Computational Life Science Seminar

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ARTICLES
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nature genetics

Corrected: Publisher Correction

Inferring whole-genome histories in large population datasets

Jerome Kelleher*, Yan Wong, Anthony W. Wohns, Chaimaa Fadil, Patrick K. Albers and Gil McVean

What does this **Title** reveal?

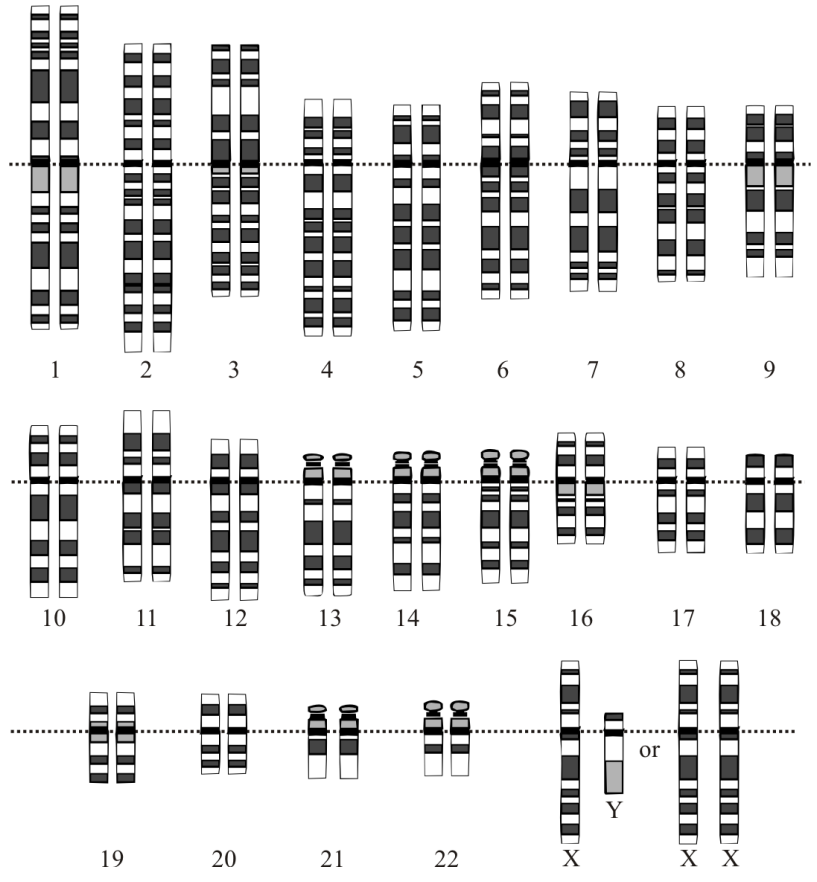
Inferring whole-genome histories in large population datasets

SYNONYMS FOR *inferring*

- ascertain
- assume
- construe
- deduce
- derive
- interpret
- presume
- presuppose
- reckon
- speculate

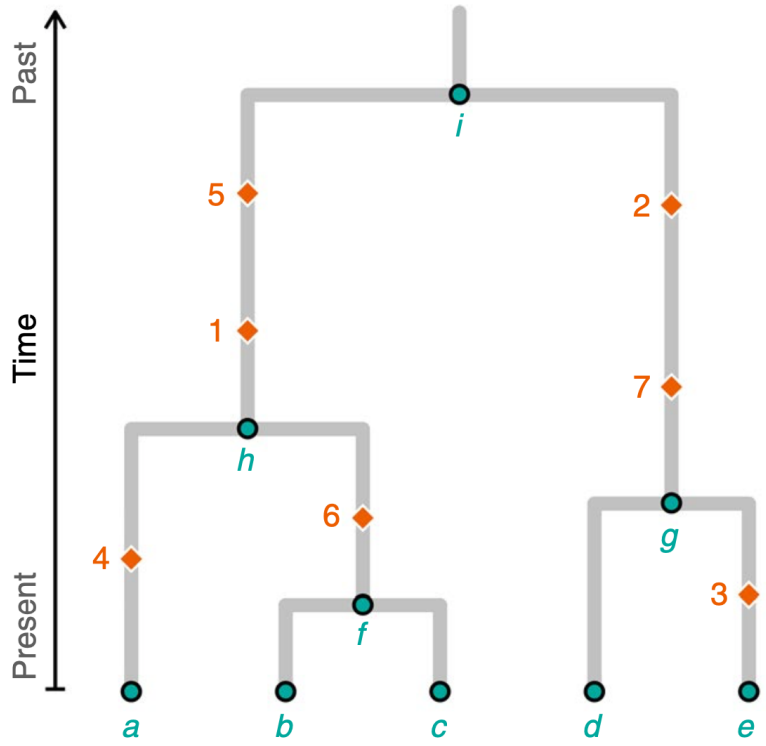
source: thesaurus.com

Inferring whole-genome histories in large population datasets



source: National Human Genome Research Institute

Inferring whole-genome **histories** in large population datasets



source: Kelleher et al., 2019

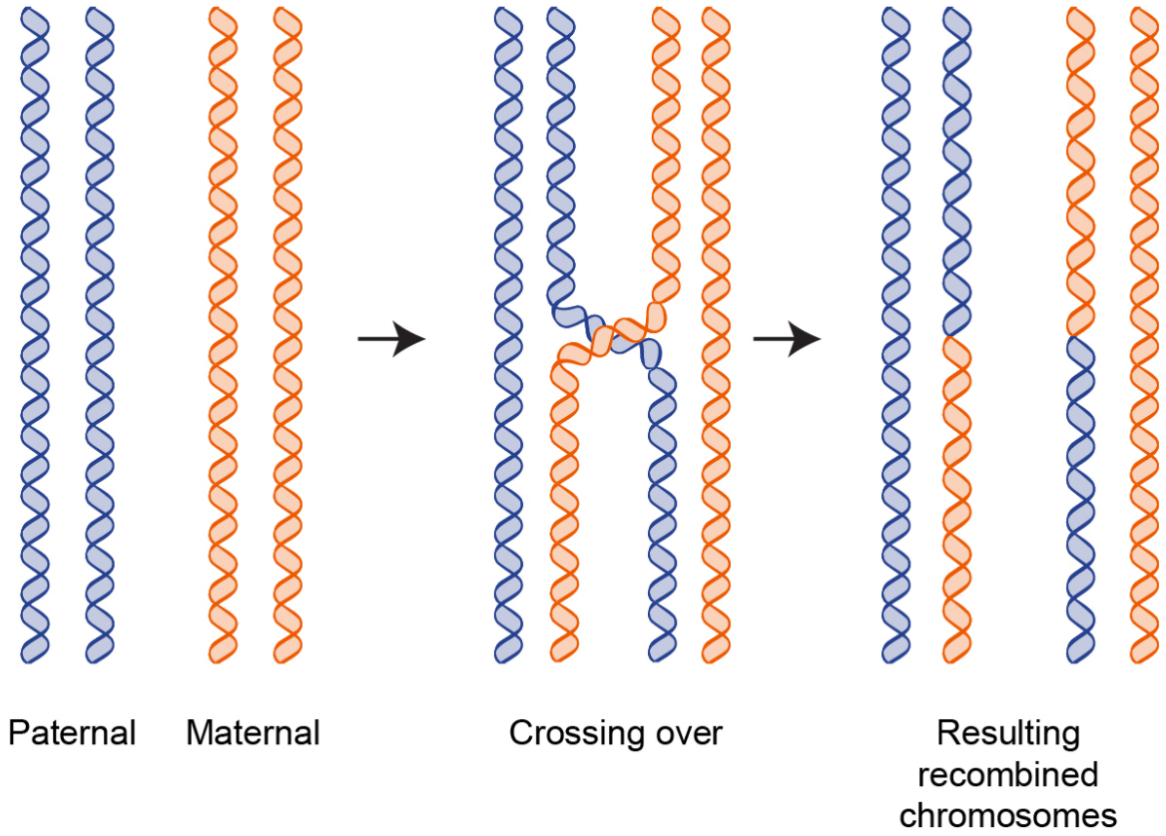
Inferring whole-genome **histories** in large population datasets

Sample haplotype	Position	1	2	3	4	5	6	7	8	9	10
	P1	A	T	A	A	C	G	G	G	C	A
	P2	T	T	G	G	C	G	G	G	C	A
	M1	T	T	A	A	C	G	G	G	C	A
	M2	T	T	A	A	C	G	G	C	C	A
	C1	A	T	A	G	C	G	G	G	C	A
	C2	T	T	G	G	C	T	G	C	C	A

Paternal
Maternal
Child

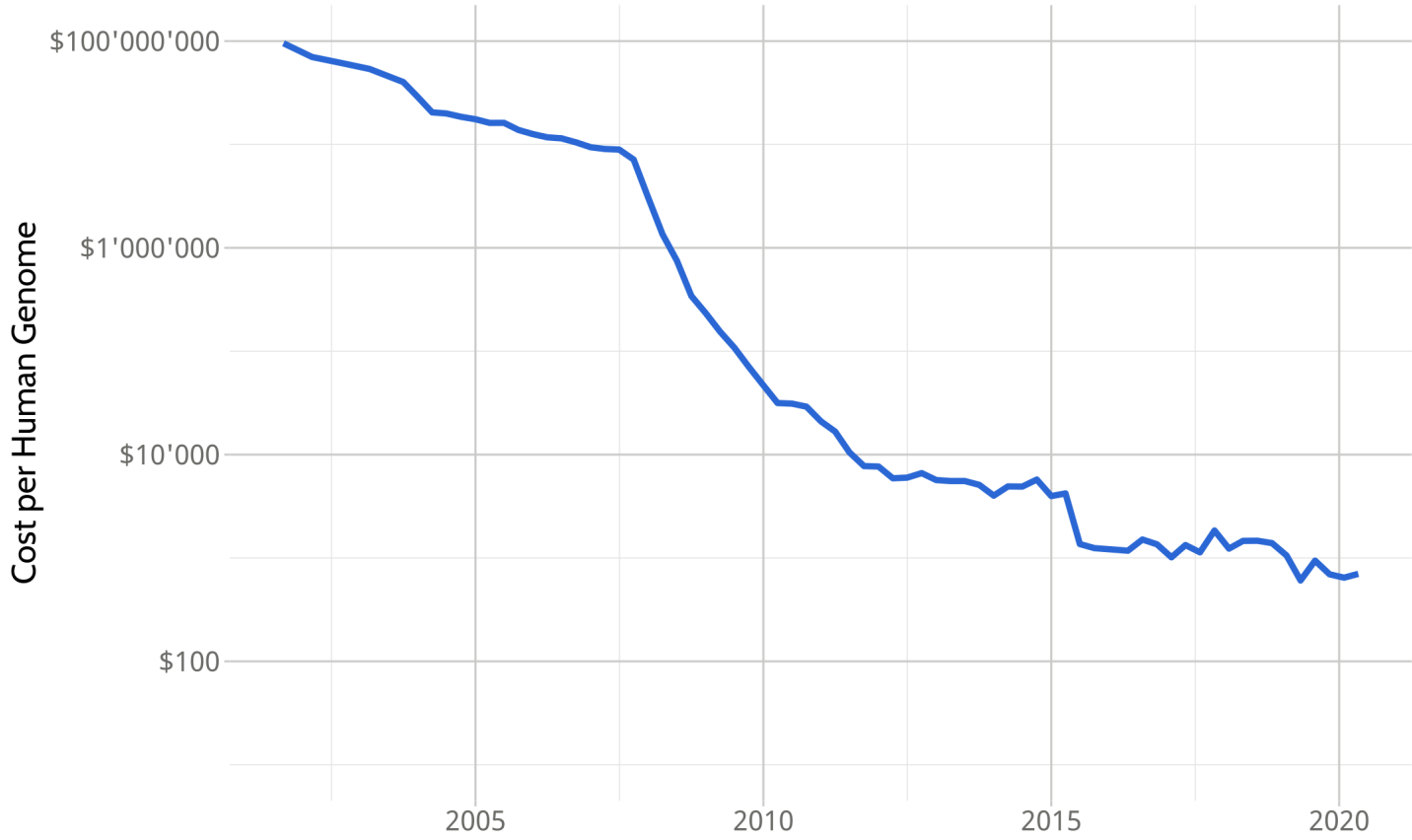
{A, T, G, C} ancestral
{A, T, G, C} derived

Inferring whole-genome histories in large population datasets



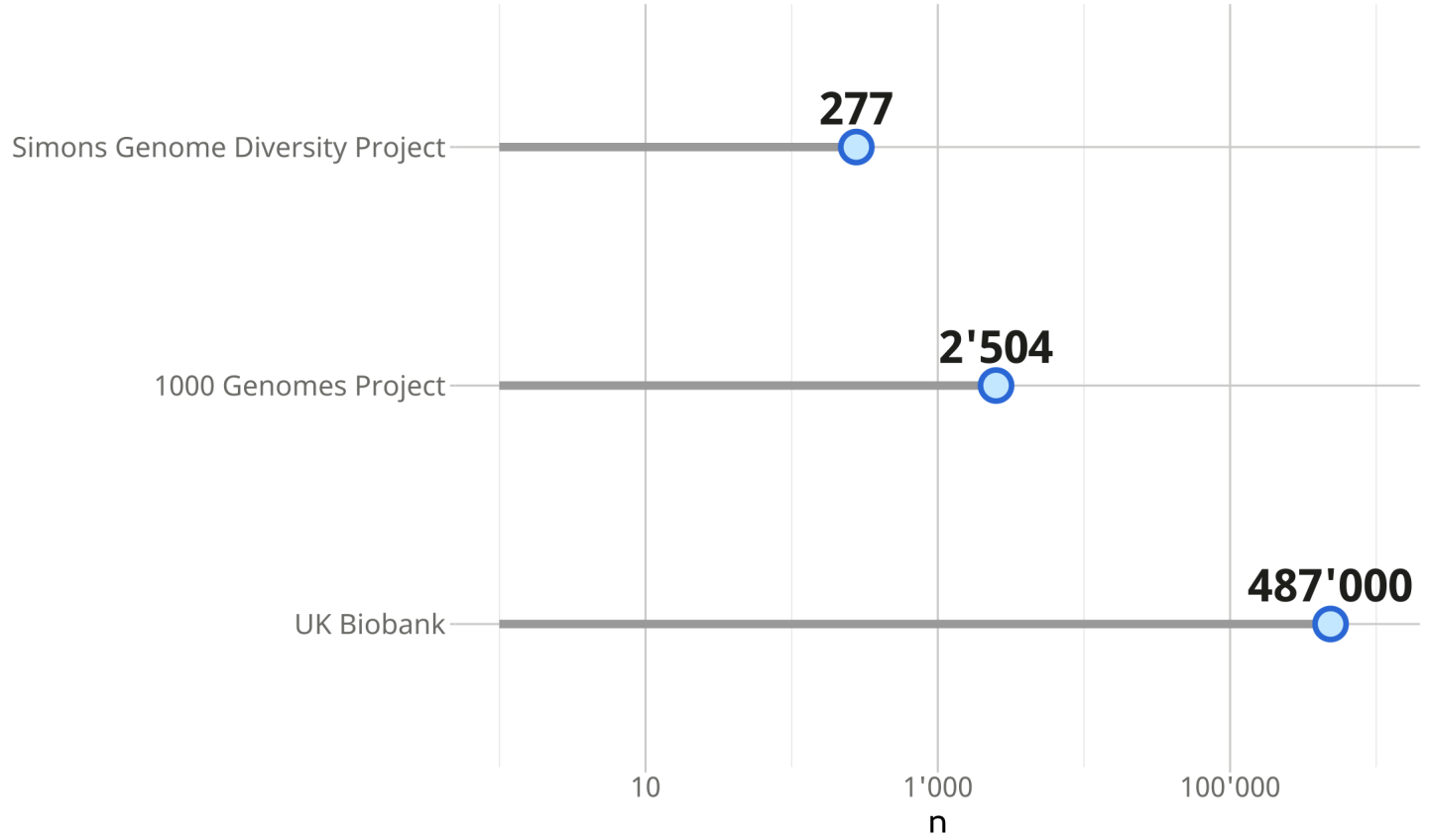
source: genome.gov

Inferring whole-genome histories in large population datasets



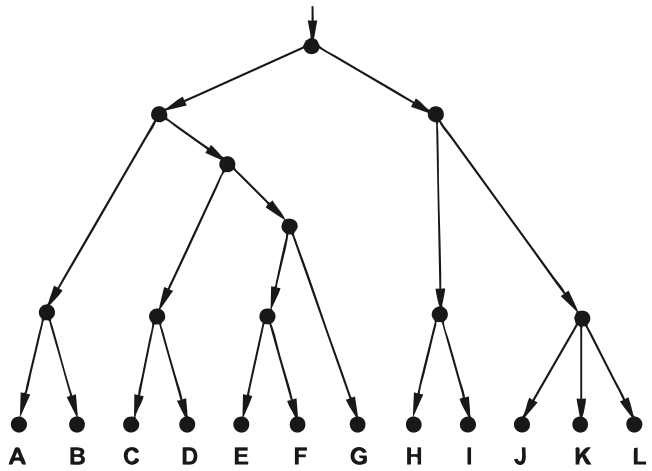
source: genome.gov/sequencingcosts

Inferring whole-genome histories in large population datasets



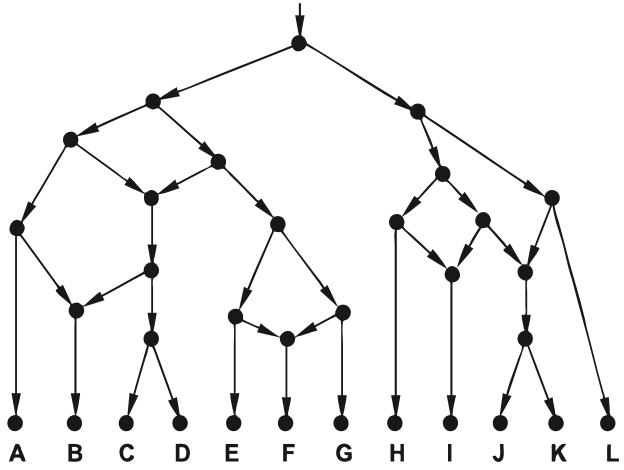
Current situation

Tree



source: Adapted from Morrison, 2016

Network

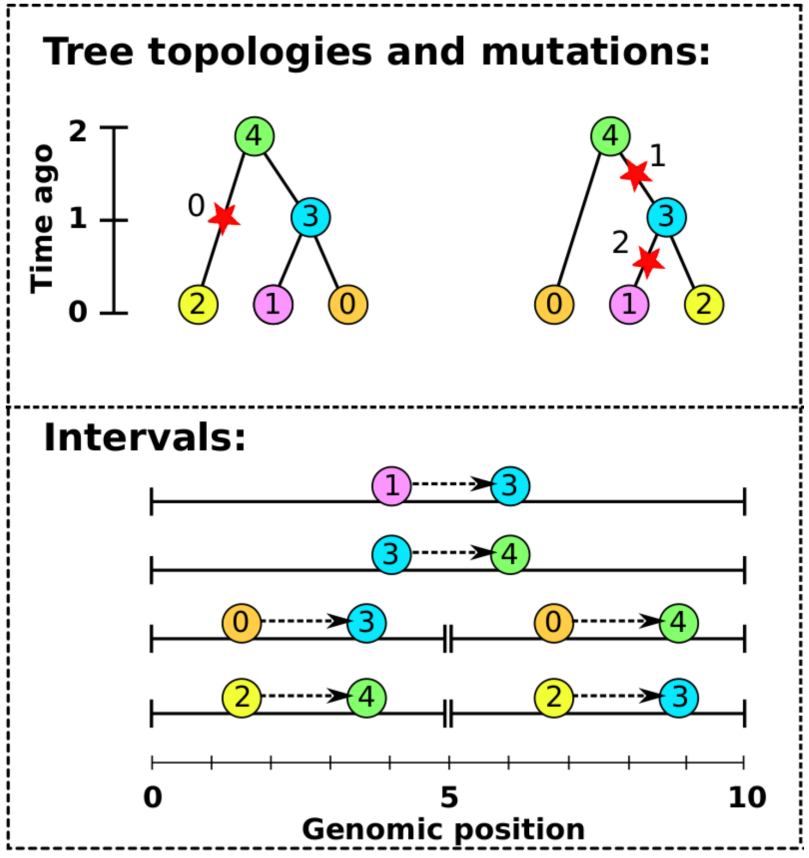


source: Adapted from Morrison, 2016

What's the Author's proposed **Solution**?

source: github.com/tskit-dev

tree sequence



source: Kelleher et al., 2018

Nodes:

ID	time
0	0.0
1	0.0
2	0.0
3	1.0
4	2.0

Edges:

left	right	parent	child
0	10	3	1
0	10	4	3
0	5	3	0
0	5	4	2
5	10	3	2
5	10	4	0

Sites:

ID	position	ancestral state
0	2.5	A
1	7.5	G

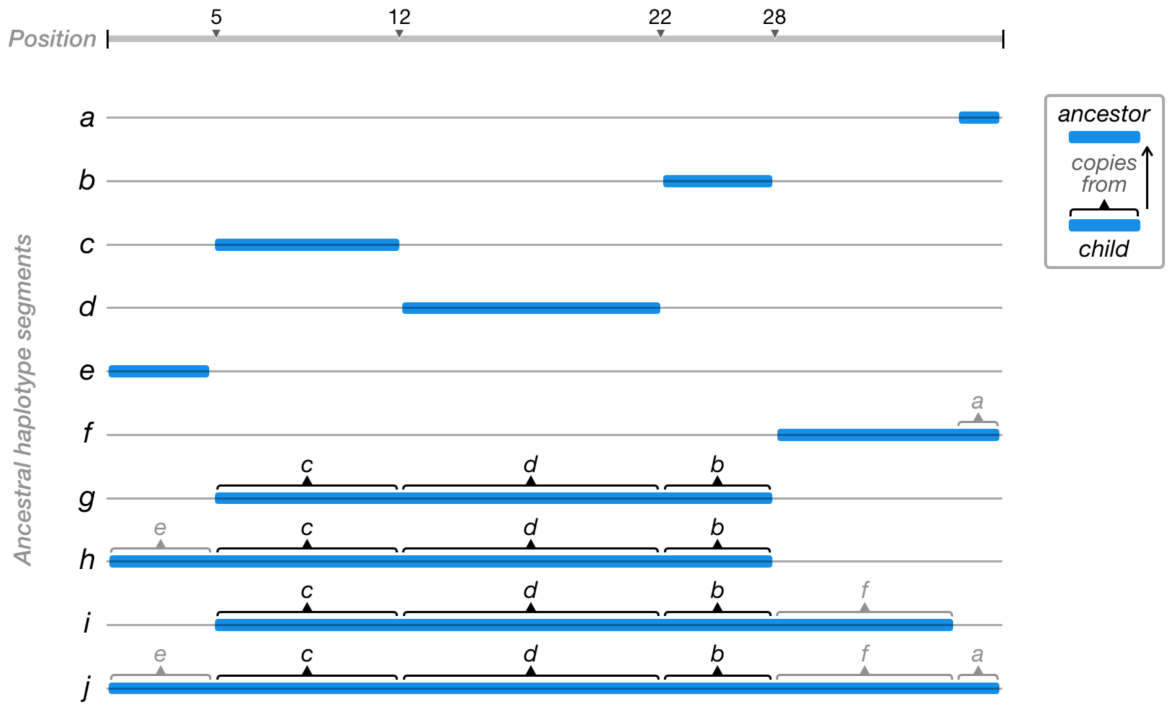
Mutations:

ID	site	node	derived state
0	0	2	T
1	1	3	C
2	1	1	G

source: Kelleher et al., 2018

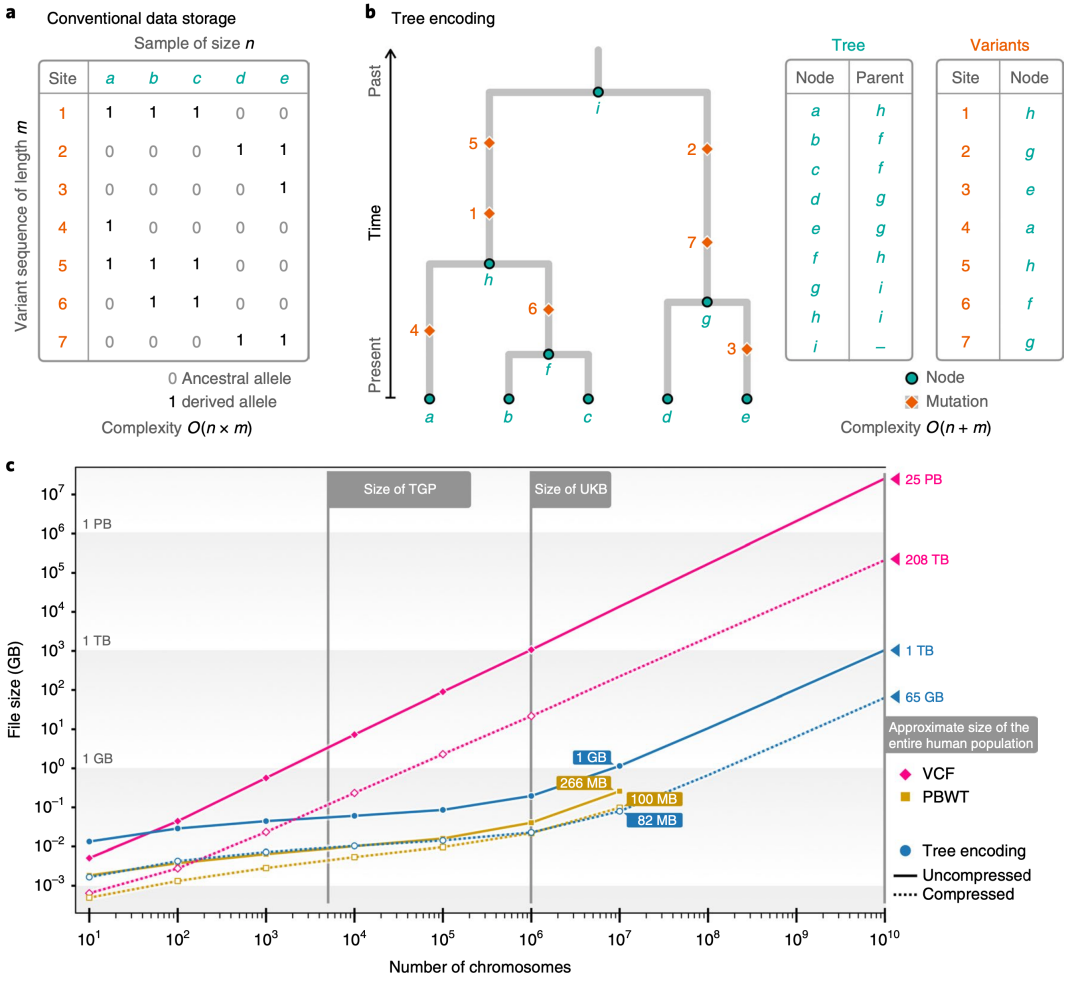
tsinfer

Building ancestors and inferring edges



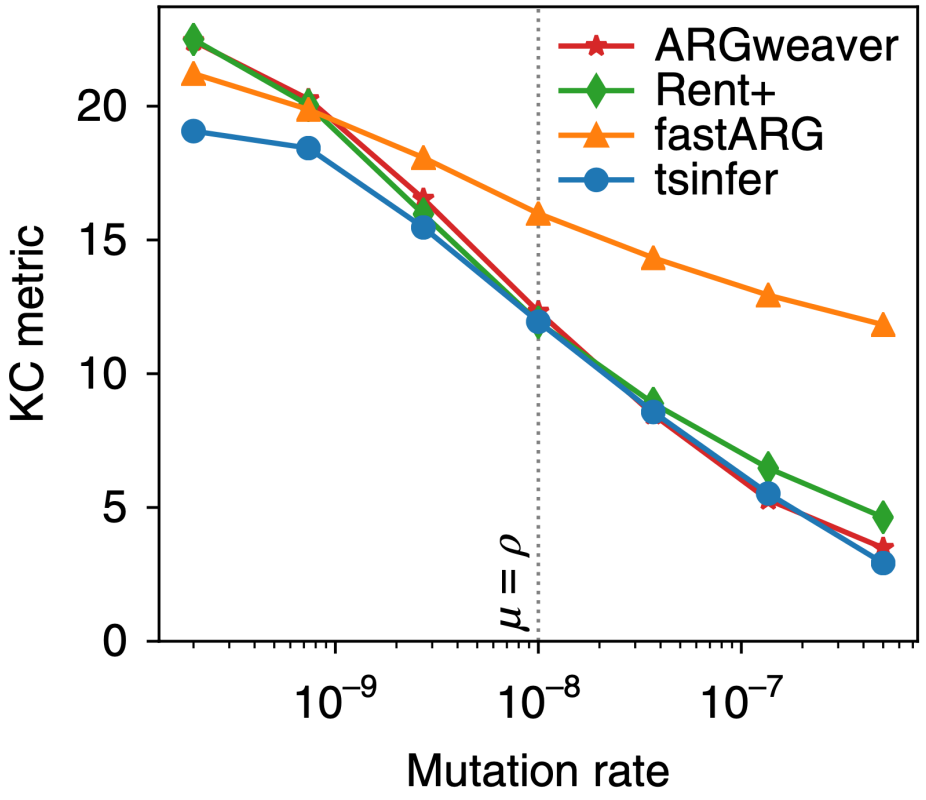
source: Kelleher et al., 2019

Comparison to state-of-the-art Storage Space



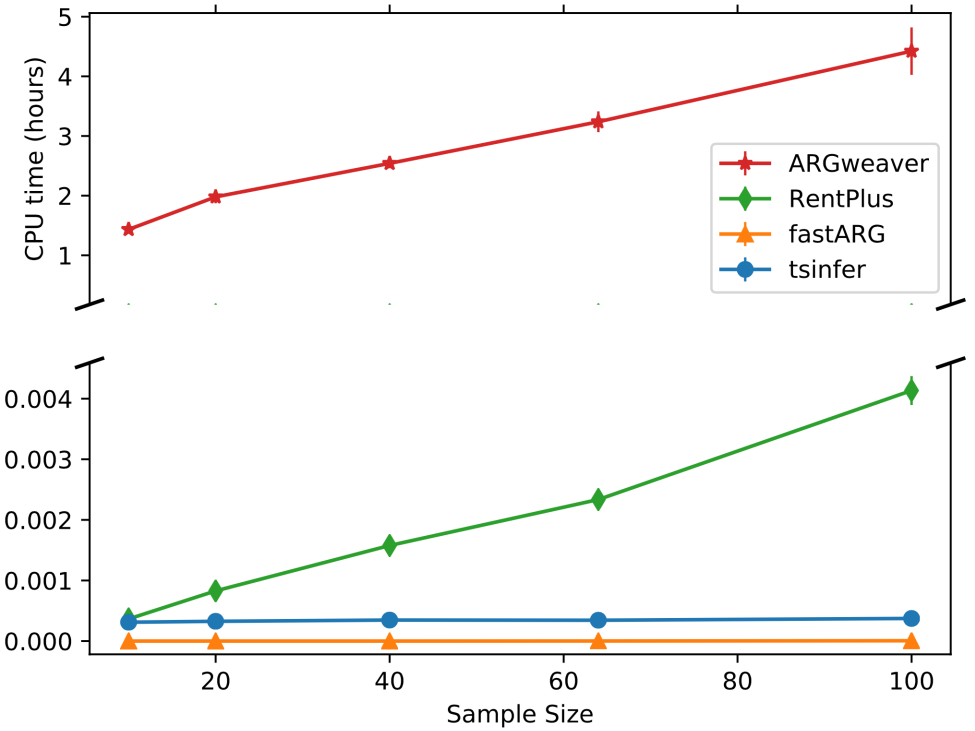
source: Kelleher et al., 2019

Comparison to state-of-the-art



source: Kelleher et al., 2019

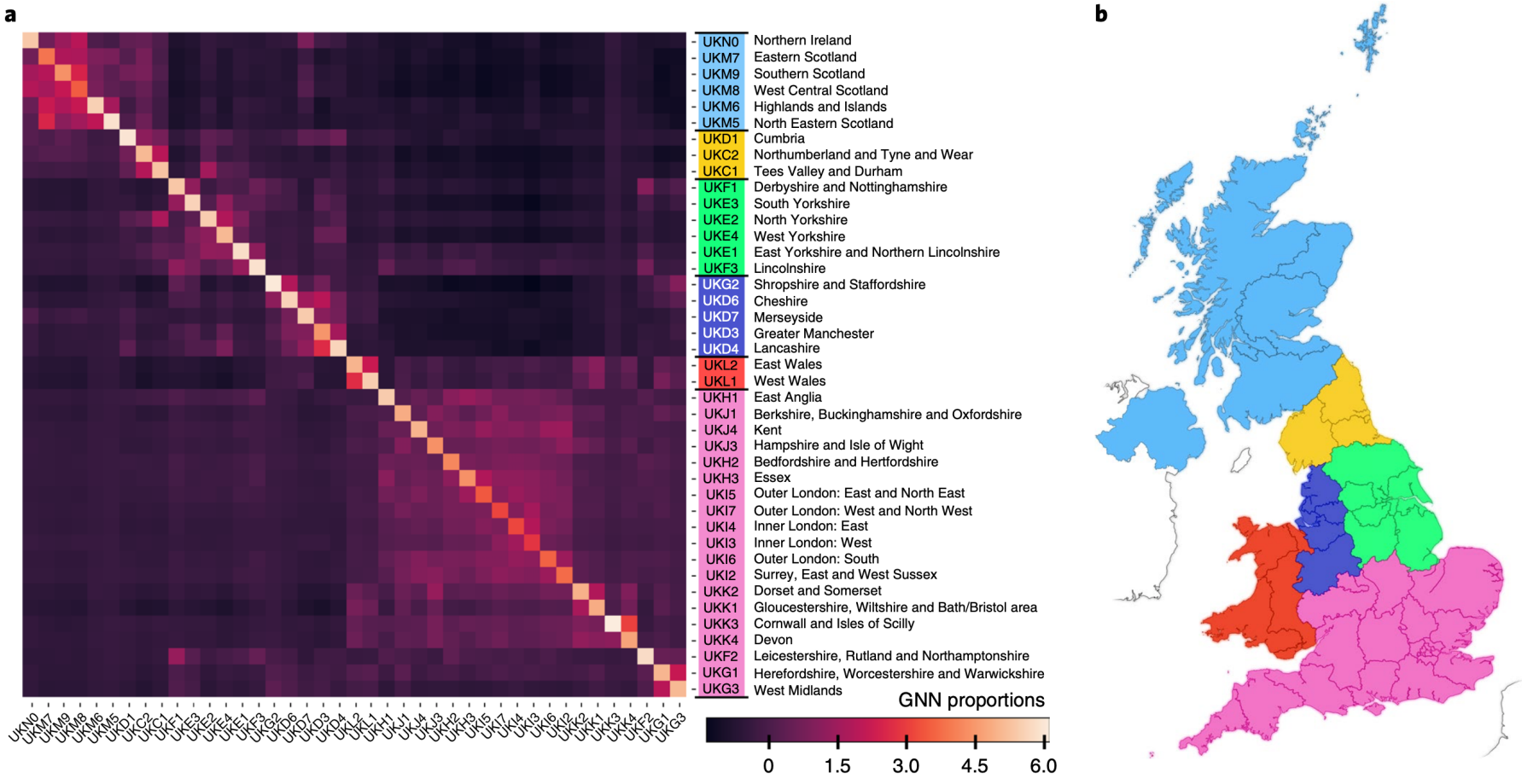
Accuracy and **Speed**



source: Kelleher et al., 2019

Application example

UK Biobank population structure



source: Kelleher et al., 2019

Limitations

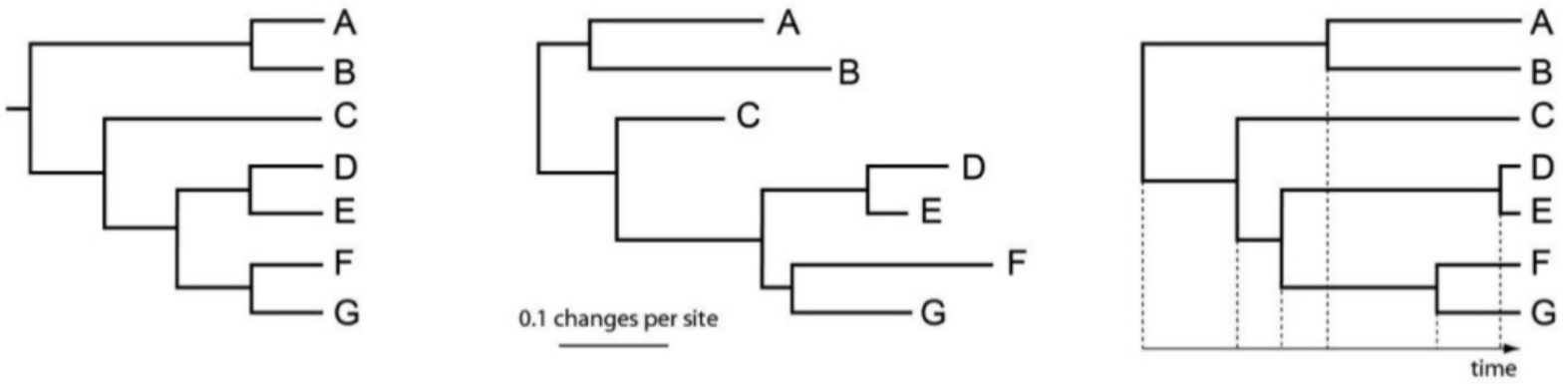
assumed each mutation has a single origin

mutation/recombination ratio has to be sufficiently high

only ordering of tree nodes (relative age)

Drawbacks

Cladogram vs. Phylogram vs. Chronogram



source: Riutort, 2016

Outlook

From topologies to branch lengths (`tsdate`)

Improved sequencing technologies

Possible application for genomes of other Species

Genome Watch | Published: 21 September 2020

Recombination should not be an afterthought

Russell Y. Neches ✉, Matthew D. McGee & Nikos C. Kyrpides

Nature Reviews Microbiology **18**, 606(2020) | Cite this article

1073 Accesses | **17** Altmetric | Metrics

This month's Genome Watch highlights how the search for the origins of SARS-CoV-2 emphasizes the need for integrated phylogenetic methods.

RESEARCH ARTICLE

Bayesian inference of reassortment networks reveals fitness benefits of reassortment in human influenza viruses

Nicola F. Müller, Ugnė Stolz, Gytis Dudas, Tanja Stadler, and Timothy G. Vaughan

PNAS July 21, 2020 117 (29) 17104-17111; first published July 6, 2020; https://doi.org/10.1073/pnas.1918304117

Edited by David M. Hillis, The University of Texas at Austin, Austin, TX, and approved May 11, 2020 (received for review October 22, 2019)

Inferring whole-genome histories in large population datasets


INFER THE ANCESTRY
OF EVERYONE

Appendix

(Dis)Advantages of open source code and data

👍

- replicability of results
-

👎

- sensitive data not protected
-

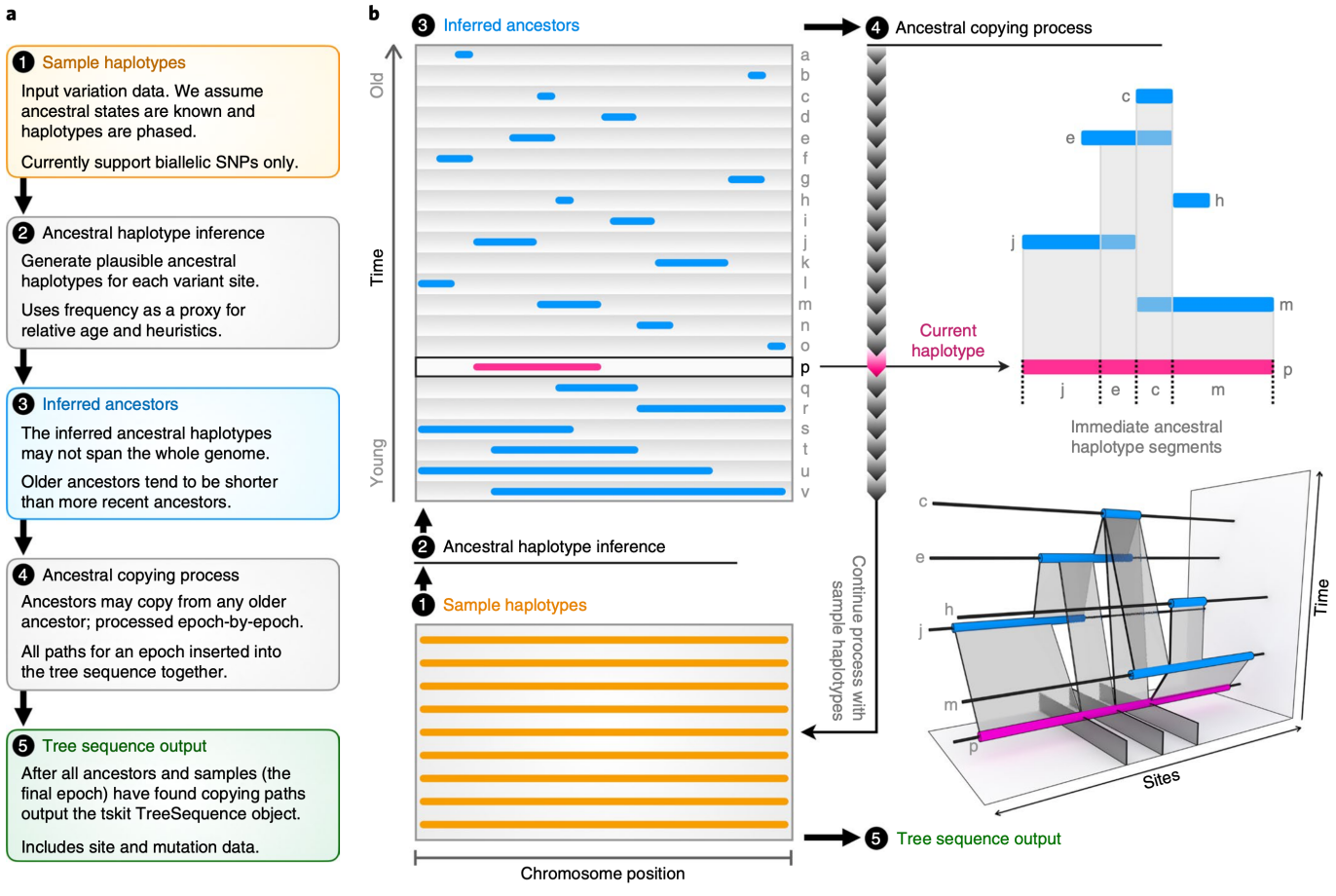


Fig. 2 | A schematic of the major steps of the inference algorithm. a, Flowchart of algorithm steps. **b**, Schematic overview. Starting from a set of sample haplotypes extending over the genome (1), we use the ancestral haplotype inference method (2) to reconstruct fragments of ancestral sequence (3), then infer copying paths among these ancestors (4). The ancestral copying process is shown on the right, using an arbitrary haplotype (*p*) for illustration. As we move from left to right along *p*, we infer that it has most recently copied from *j*, *e*, *c* and then *m*. Incorporating the copying history of all older haplotypes (for example, *m* copied partly from *c* and partly from *h*), partial coalescent trees emerge in the bottom-right panel. Once copying paths have been found for all ancestors and samples, we output a tskit tree sequence (5).

source: Kelleher et al., 2019

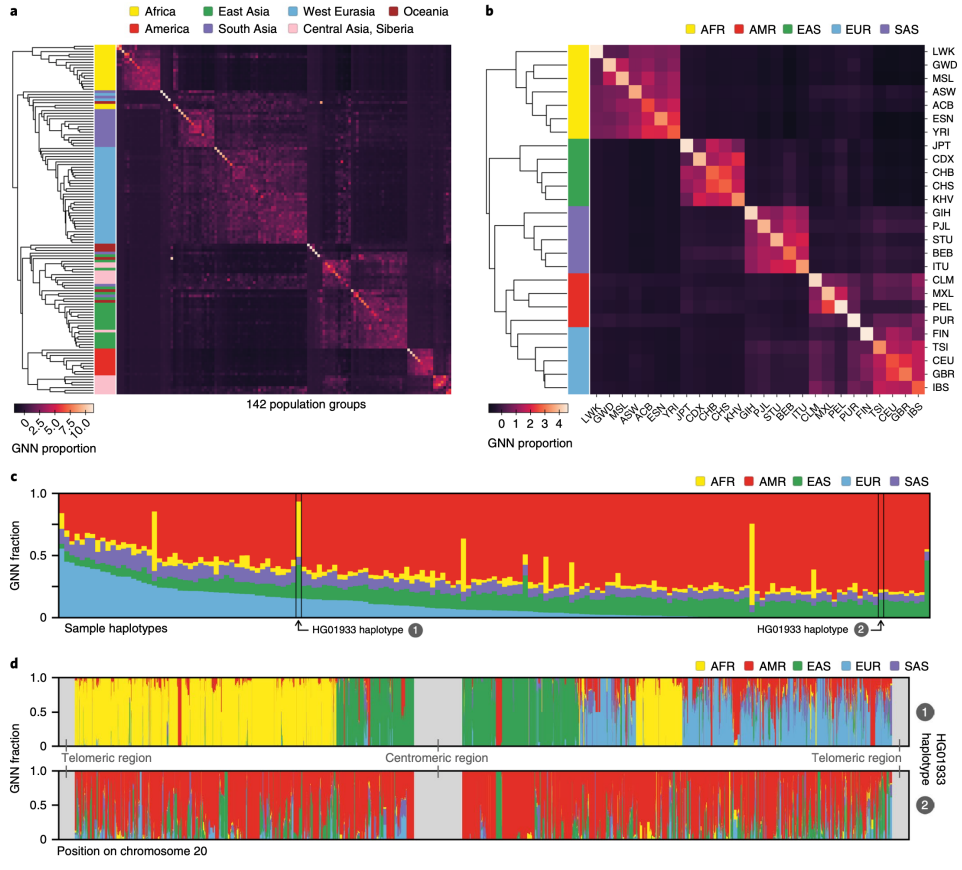
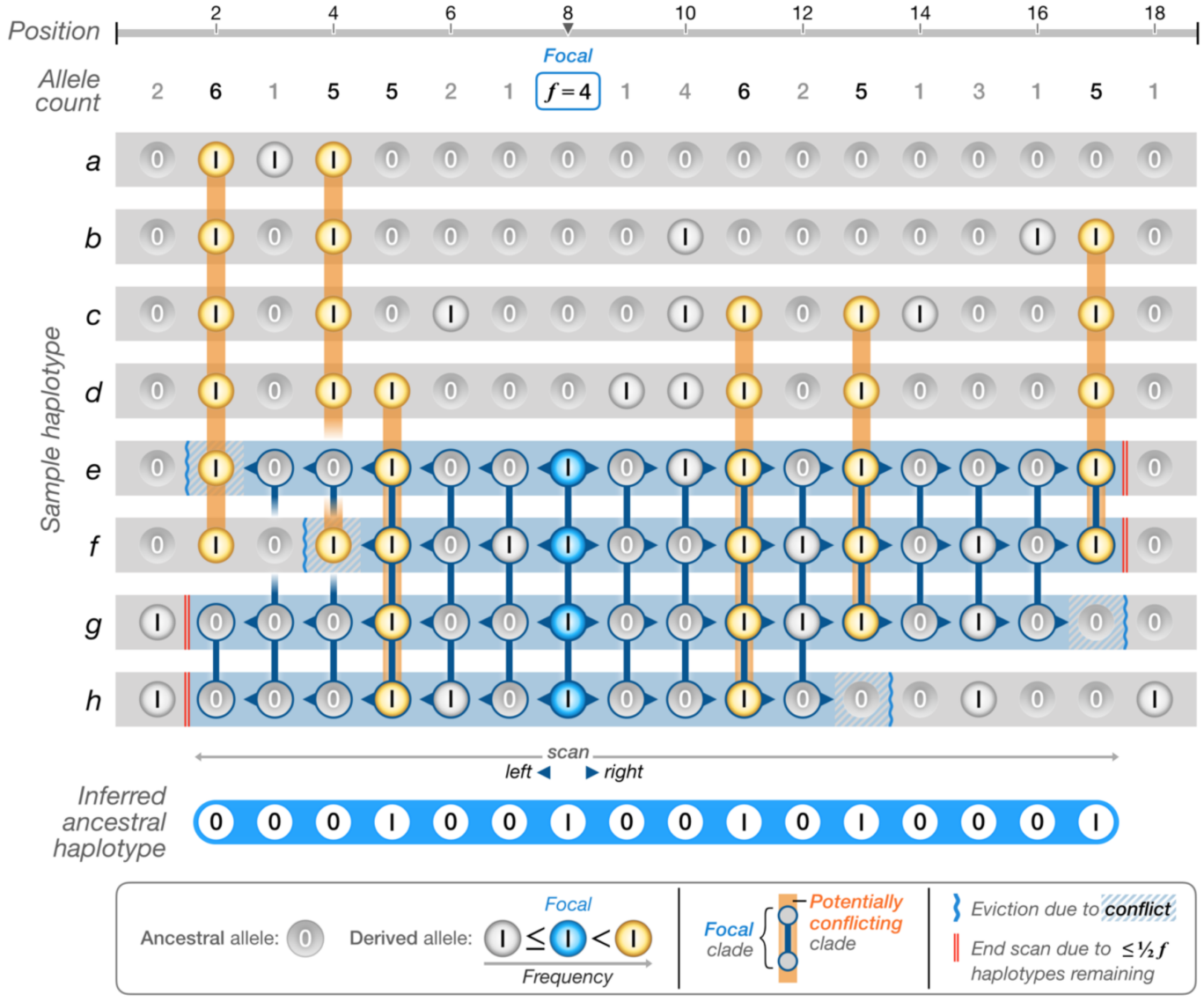
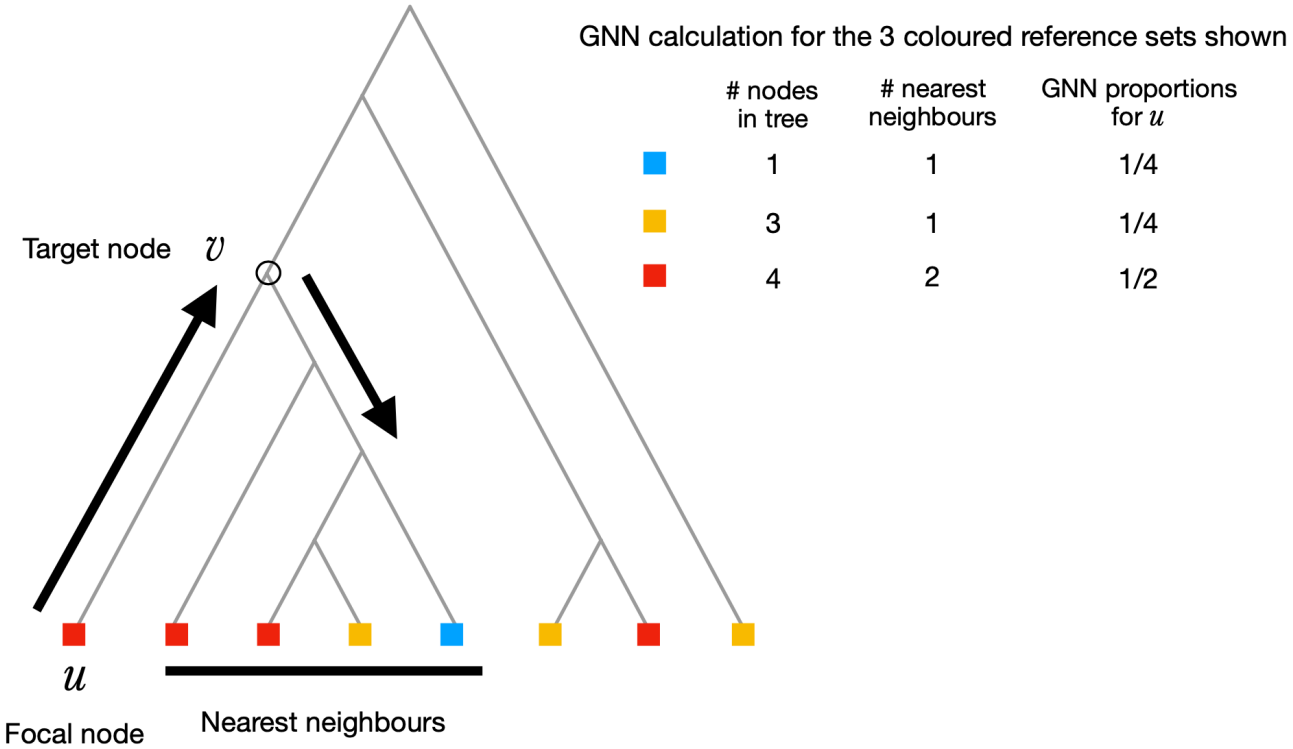


Fig. 4 | Tree sequence characterization of global genome diversity. a, *Z*-score-normalized GNN proportions for SGDP by population ($n = 278$ individuals). The GNN matrix was first *z*-score normalized by column and the rows were then hierarchically clustered. See Supplementary Fig. 16 for a larger version with population labels. **b**, As for **a**, but for the TGP data ($n = 2{,}504$ individuals). AFR, Africa; AMR, America; EAS, east Asia; EUR, Europe; SAS, south Asia; population codes are TGP abbreviations[30]. **c**, Average GNN proportions for all individuals within the Peruvian population in TGP. Colors indicate continental-level groupings. **d**, The GNN proportions across the chromosome for the two haplotypes of HG01933, from the Peruvian population in TGP. HG01933 was chosen as an example of an individual who showed evidence of very recent admixture from multiple source populations. We note that apparent short tracts of different ancestry most likely do not reflect true changes in recent ancestry, but arise through the stochastic nature of genealogical processes and errors in inference.

source: Kelleher et al., 2019



source: Kelleher et al., 2019



source: Kelleher et al., 2019

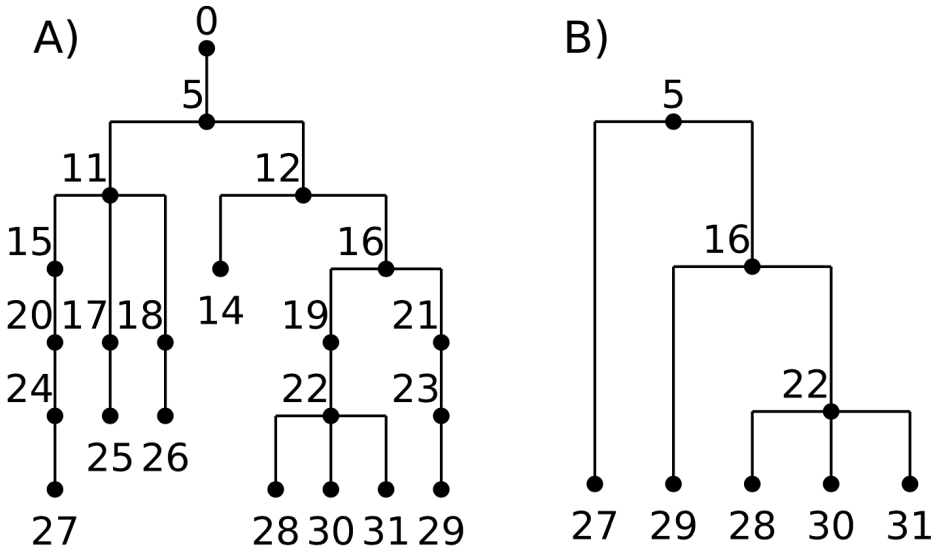


Fig 4. An example of a marginal genealogy from a Wright-Fisher simulation with $N = 5$. (A) the original tree including all intermediate nodes and dead-ends, and **(B)** the minimal tree relating all of the currently-alive individuals (27–31).

source: Kelleher et al., 2018