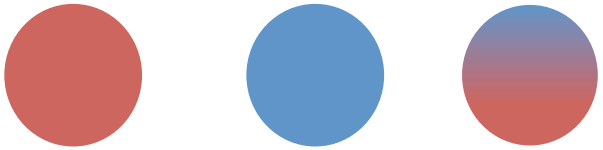
1000 Genomes and Population Genomics

As small groups separate, they evolve in isolation

How do the frequencies of alleles change over time?

- Selection
- Genetic Drift
- Hardy-Weinberg



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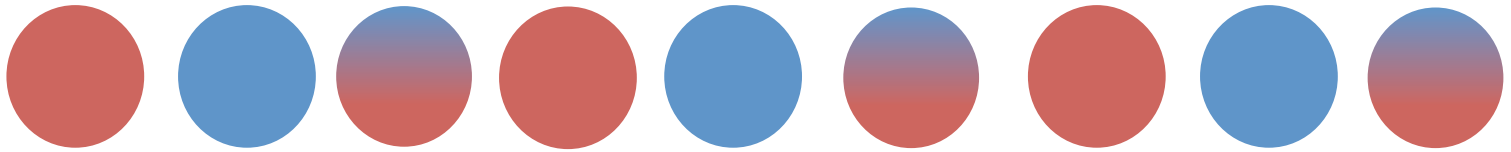
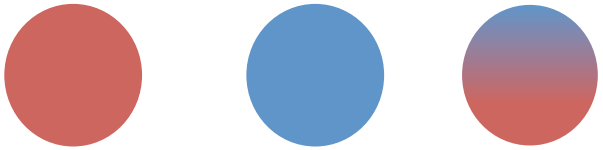
Creates 3 genotypes AA, aa, and Aa



Gen 0



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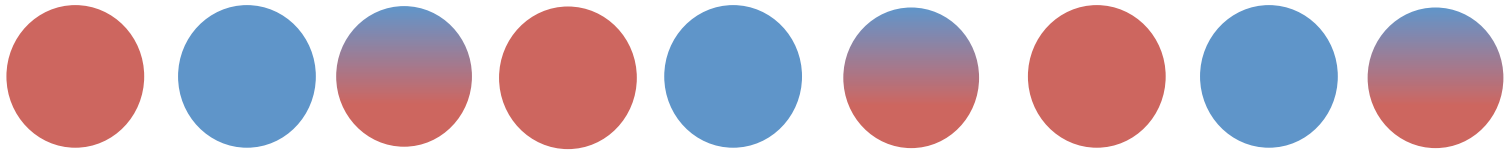

Gen 0

Frequency of allele A; p
Frequency of allele a: q
p+q=1

Frequency of AA: $D=p^2$
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Assume no selection and no mutation
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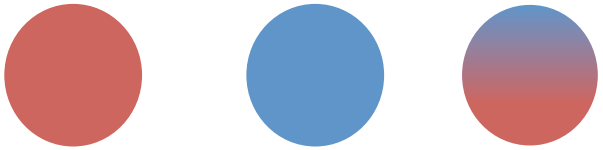
Assume infinite population sizes (no restrictions on numbers)



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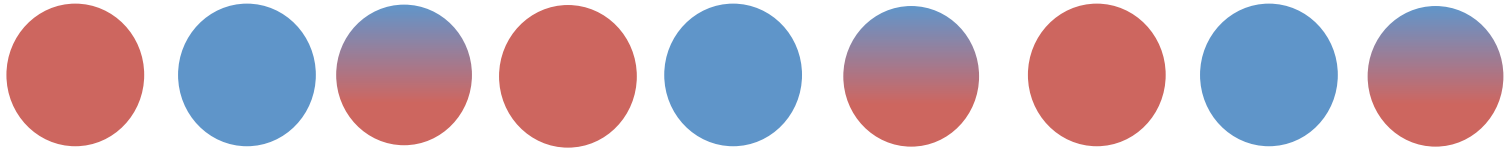

Gen 0

Mating	Probability	Offspring Genotype frequencies		
		AA	Aa	aa
AA x AA	D^2	1	0	0
AA x Aa	2DH	½	½	0
AA x aa	2DR	0	1	0
Aa x Aa	H^2	¼	½	¼
Aa x aa	2HR	0	½	½
aa x aa	R^2	0	0	1
Total for Gen 1		D’	H’	R’

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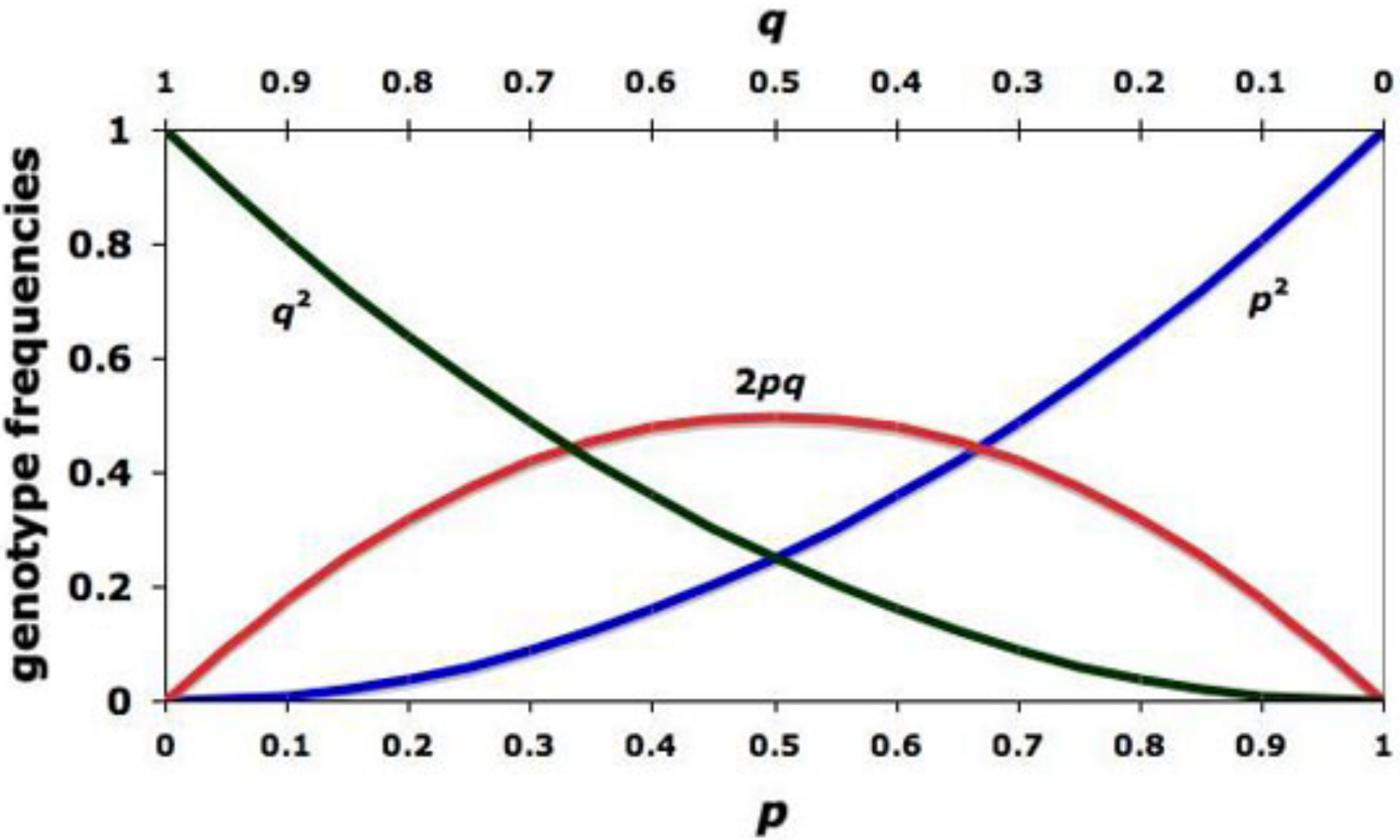
Total for Gen 1		D’	H’	R’

$$D' = D^2 + \frac{2DH}{2} + \frac{H^2}{4} = \left(D + \frac{H}{2}\right)^2 = \left(p^2 + p(1-p)\right)^2 = \left(p^2 + p - p^2\right) = p^2$$

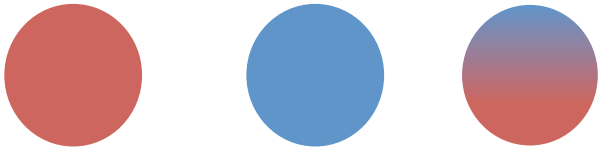
$$R' = \frac{H^2}{4} + \frac{2HR}{2} + R^2 = \left(R + \frac{H}{2}\right)^2 = \left(q^2 + q(1-q)\right)^2 = (q^2 + q - q^2) = q^2$$

Genotypes are stable over time

$$H' = \frac{2DH}{2} + 2DR + \frac{H^2}{2} + \frac{2HR}{2} = 2\left(D + \frac{H}{2}\right)\left(R + \frac{H}{2}\right) = 2pq$$



Andrews, C. (2010) The Hardy-Weinberg Principle. *Nature Education Knowledge* **3**(10):65



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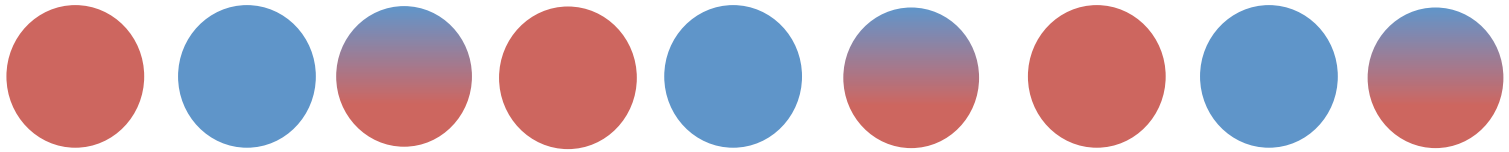

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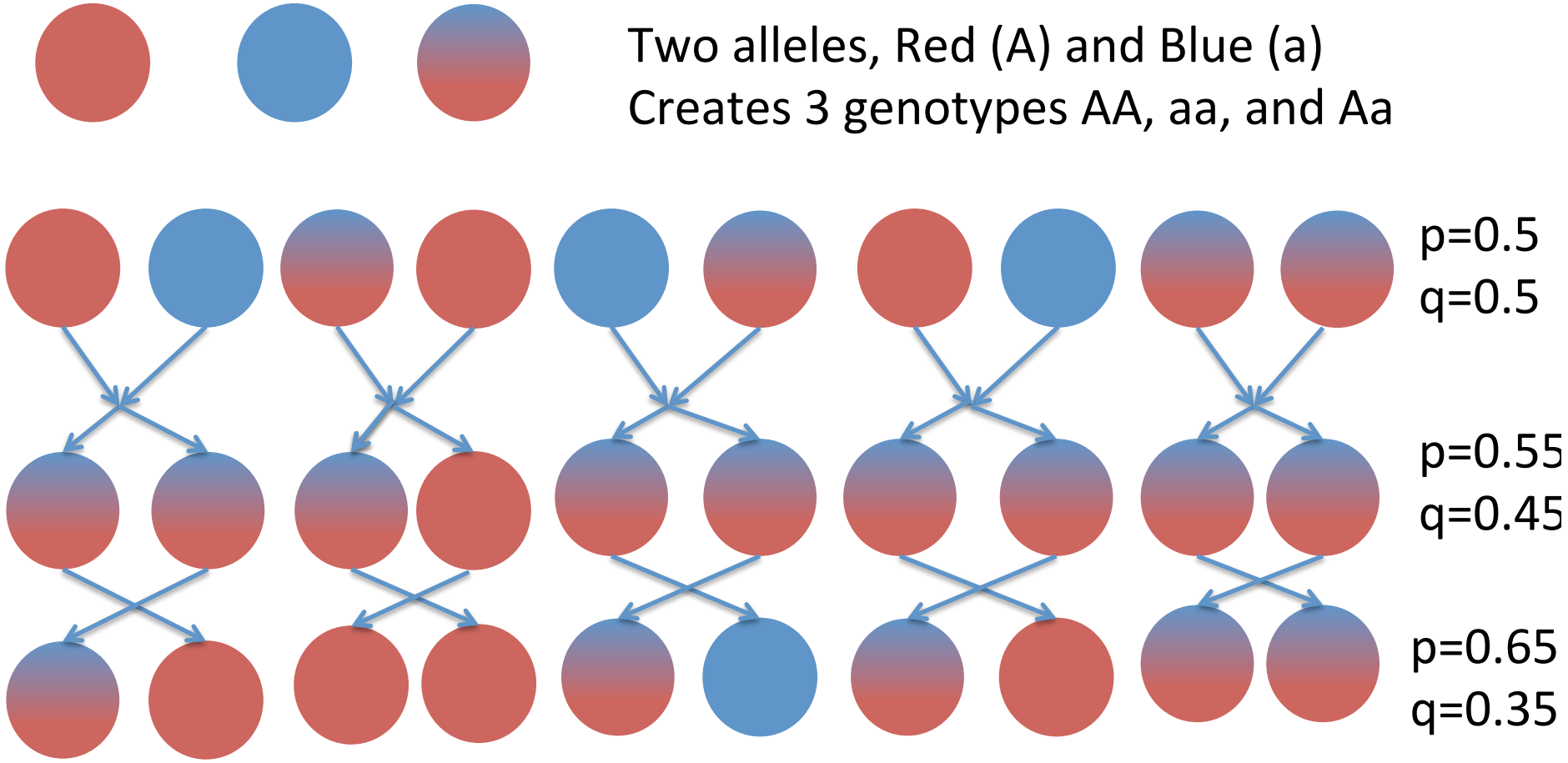
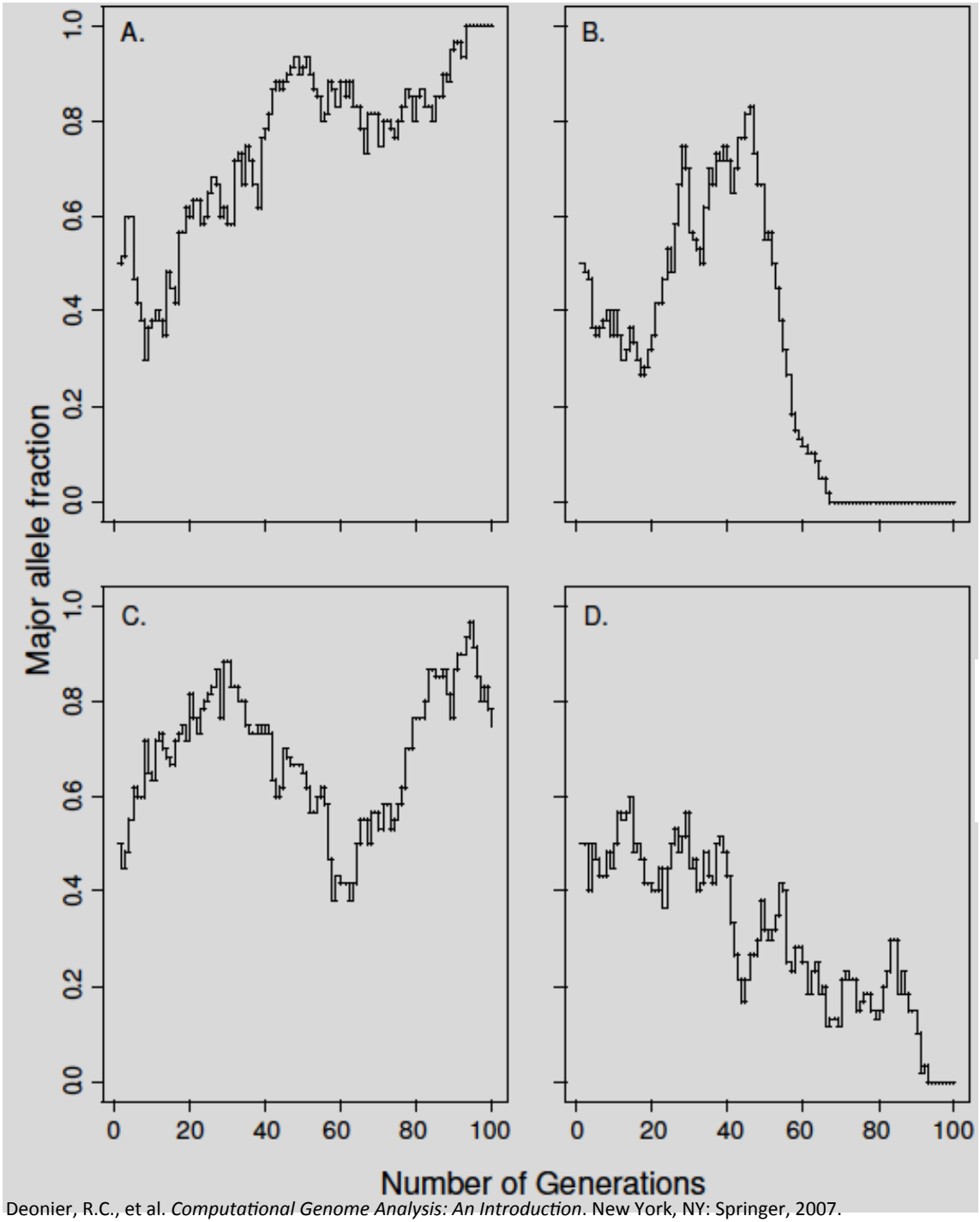


Genetic Drift



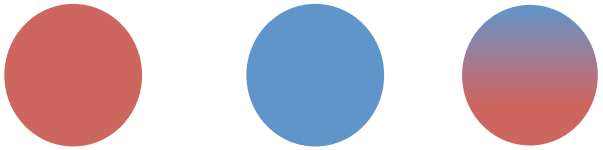
Deonier, R.C., et al. *Computational Genome Analysis: An Introduction*. New York, NY: Springer, 2007.

If not infinite number of offspring, then random fluctuations in number of alleles can cause dramatic changes in allele frequency

These drifts are more pronounced in a smaller population

$$h(n) = \left(1 - \frac{1}{2N}\right)^n h(0).$$

Heterozygosity is lost at a geometric rate with the number of generations (n) that depends on the number of individuals (N)



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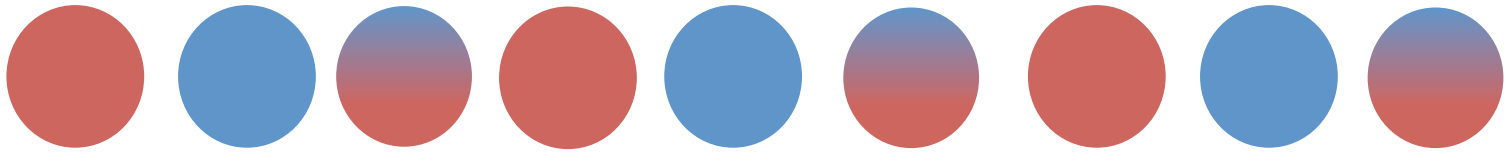

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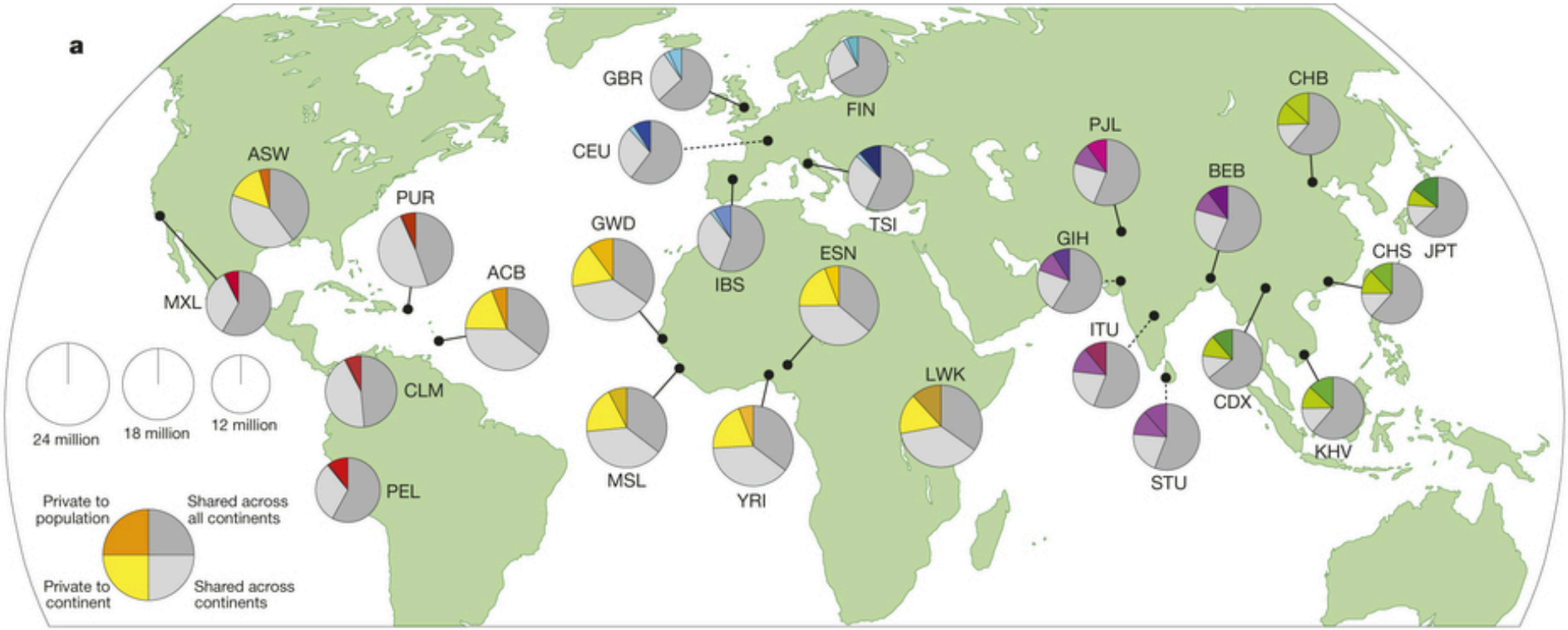
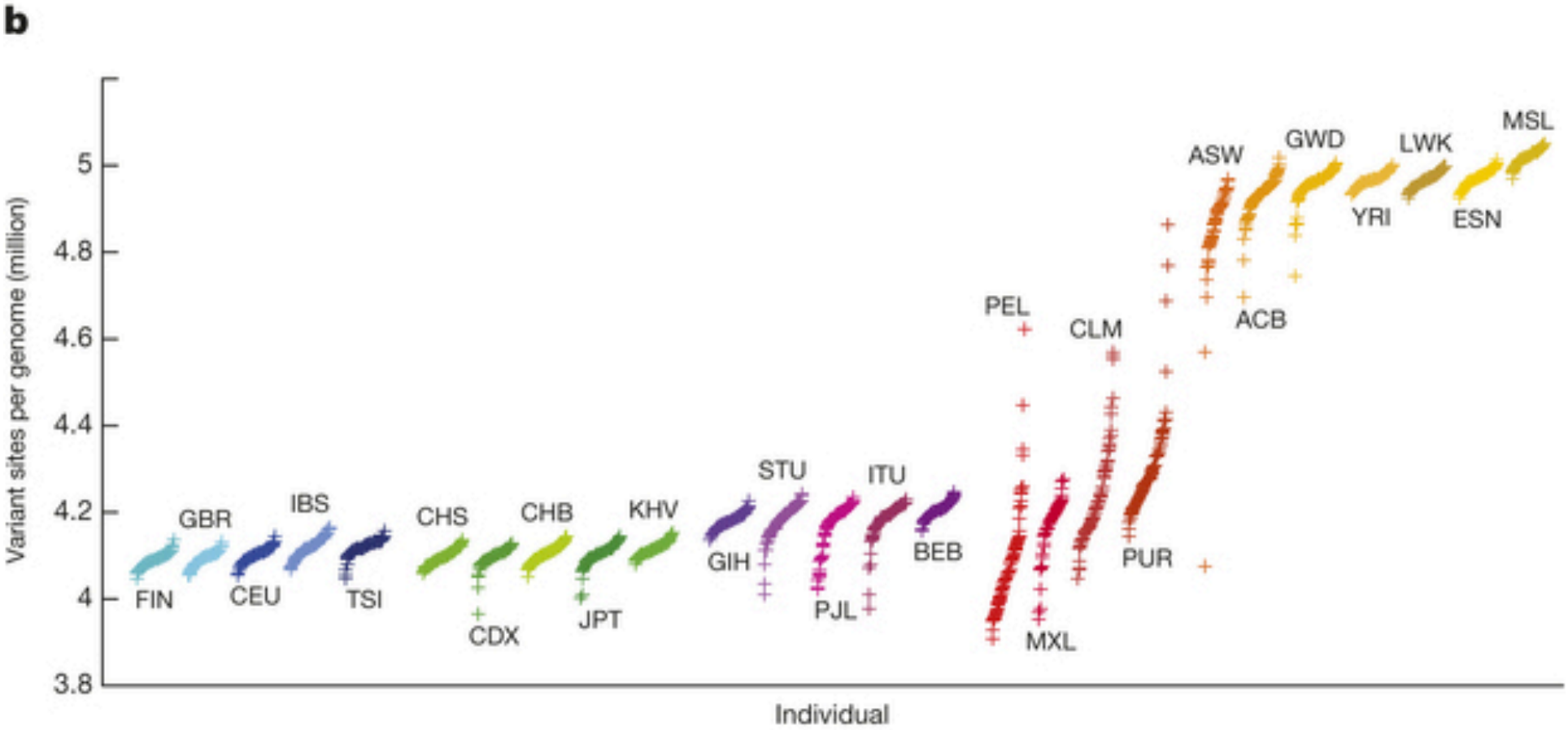


The 1000 Genomes Project Consortium; *Nature* **526**, 68–74 (01 October 2015) doi:10.1038/nature15393



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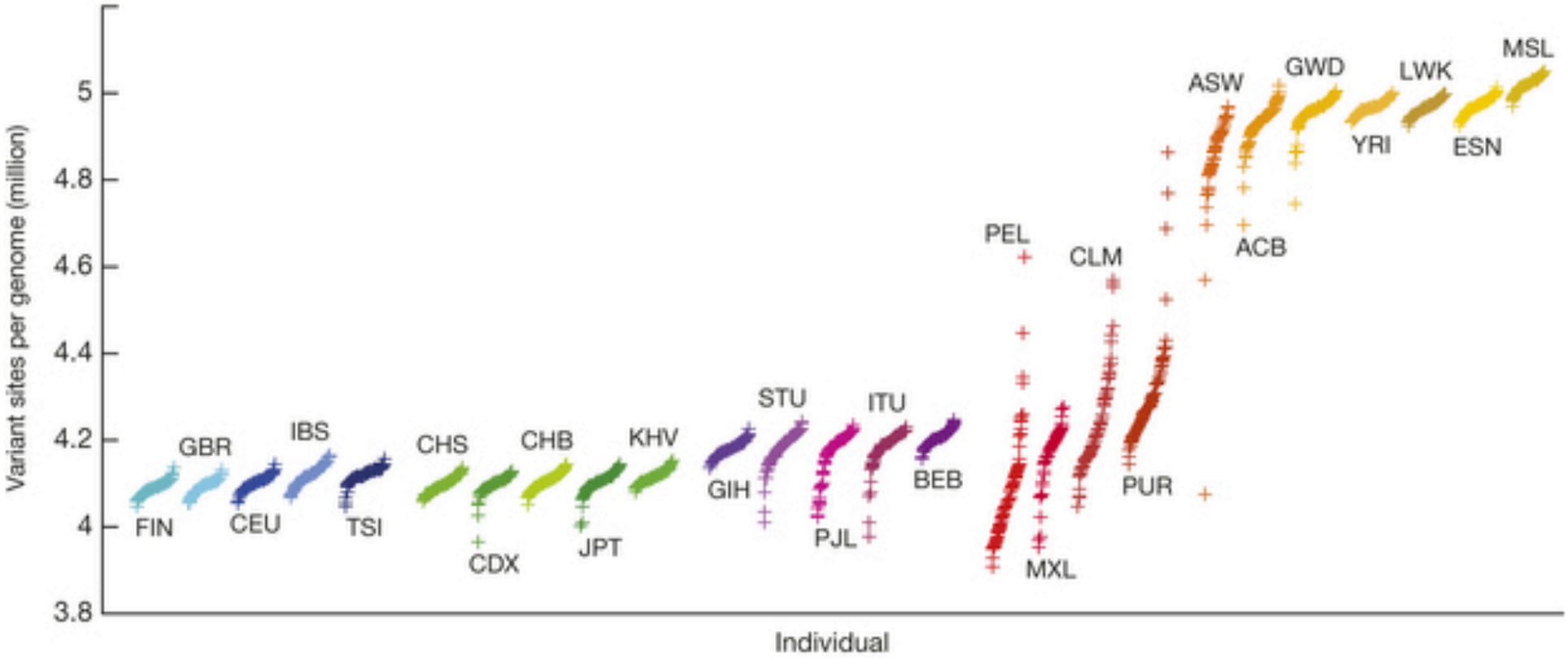
Why does the higher level of variants per genome support the out of Africa hypothesis of human evolution and migration?



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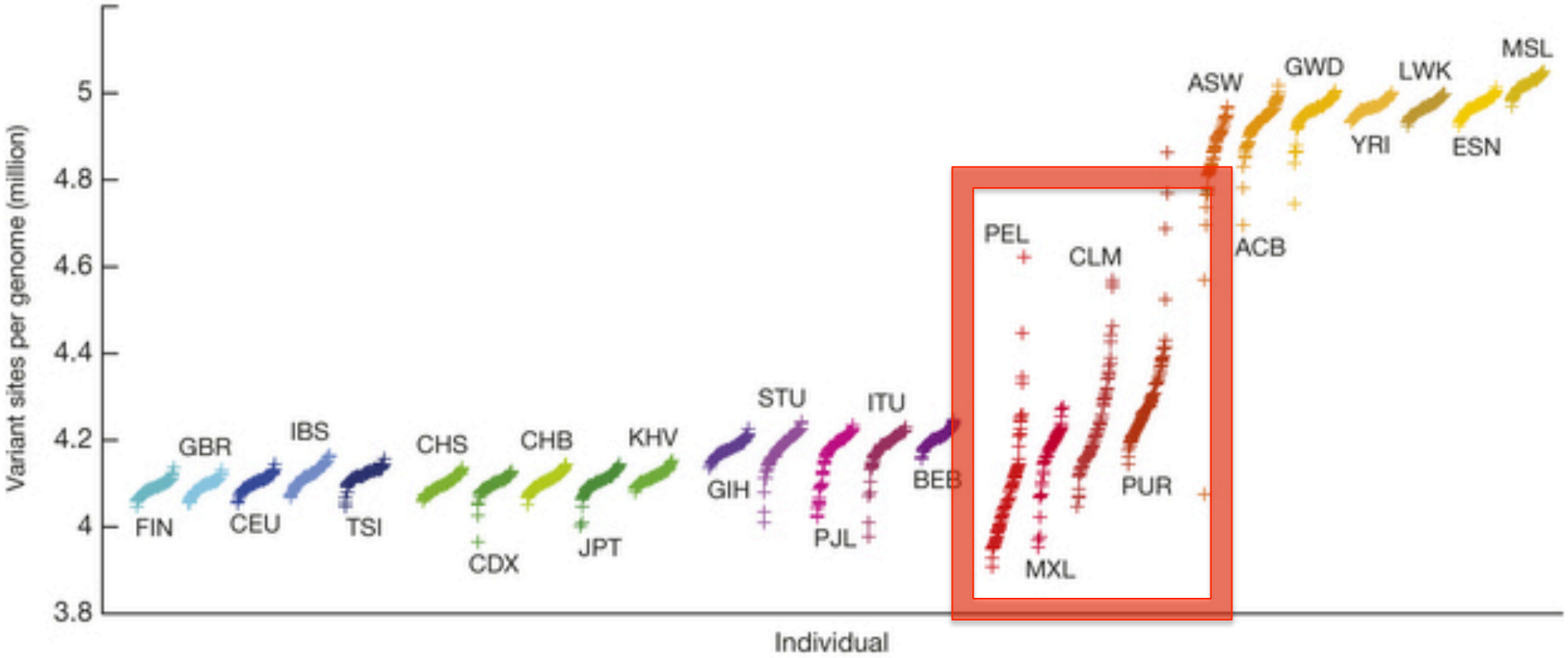
The populations not in Africa are more similar to each other than those within Africa, indicating a common set of ancestors from Africa (founder population), while within Africa, the least common ancestor is further back, evolutionarily.



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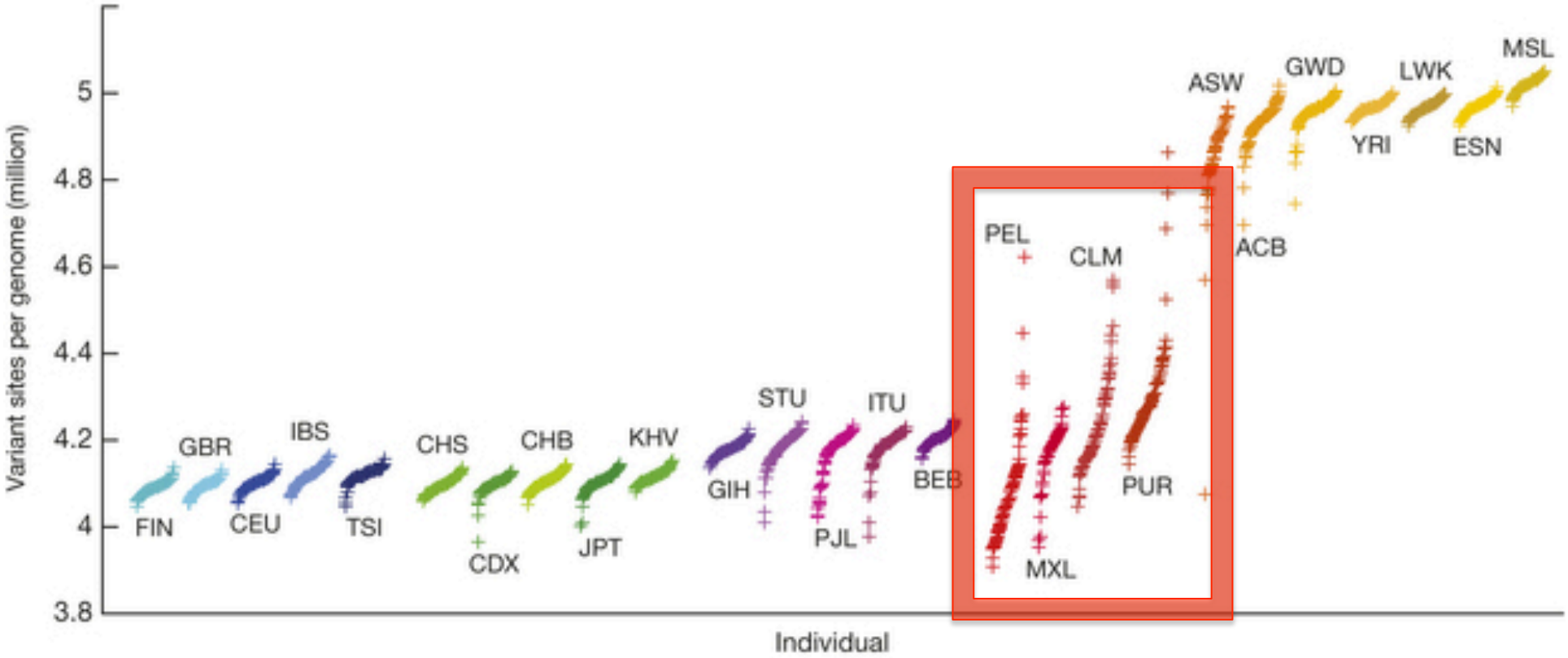
What's going on with these populations? Why do they seem to split the non-African and African patterns?



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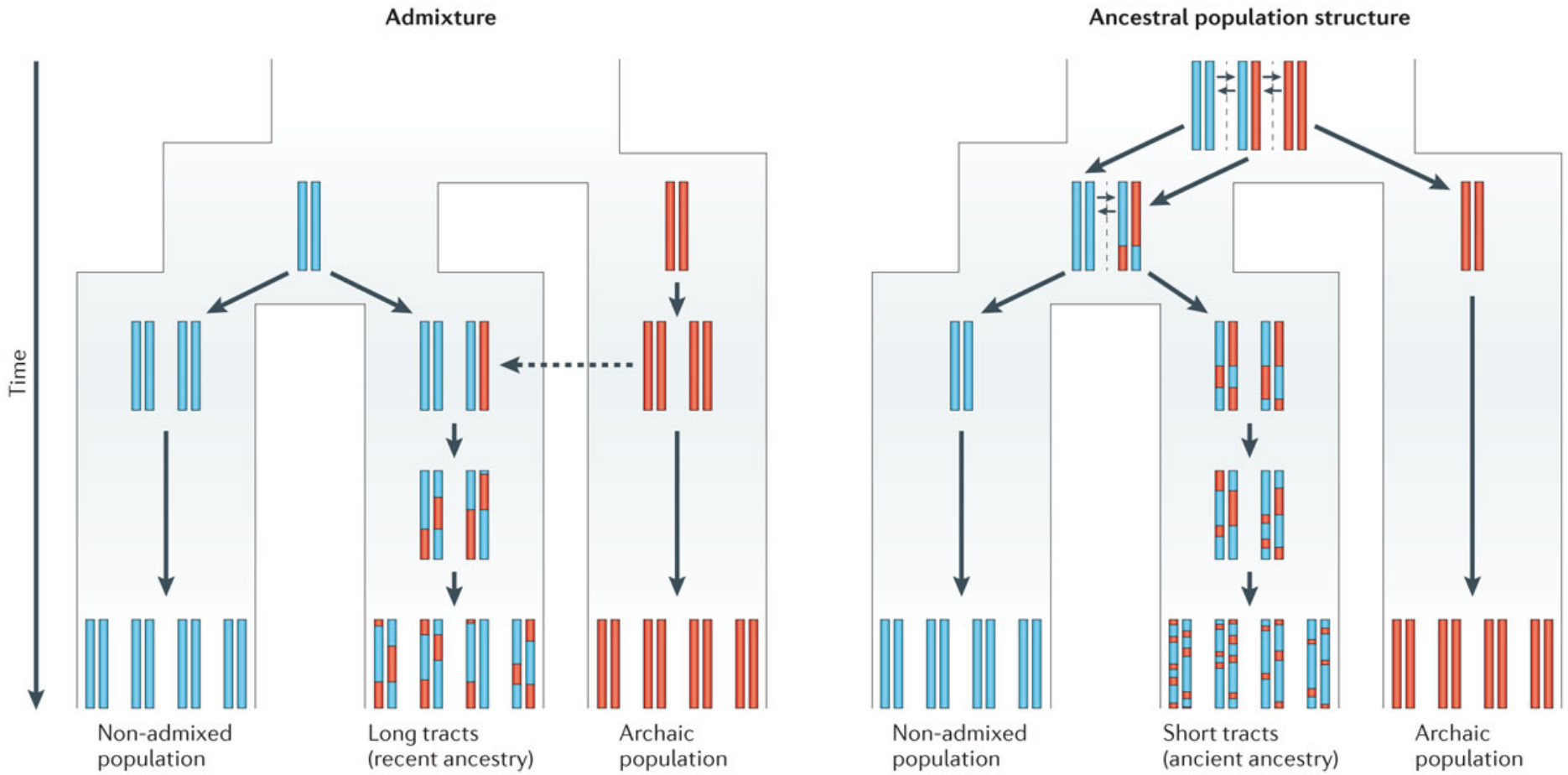
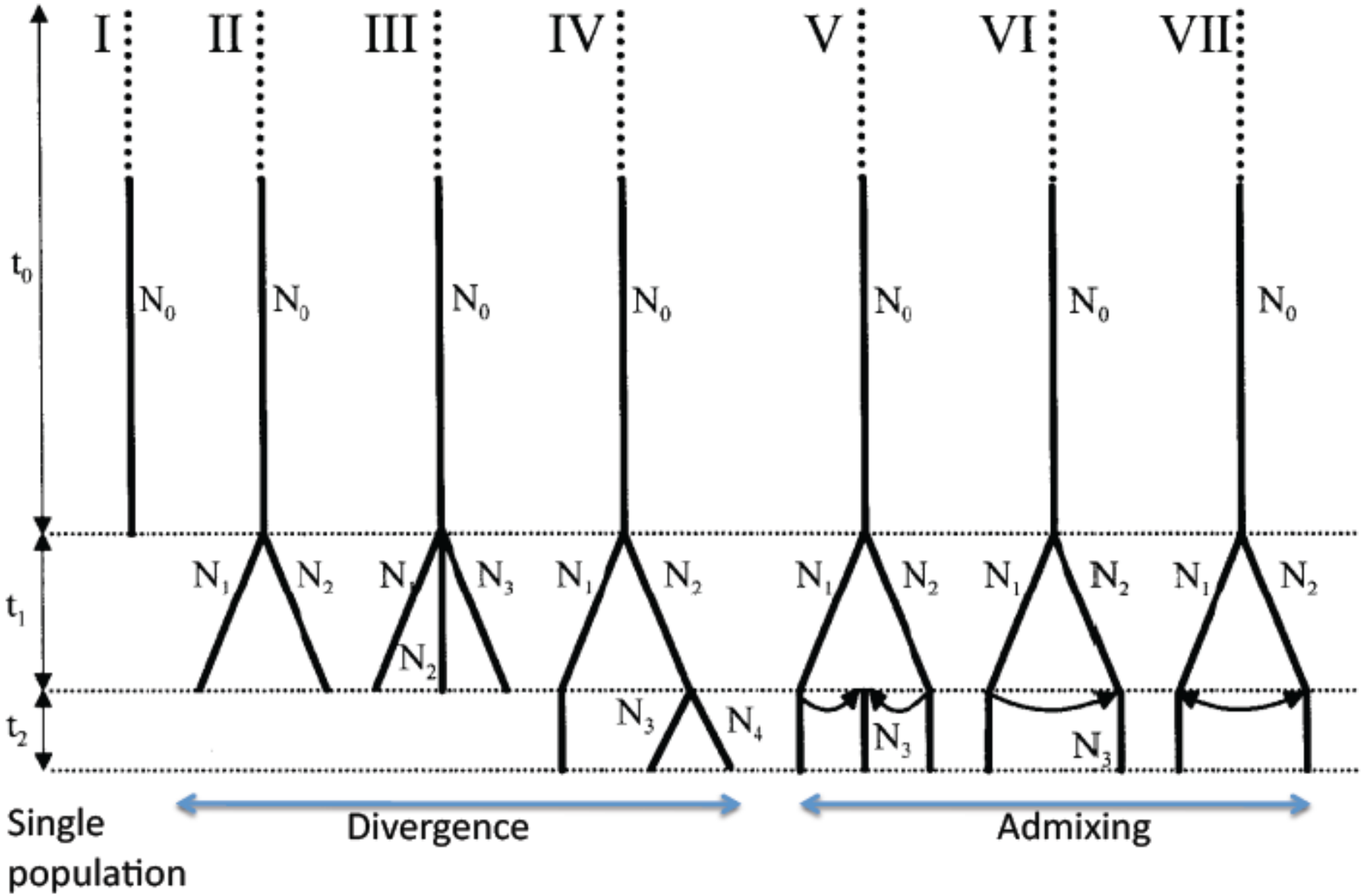
They are the populations that have the highest admixture of African with non-African. Mostly places that were central to the African slave trade.



Nature Reviews Genetics 16, 359–371 (2015) doi:10.1038/nrg3936



Adapted from Seyoung Kim

Which chromosome is not admixed or recombined? Is there other DNA in a cell that also transmits without change from generation to generation?

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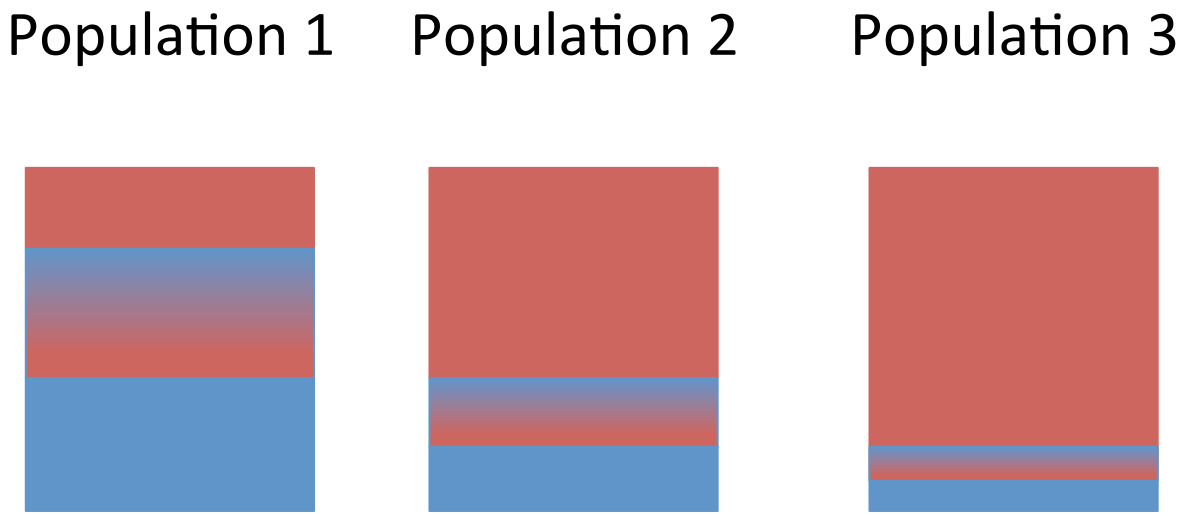
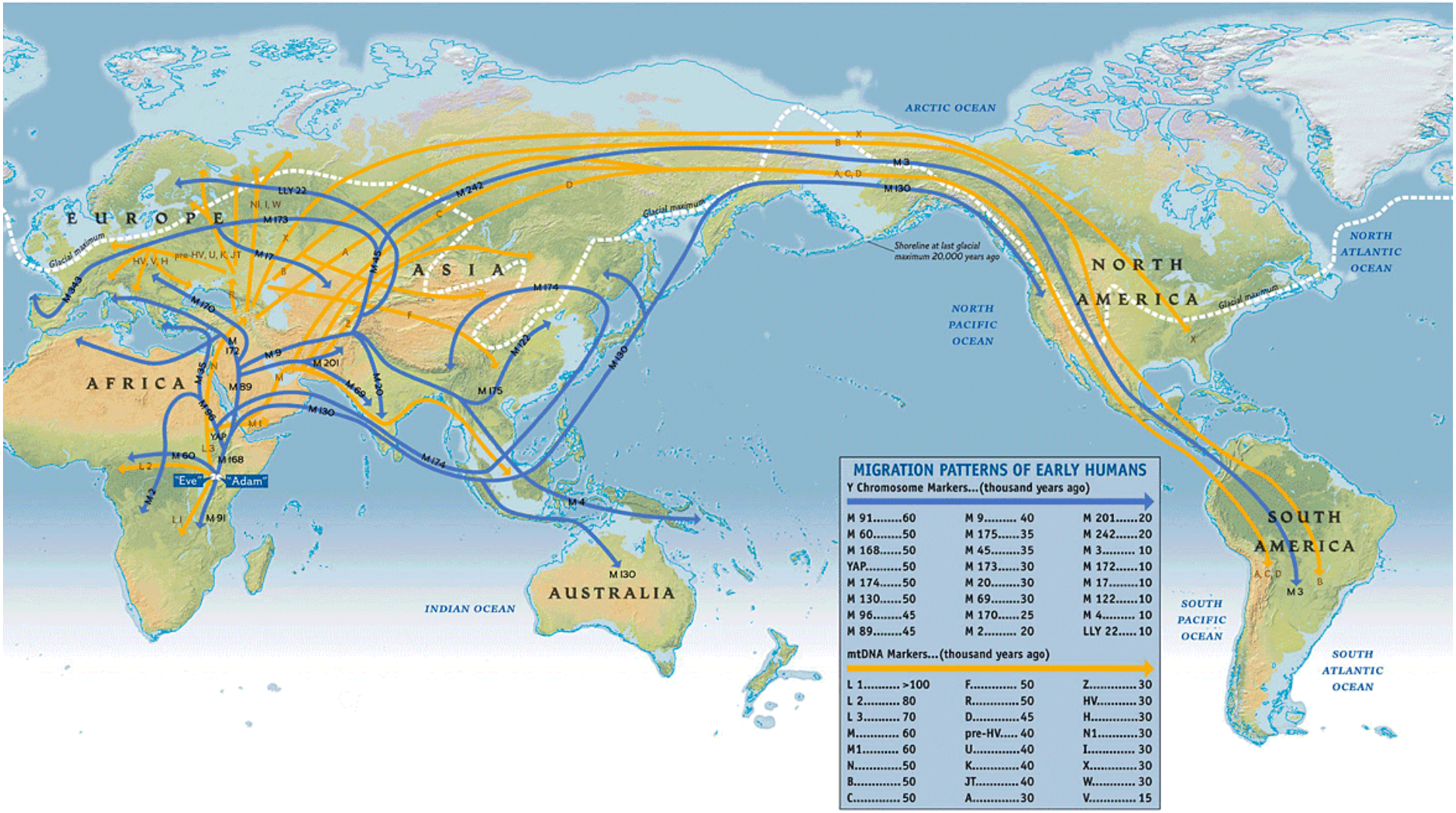
The Y chromosome doesn't have a pair, so can not recombine, and therefore doesn't get admixed.

Mitochondrial DNA is transmitted intact from the maternal line

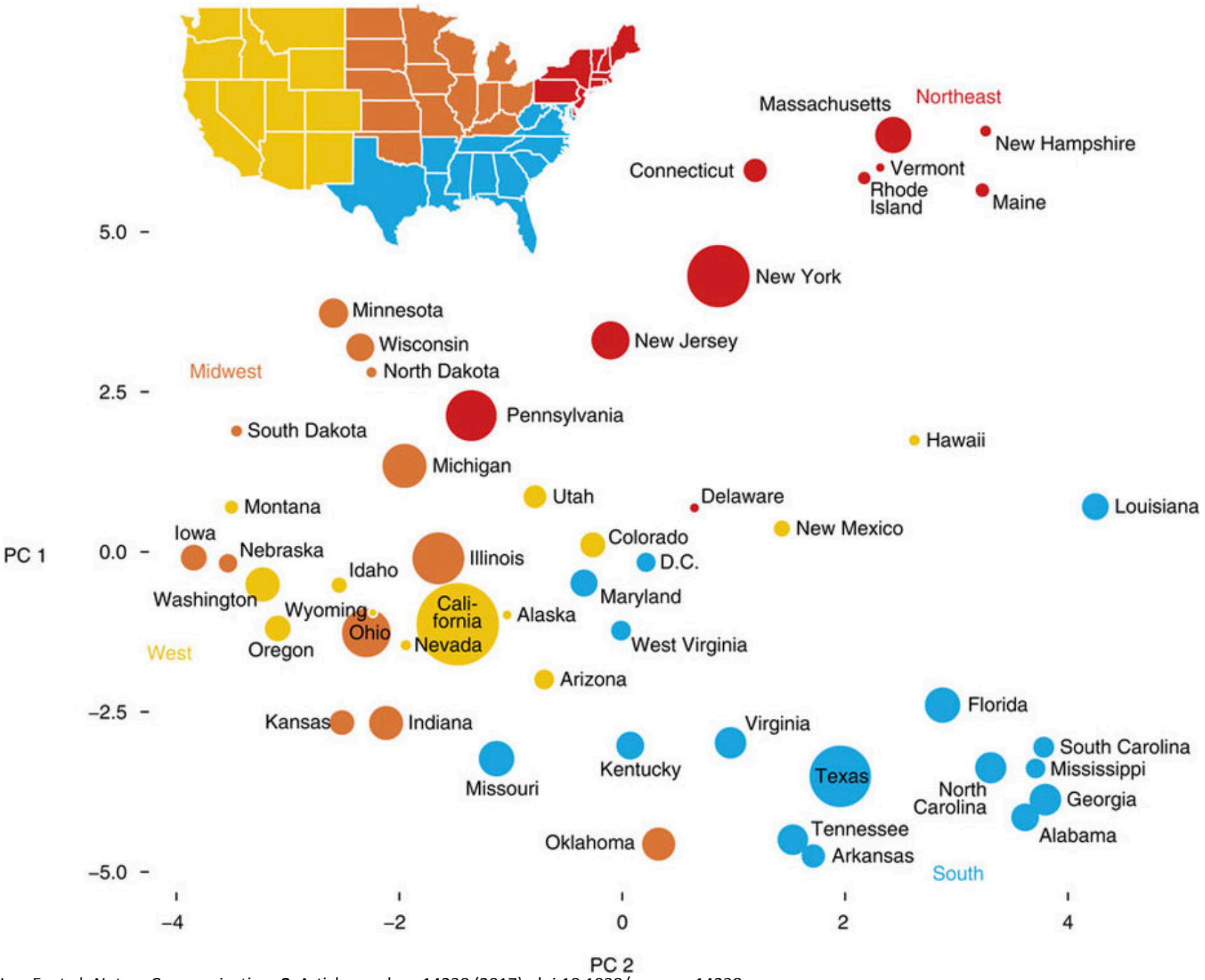
Because the allele probabilities change during evolution/migration/drift, different populations will have different probabilities of a given allele.



Allows us to predict ancestry, but also gets in the way of determining what alleles associate with a phenotype



https://genographic.nationalgeographic.com/



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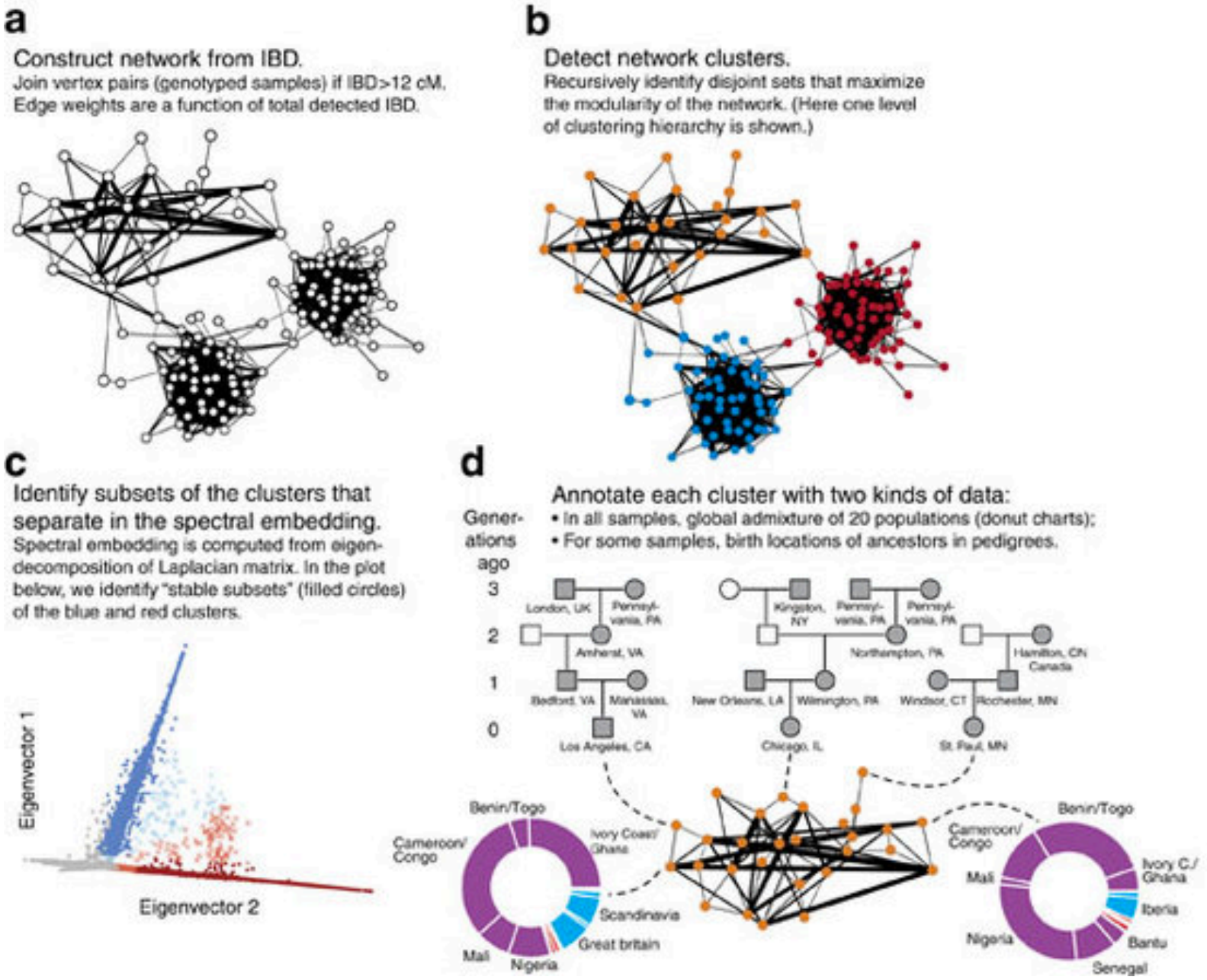

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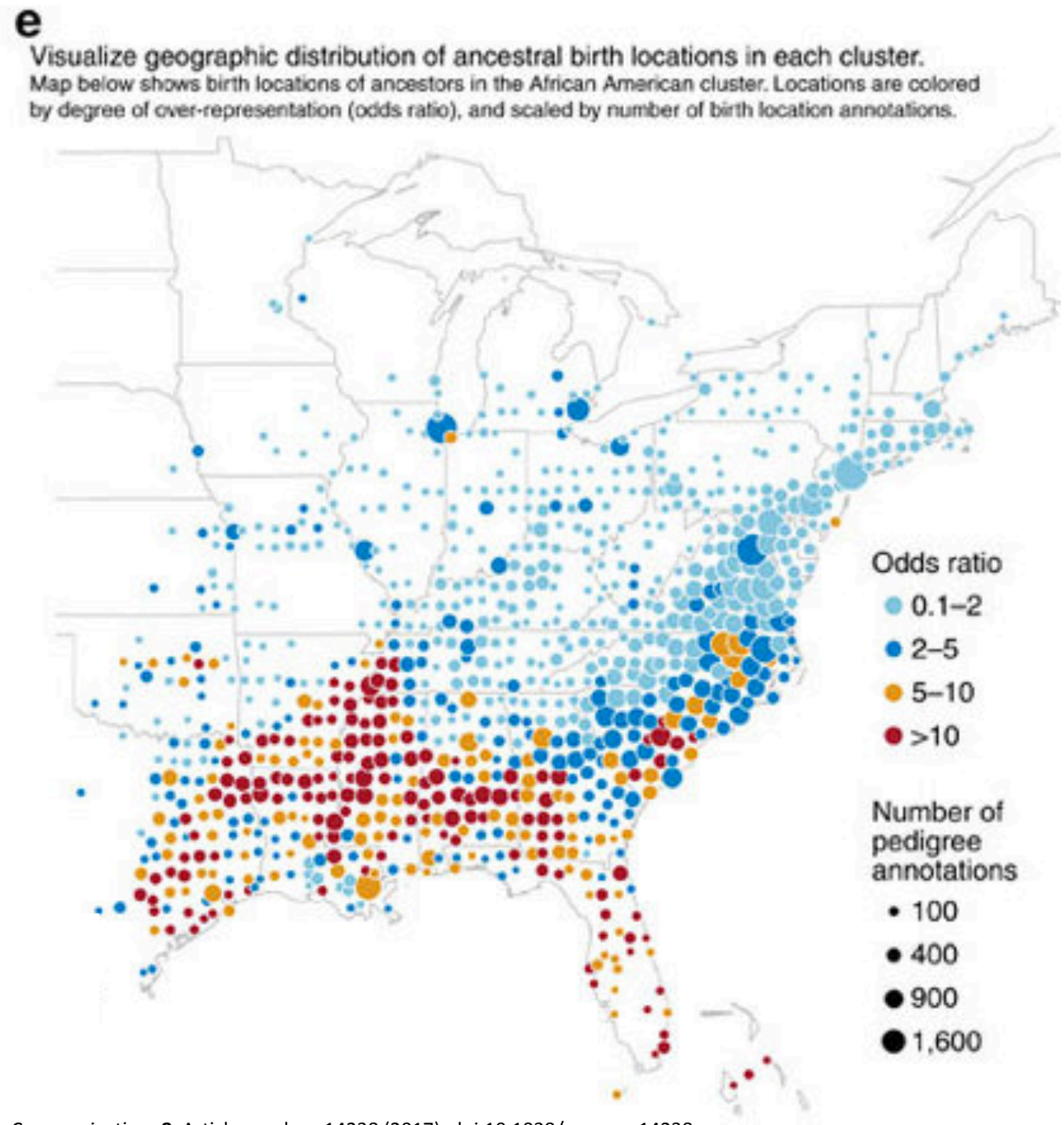

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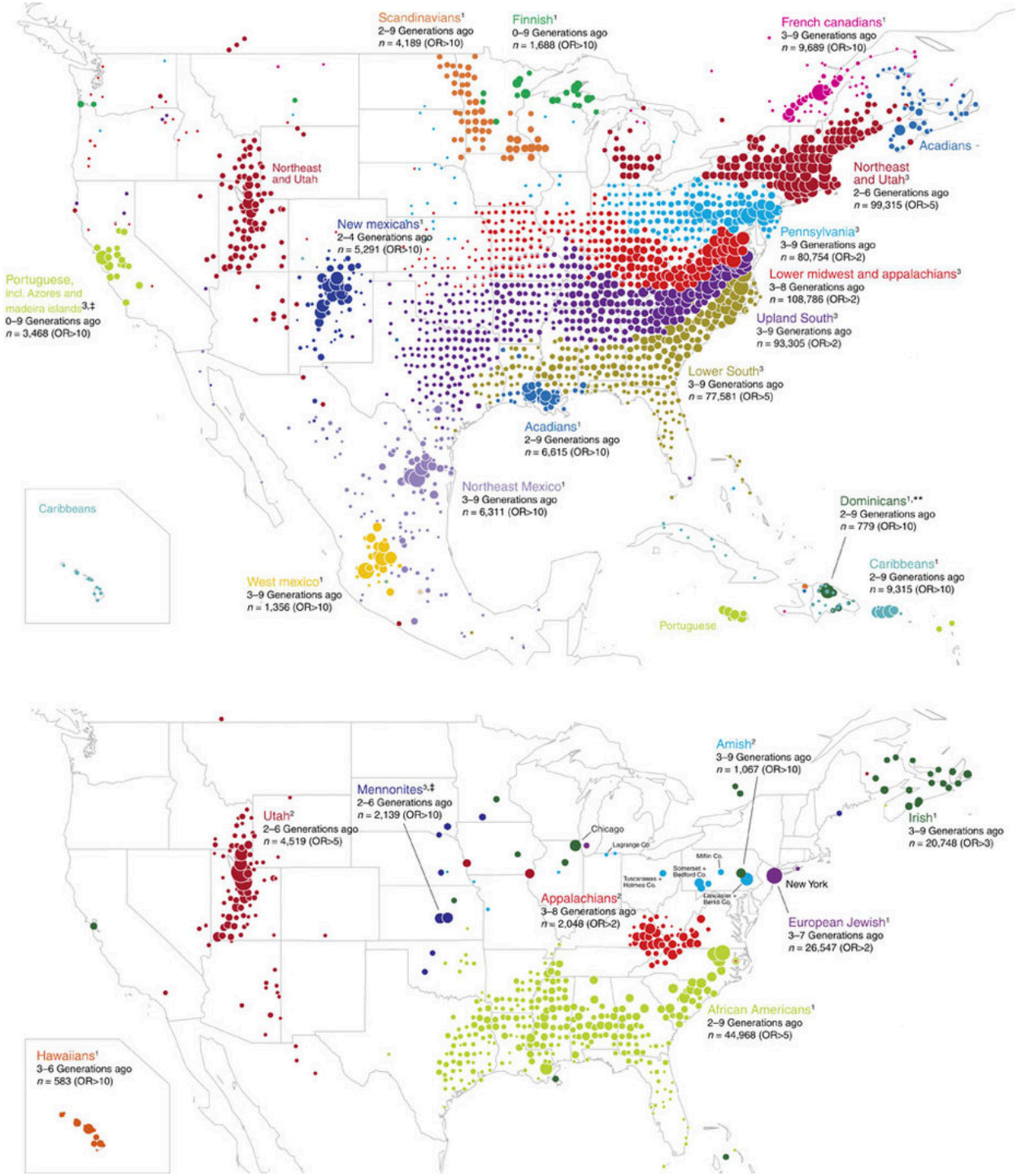

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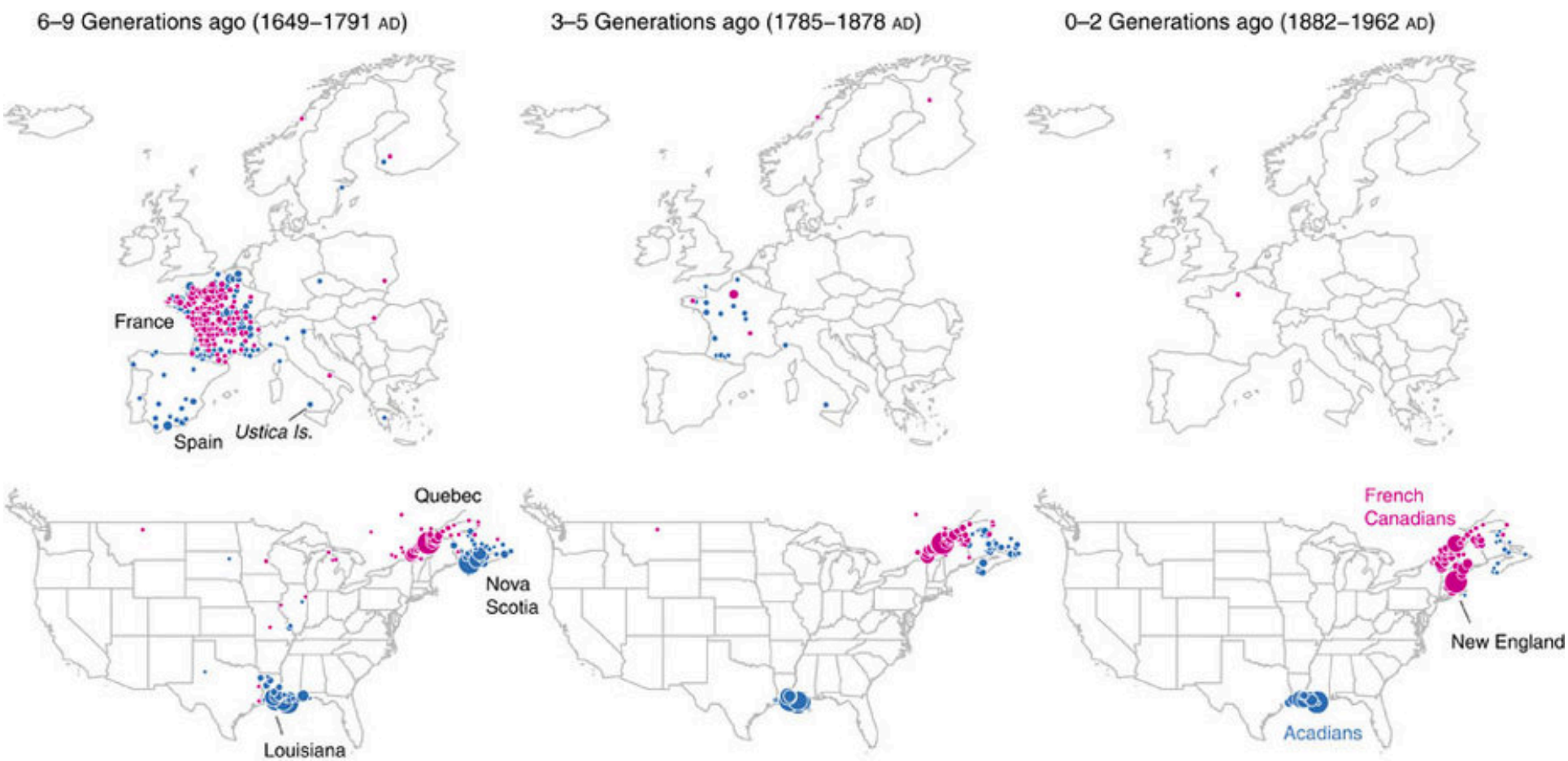

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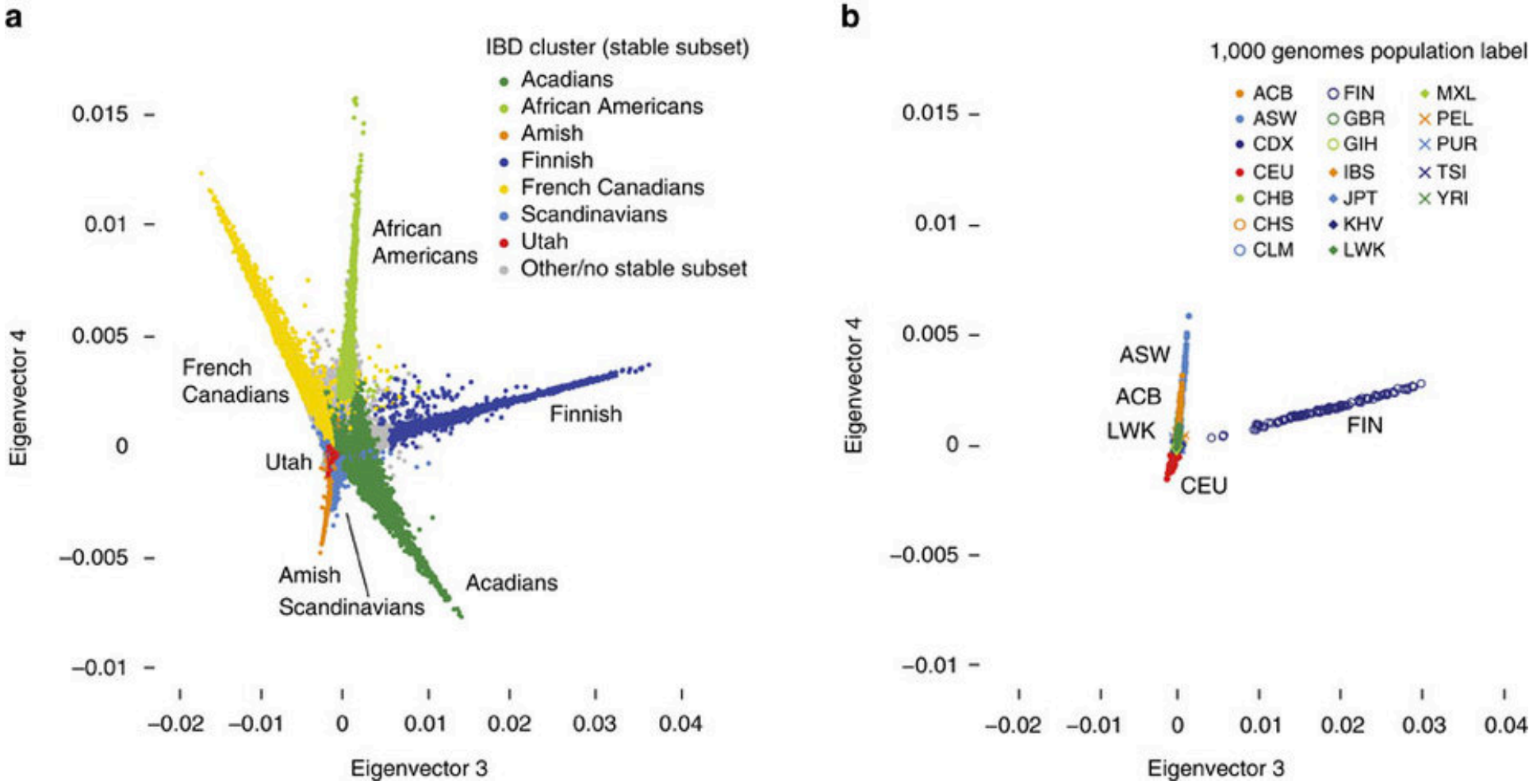

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Far more information than in 1000 Genome Project! Greater diversity in some ancestries

Difficulties in their data

- Some populations had poor ancestry data
  - African–Americans
  - Ashkenazi Jews
- Data still very biased toward European ancestry
- The way they biased the data to increase resolution in recent ancestry, omits populations that are less distincitve/more admixed
  - African-Americans communities in Northern cities for generations

Implications of this study

- Exciting that we can trace migrations so tightly
- Private data set
  - Ancestry.com is not a public repository
    - Company grew out of LDS genealogy projects
  - They got their data by having people pay for their own data

Summary

Next Class

- Guest speaker on genomics of breast and ovarian cancer
- Please come prepared to ask questions