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?

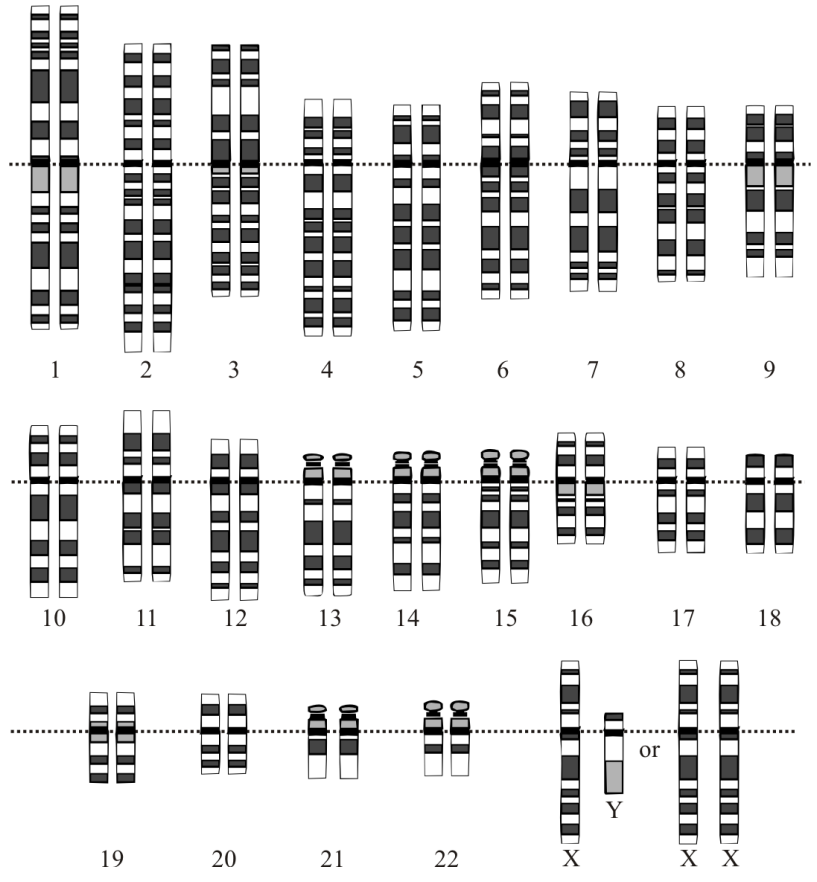
Inferring whole-genome histories in large population datasets

SYNONYMS FOR *inferring*

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

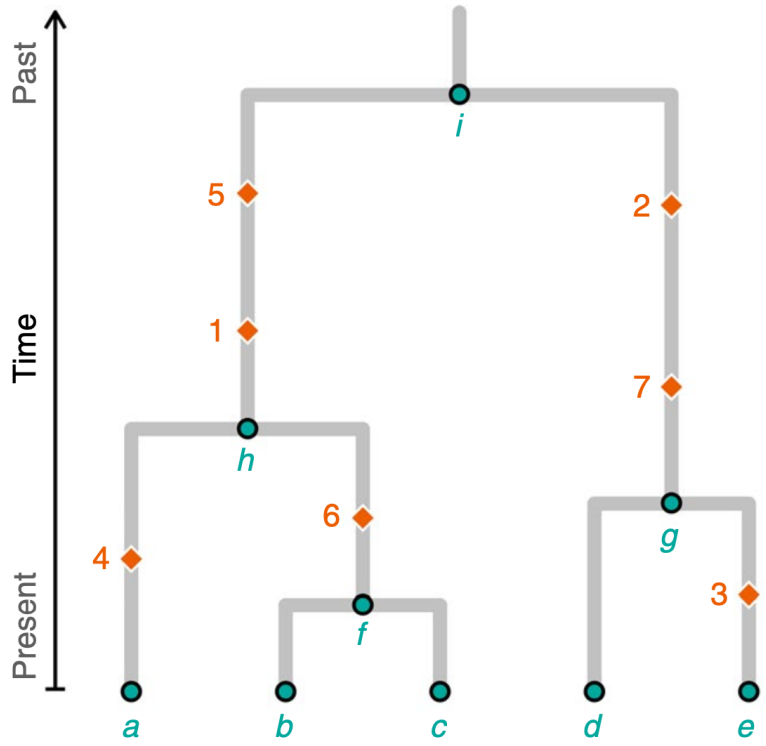
source: thesaurus.com

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

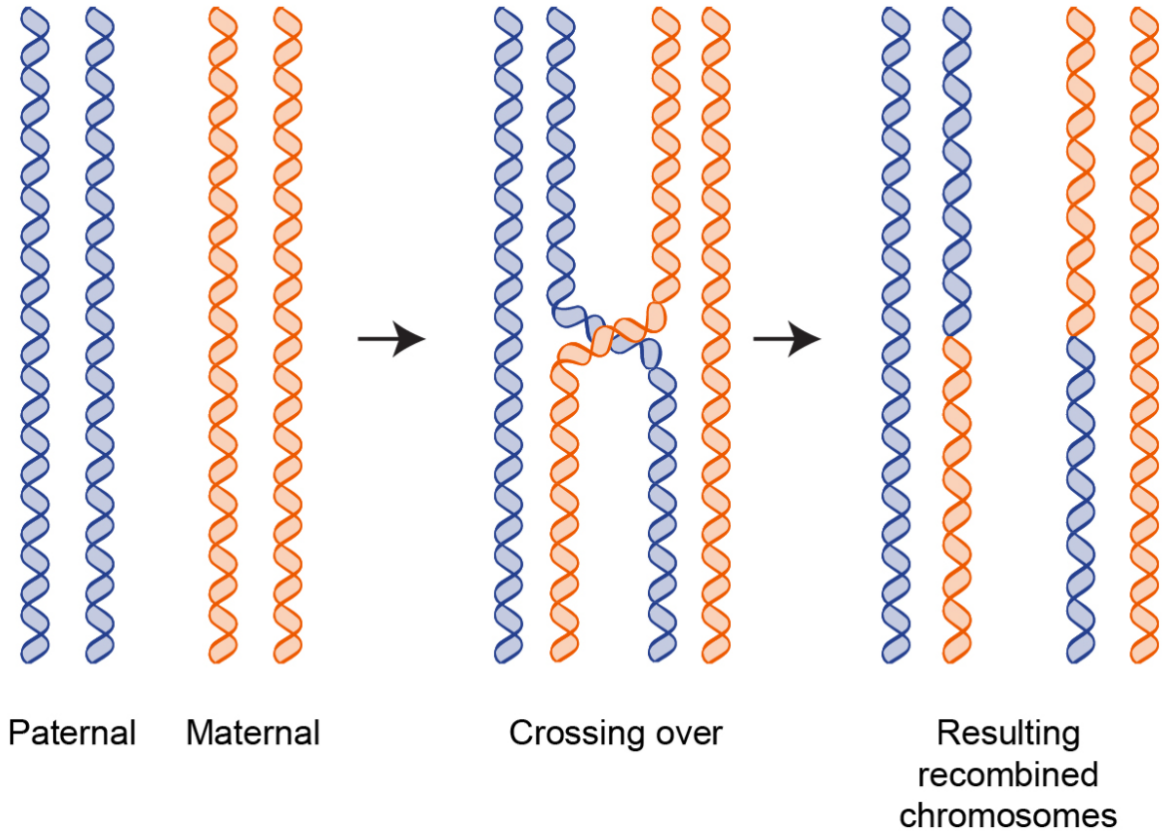
Inferring whole-genome **histories** in large population datasets

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

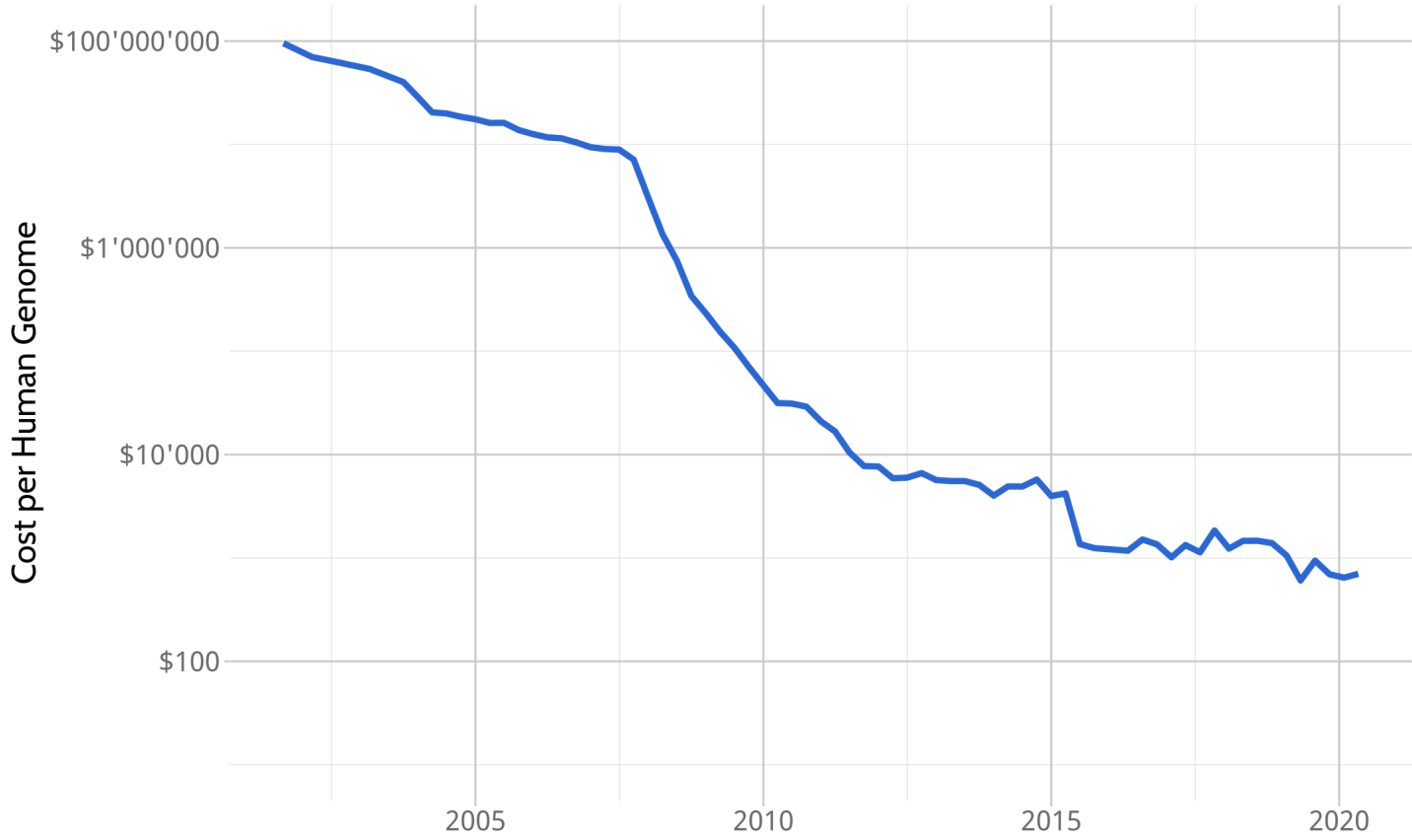
{A, T, G, C} ancestral
{A, T, G, C} derived

Inferring whole-genome histories in large population datasets



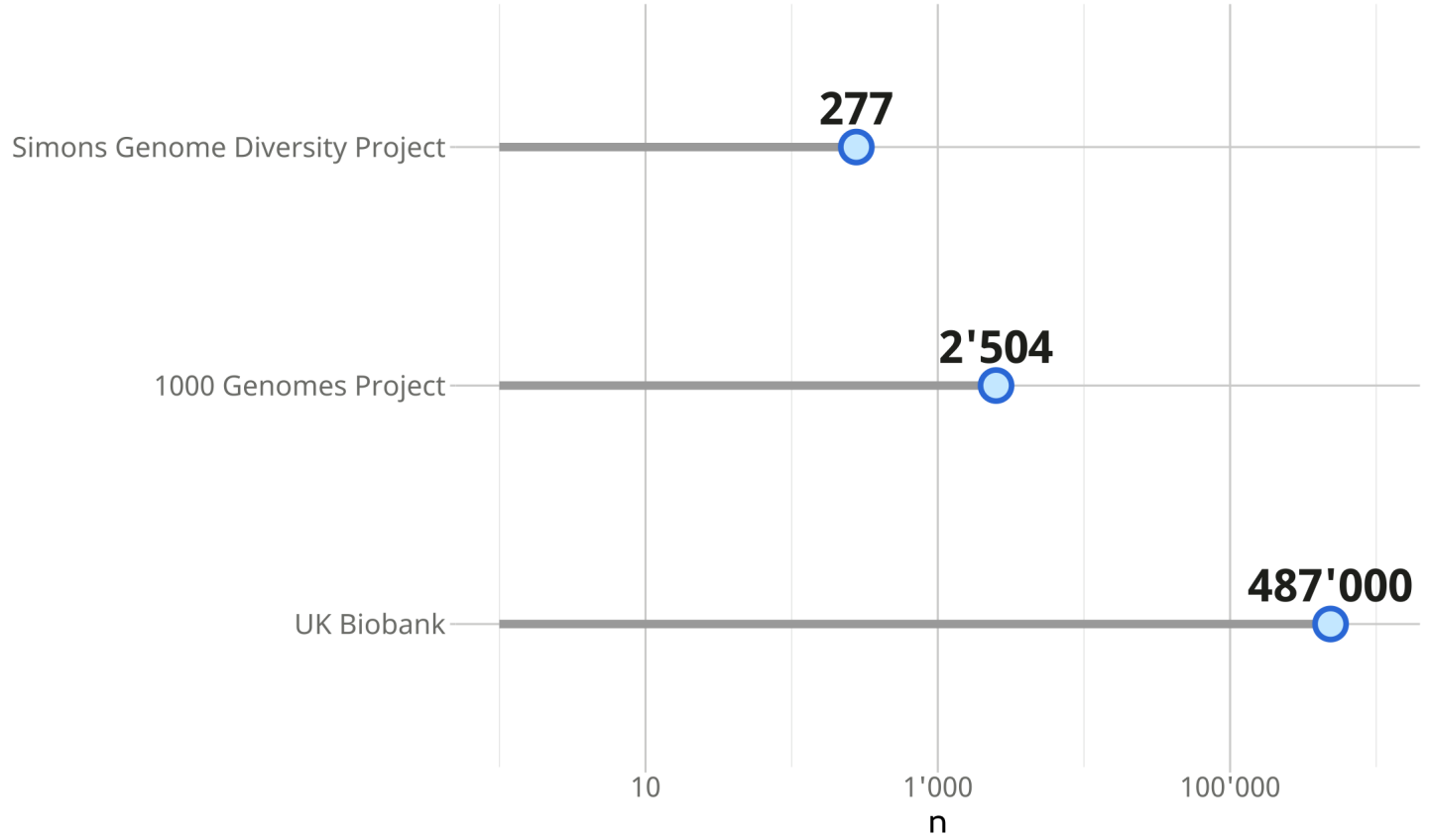
source: genome.gov

Inferring whole-genome histories in large population datasets



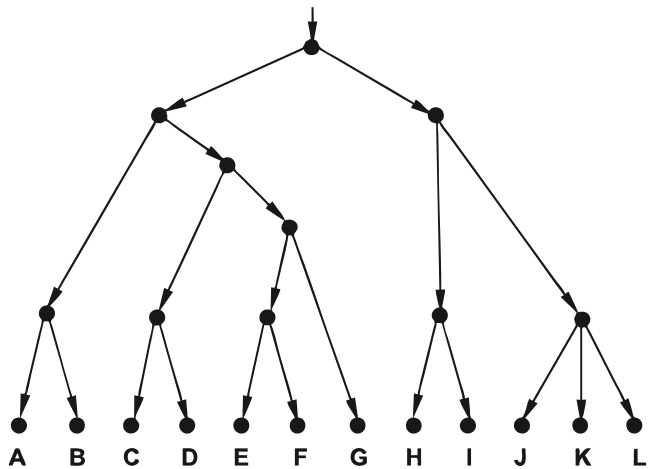
source: genome.gov/sequencingcosts

Inferring whole-genome histories in large population datasets



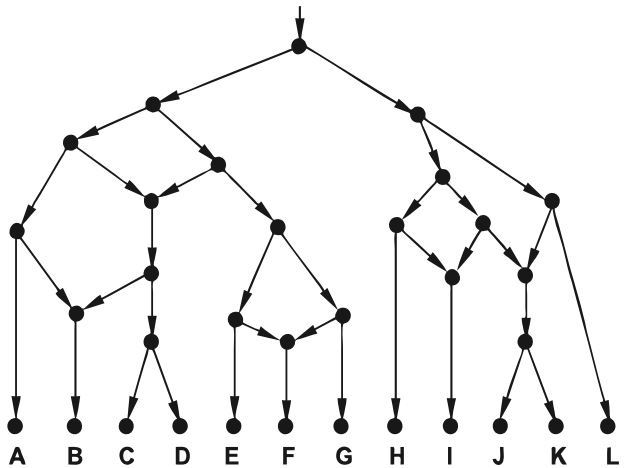
Current situation

Tree



source: Adapted from Morrison, 2016

Network



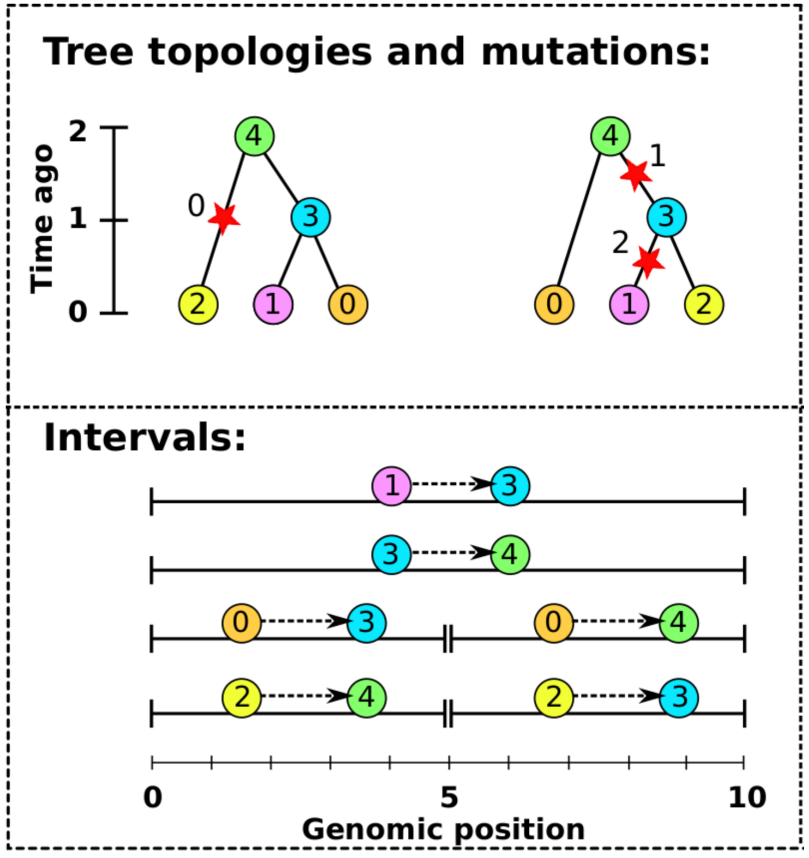
source: Adapted from Morrison, 2016

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

source: github.com/tskit-dev

tsinfer

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:

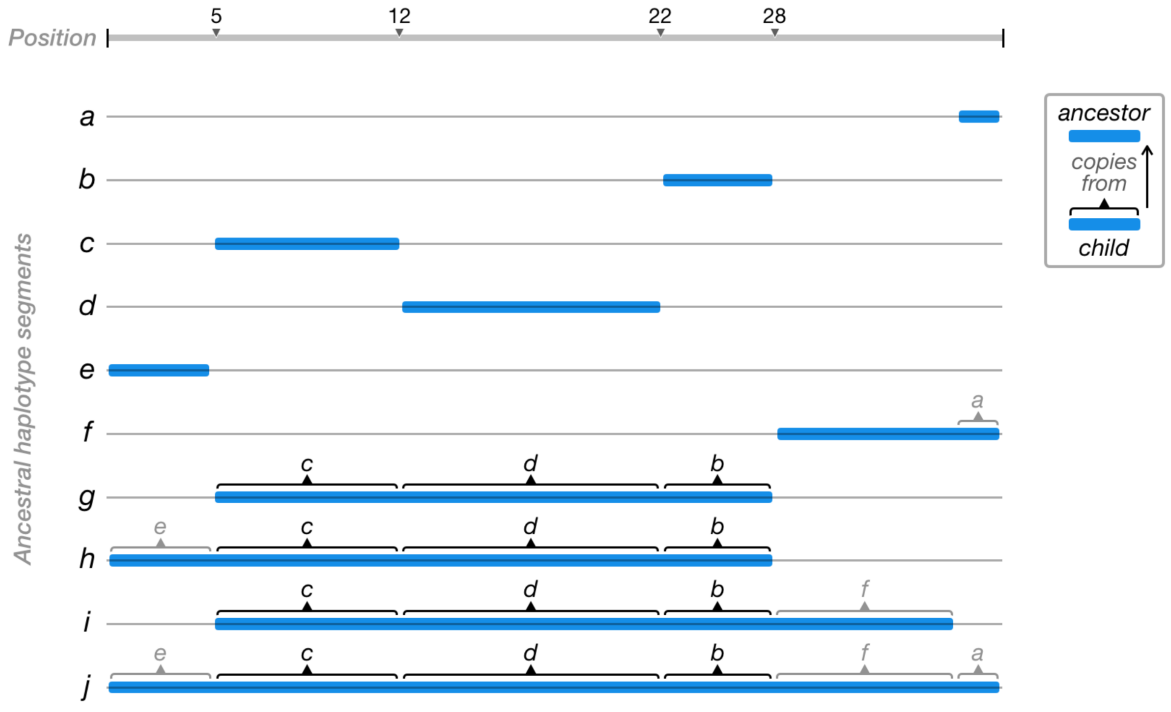
ID	position	ancestral state
0	2.5	A
1	7.5	G

Mutations:

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

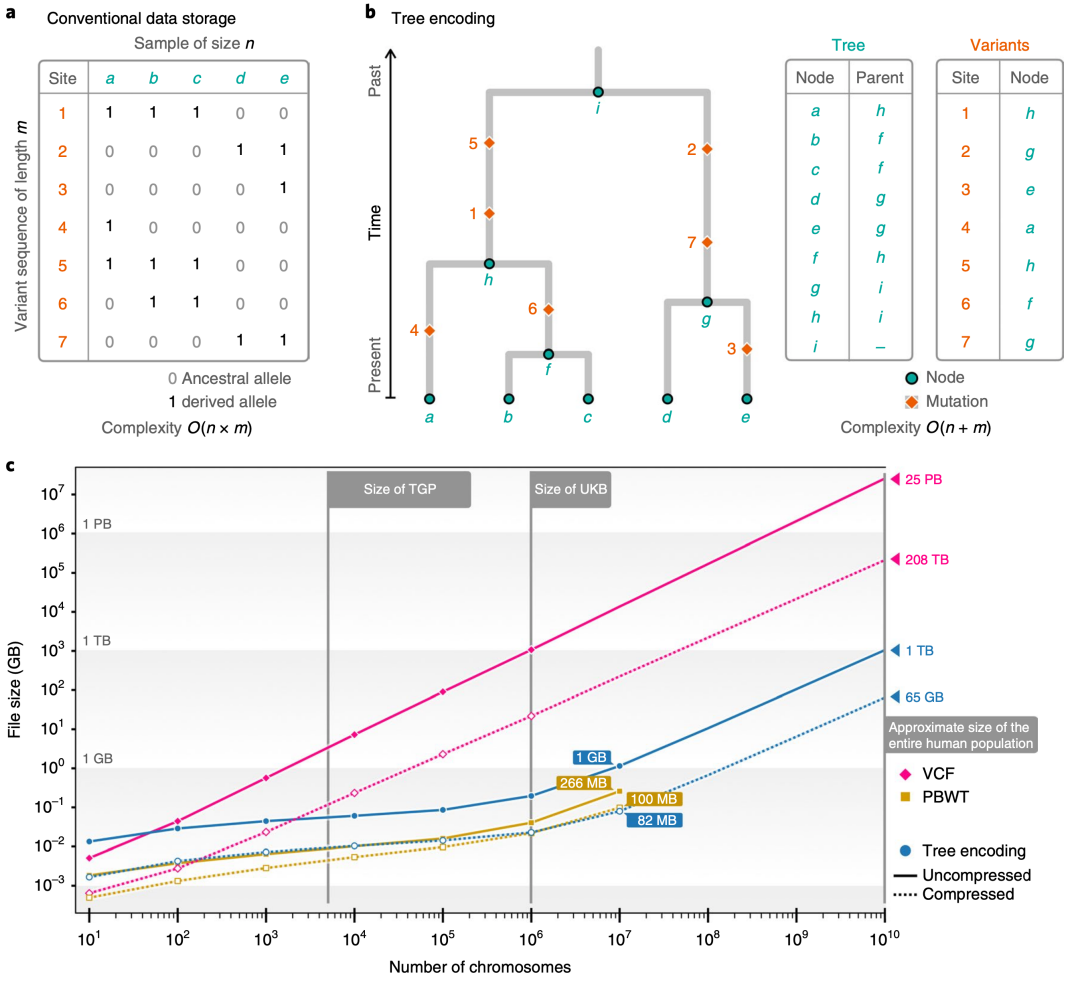
source: Kelleher et al., 2018

Ancestral haplotype inference



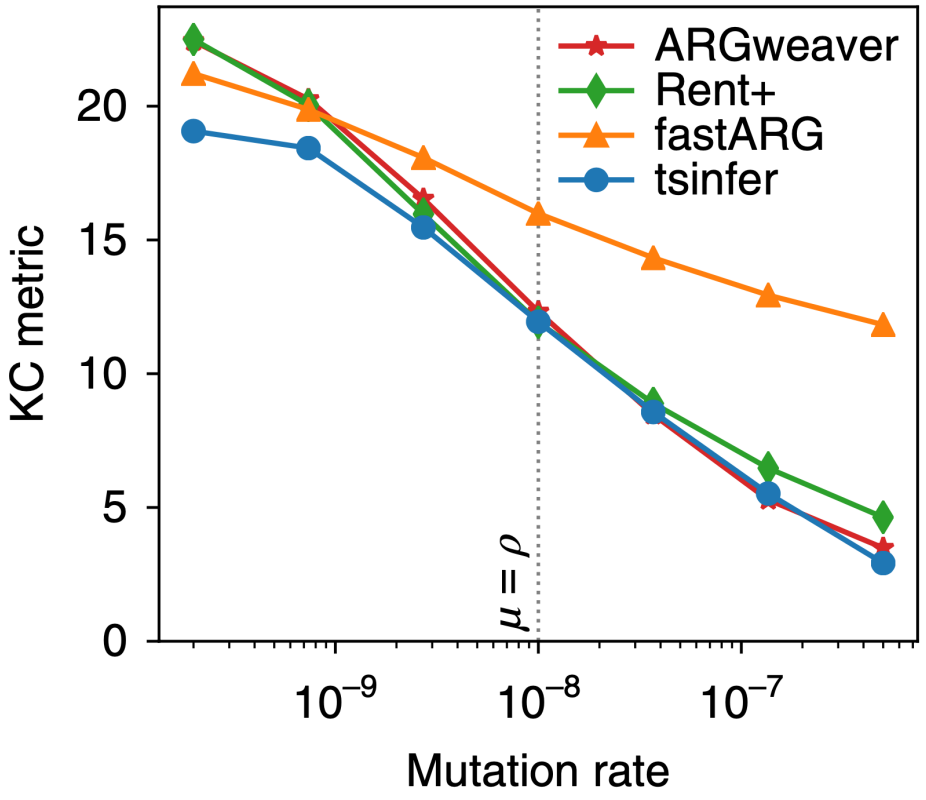
source: Kelleher et al., 2019

Comparison to state-of-the-art Storage Space



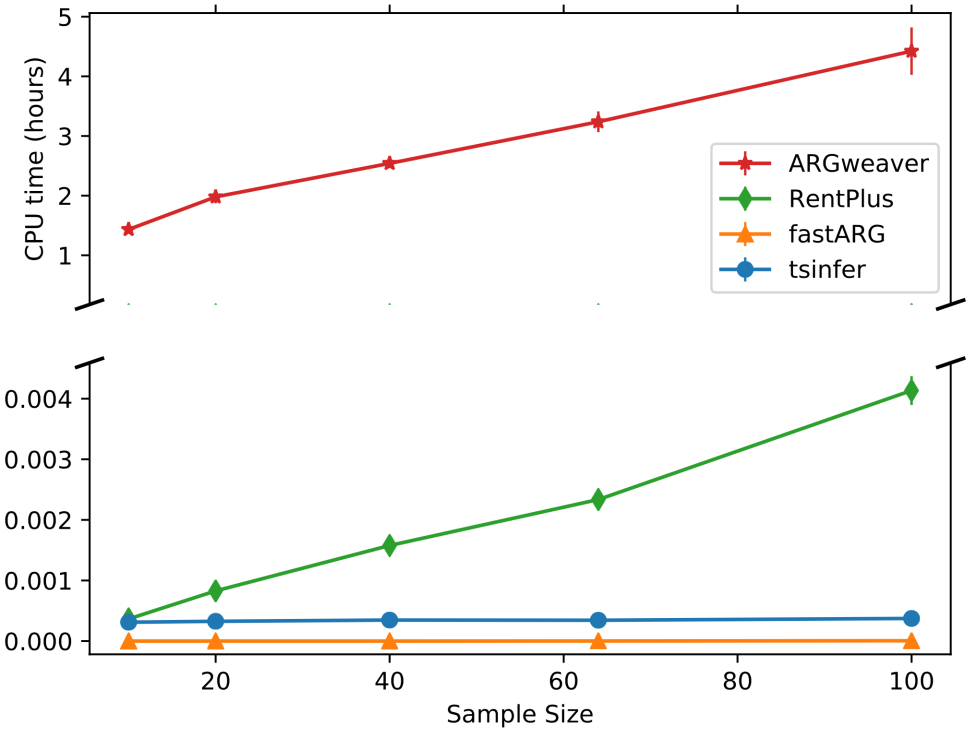
source: Kelleher et al., 2019

Comparison to state-of-the-art



source: Kelleher et al., 2019

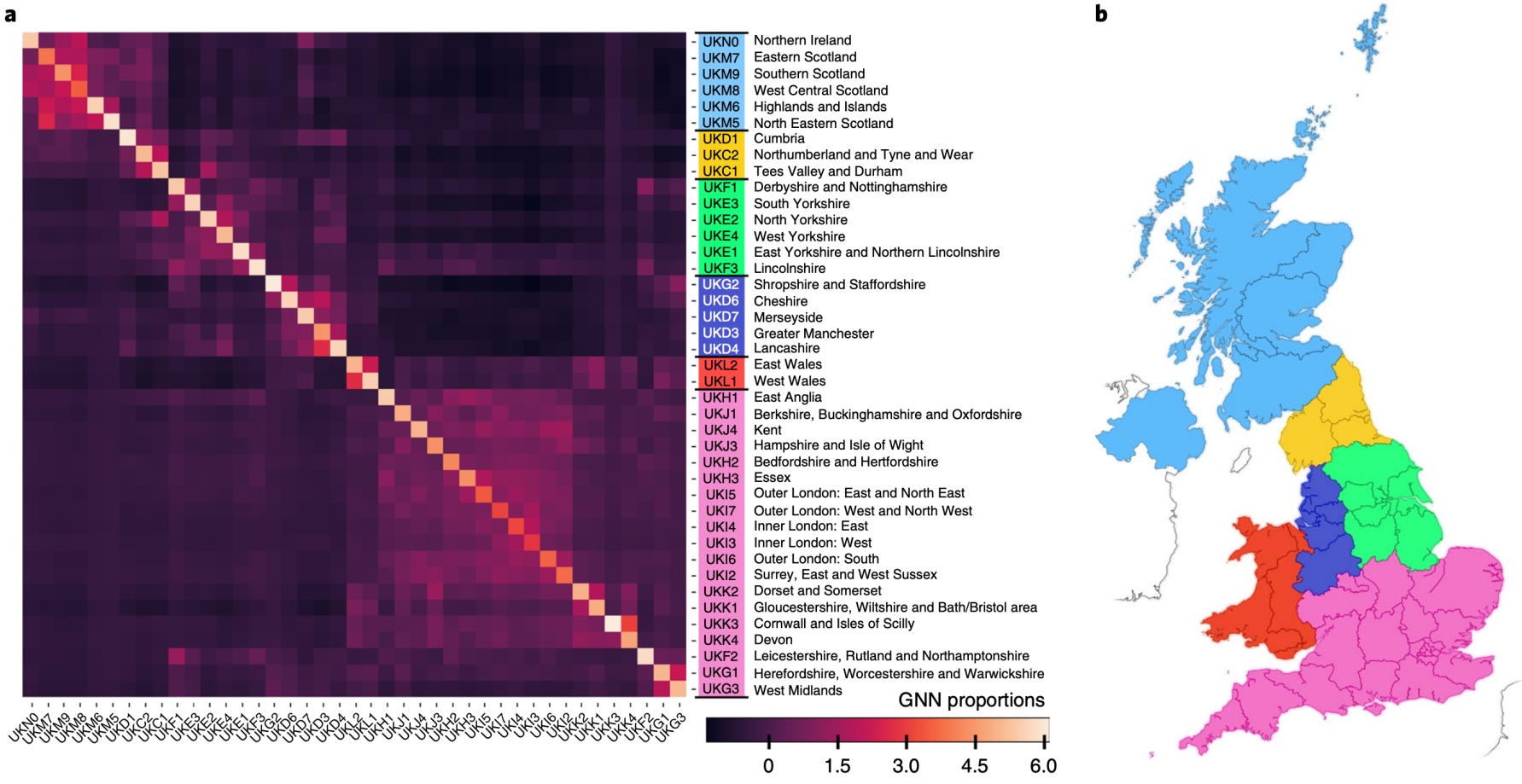
Accuracy and **Speed**



source: Kelleher et al., 2019

Application example

UK Biobank population structure



source: Kelleher et al., 2019

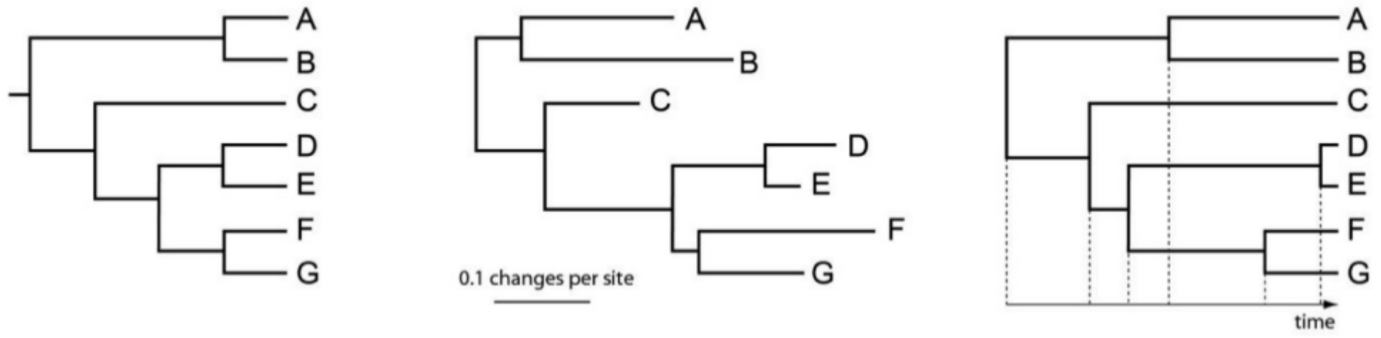
Drawbacks

Assumptions

- each variant has a single origin
- mutation/recombination ratio is sufficiently high
- haplotype frequency as proxy for 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

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

Appendix

(Dis)Advantages of open source code and data

👍

- replicability of results
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👎

- sensitive data not protected
-

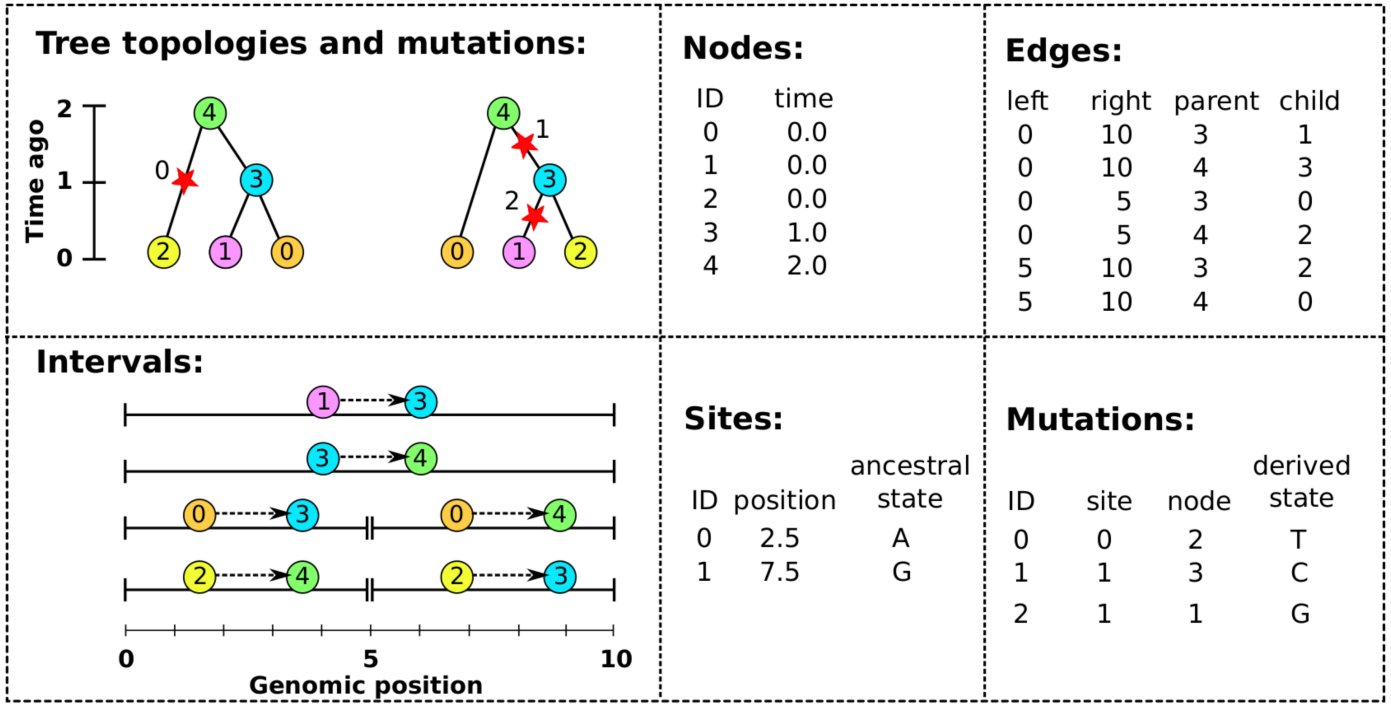

Fig 3. An example tree sequence with three samples over a chromosome of length 10. The leftmost panels show the tree sequence pictorially in two different ways: (top) a sequence of tree topologies; the first tree extends from genomic position 0 to 5, and the second from 5 to 10; and (bottom) the edges that define these topologies, displayed over their corresponding genomic segment (for instance, the edge from node 2 to node 4 is present only on the interval from 0 to 5). The remaining panels show the specific encoding of this tree sequence in the four tables (nodes, edges, sites and mutations).

source: Kelleher et al., 2018

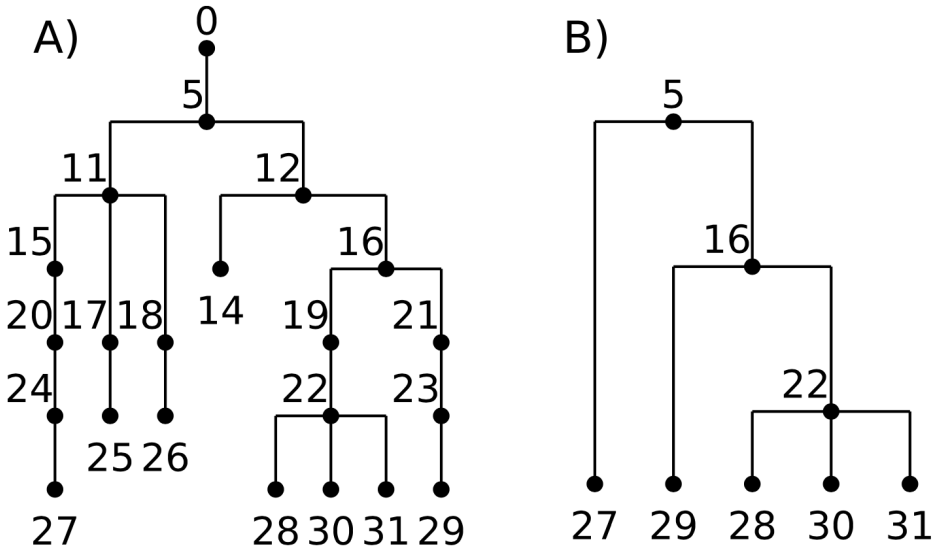

Fig 4. An example of a marginal genealogy from a Wright-Fisher simulation with $N = 5$. (A) the original tree including all intermediate nodes and dead-ends, and **(B)** the minimal tree relating all of the currently-alive individuals (27–31).

source: Kelleher et al., 2018