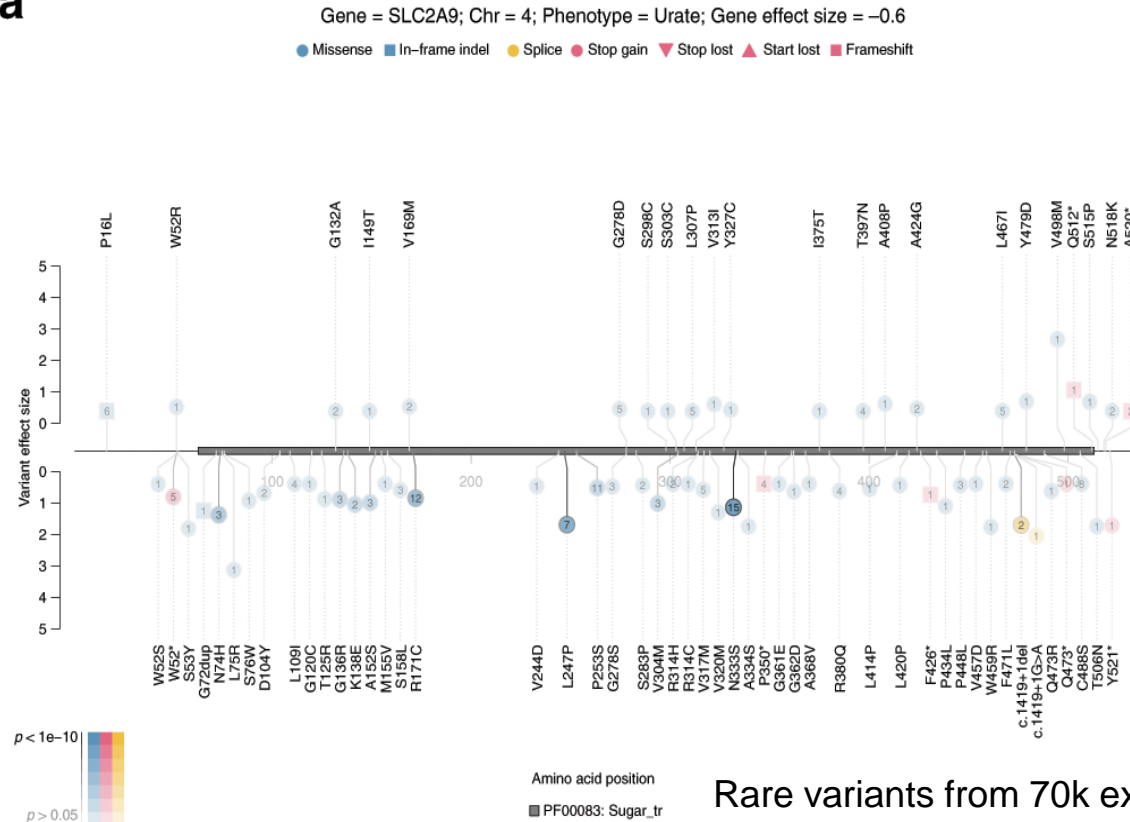
More of the same?

Selection scans and GWAS already possible with SNP chips



Rare alleles

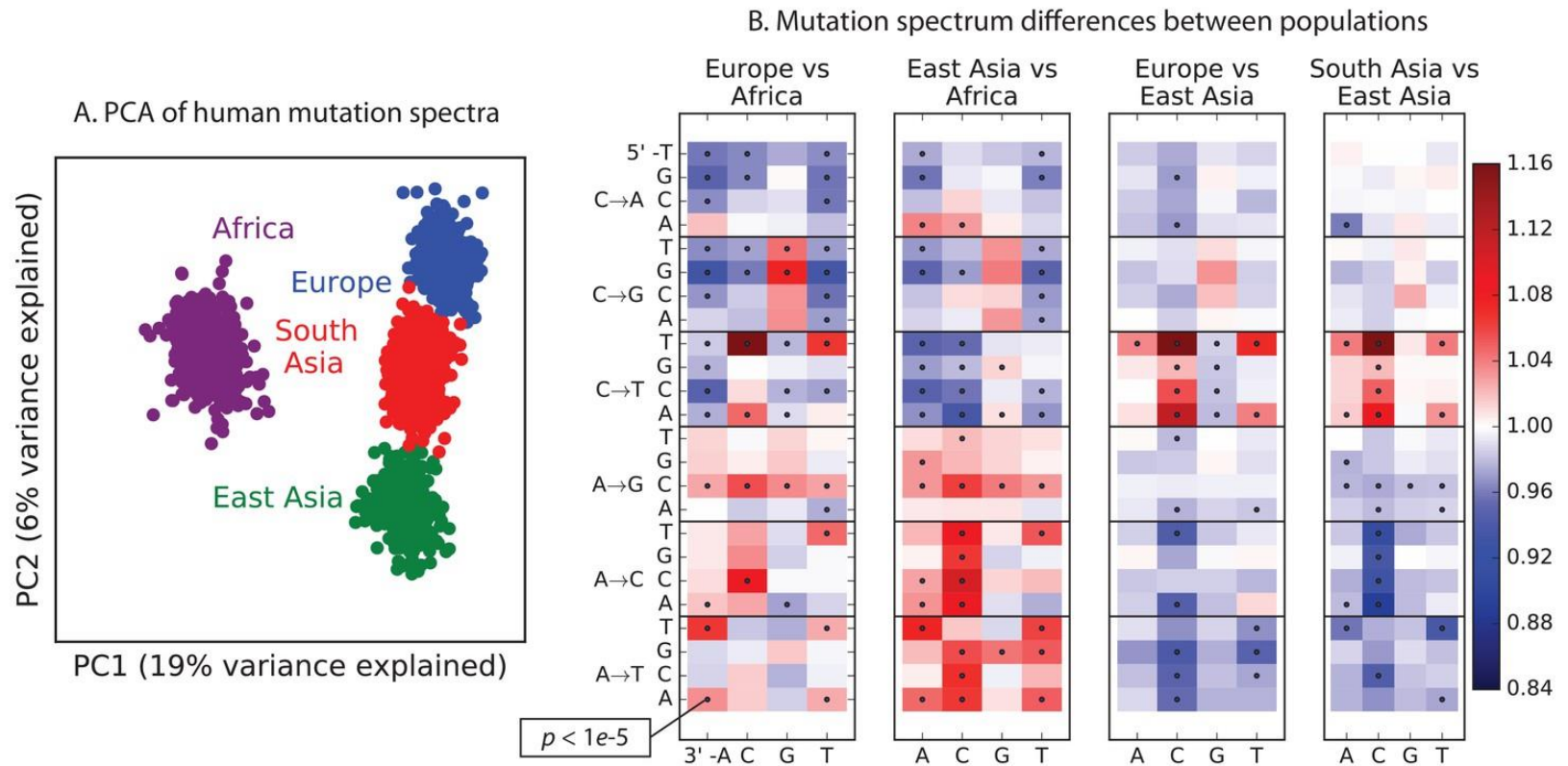
a



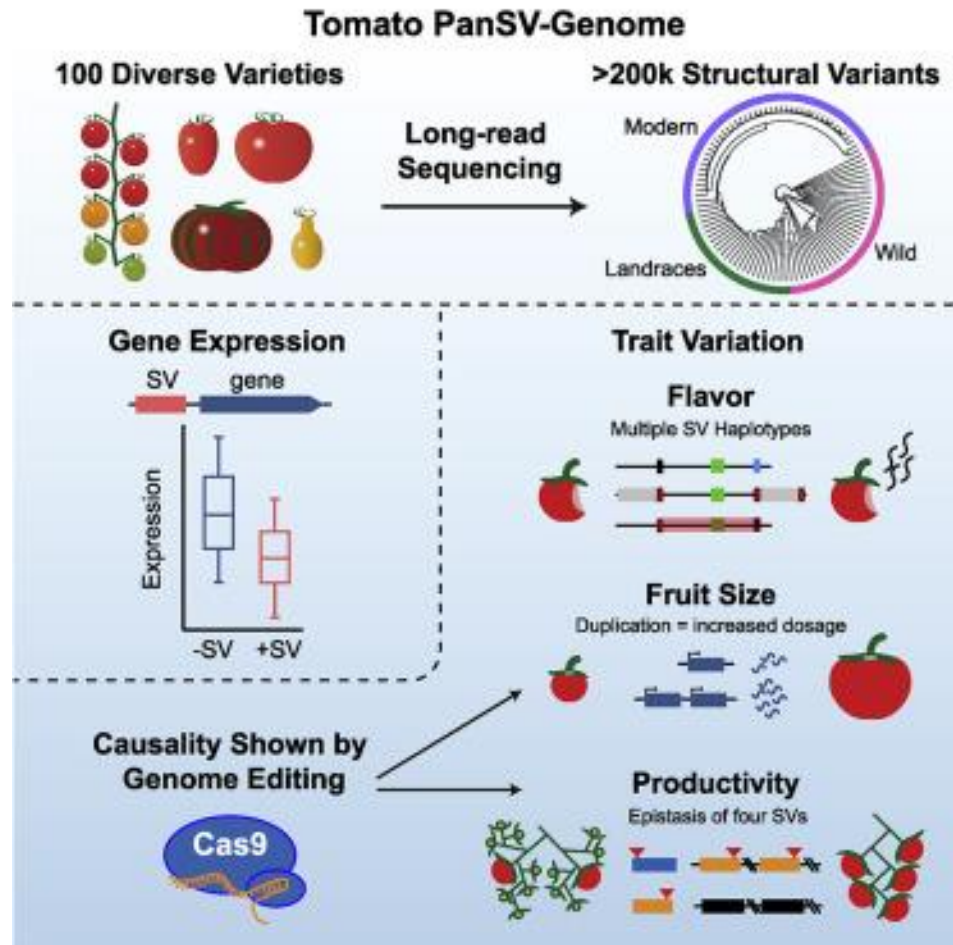
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But still a big need for functional validation of candidates!
False positives are a big issue in selection studies.

Mutation spectrum

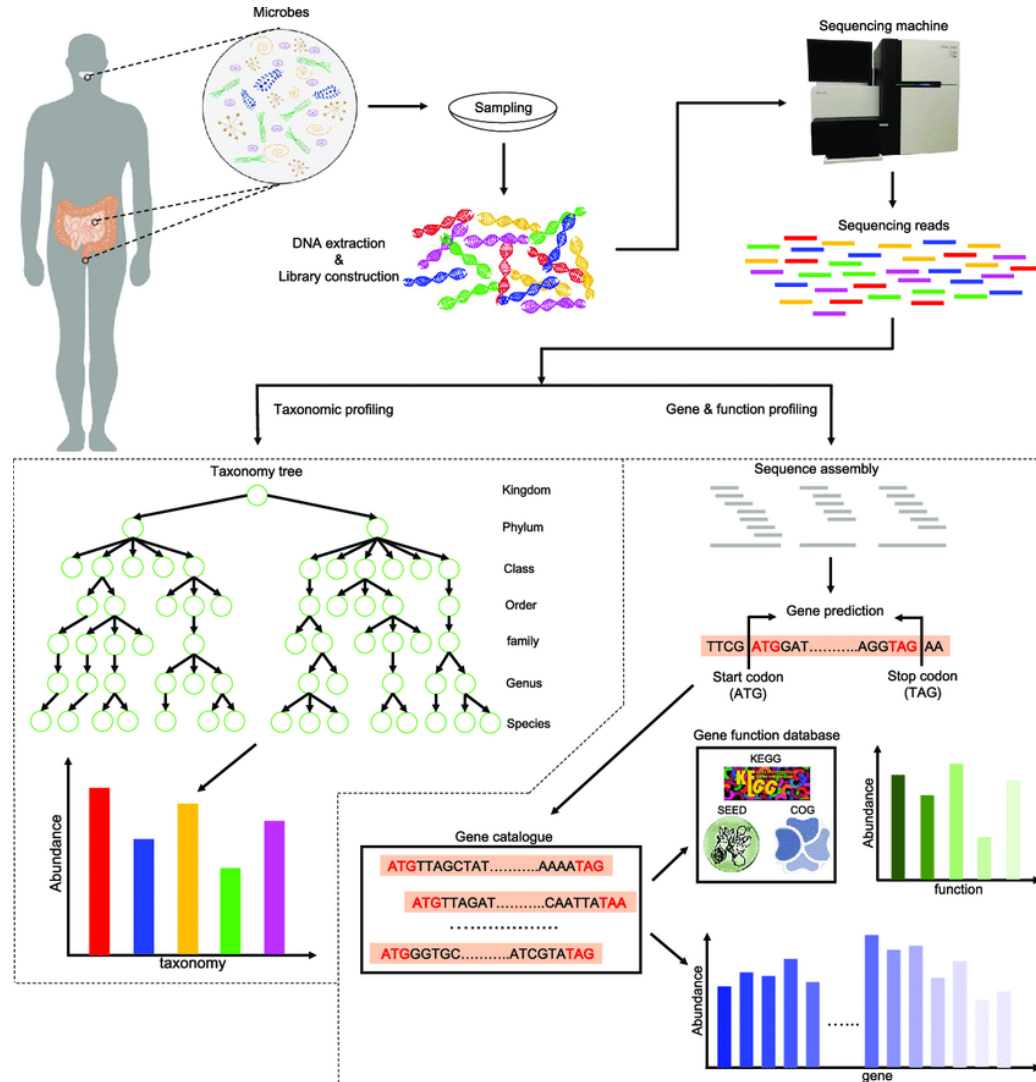


Structural variation



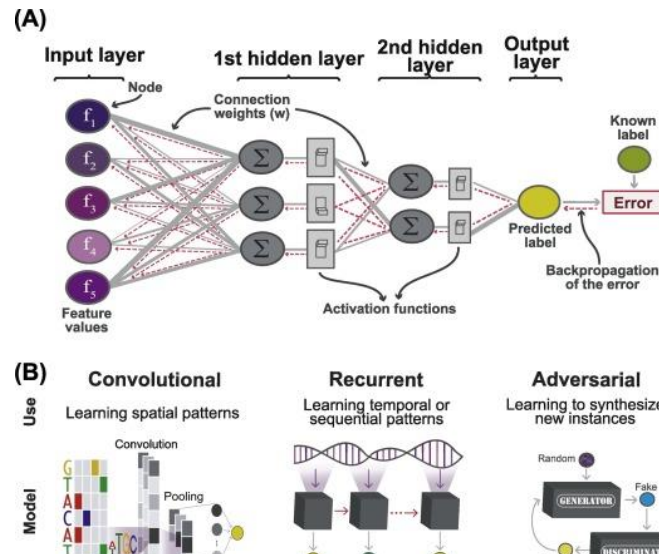
Long read sequencing helps a lot with structural variation!

Metagenome



Phenotypes might be greatly affected by other organisms

Big data and Machine Learning



A black box?
Not necessarily

Trends in Genetics

CellPress
REVIEWS

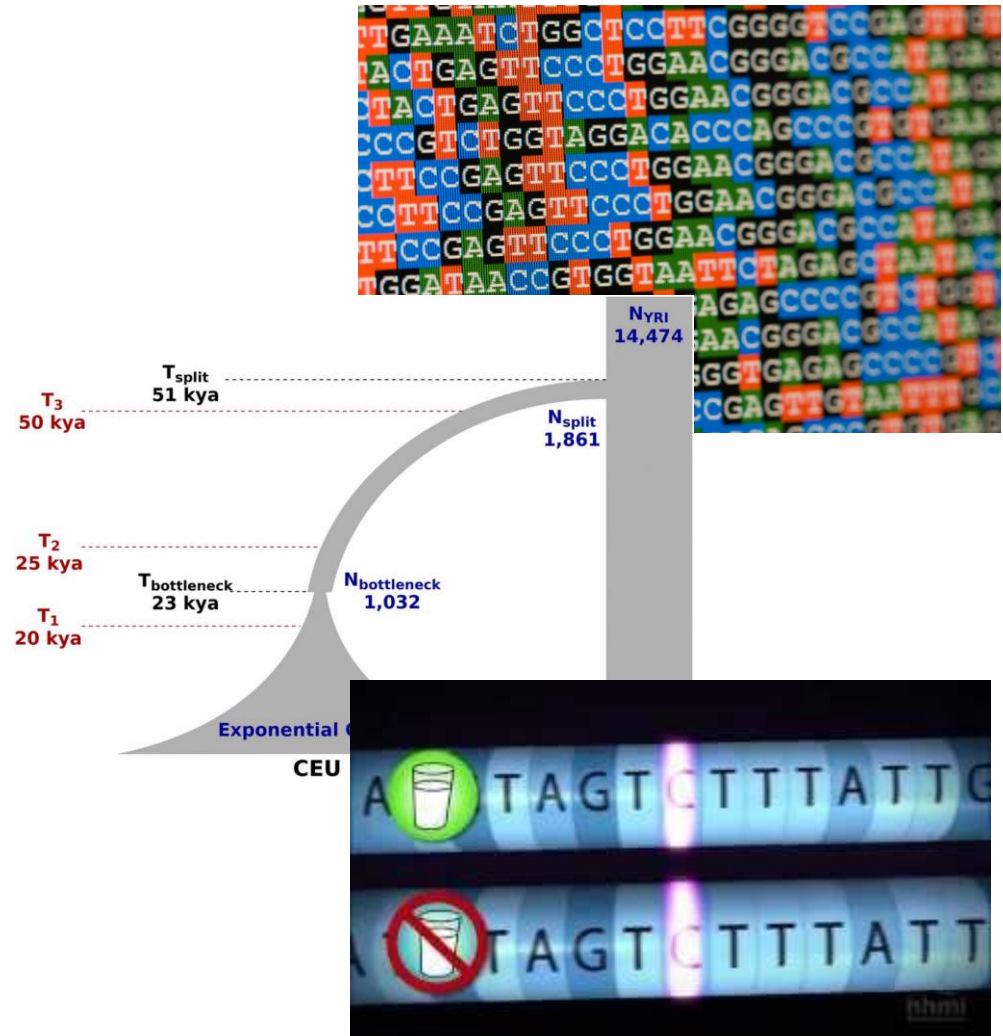
Review

Opening the Black Box: Interpretable Machine Learning for Geneticists

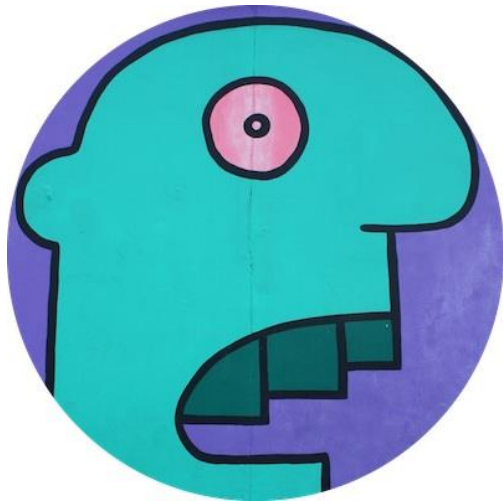
Christina B. Azodi,^{1,2,*} Jiliang Tang,³ and Shin-Han Shiu ,^{1,4,*}

Summary

- Type of data
- Demography
- Selection



EMBO Population Genomics 2023



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