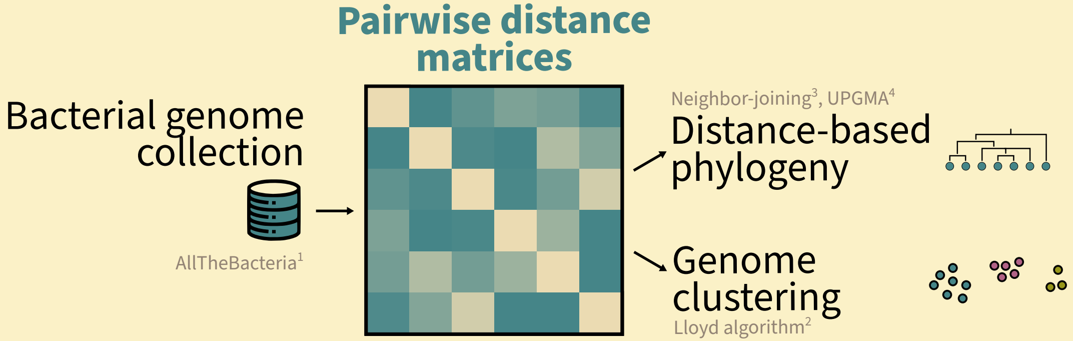
Towards space-efficient data structures for large genome-distance matrices with quick retrieval

Léo Ackermann[1], Pierre Peterlongo[1], Karel Břinda[1]

[1] Inria, Genscale, Rennes

29th November 2024

Importance of pairwise distance matrices


Pairwise distance matrices
Bacterial genome collection
AllTheBacteria[1]
Neighbor-joining[3], UPGMA[4]
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Genome clustering
Lloyd algorithm[2]

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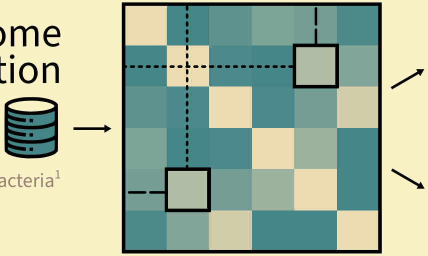

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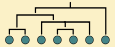

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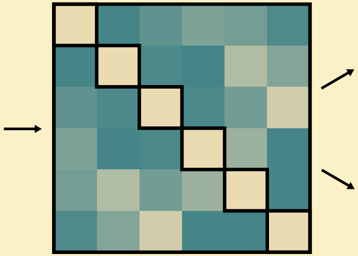

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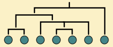

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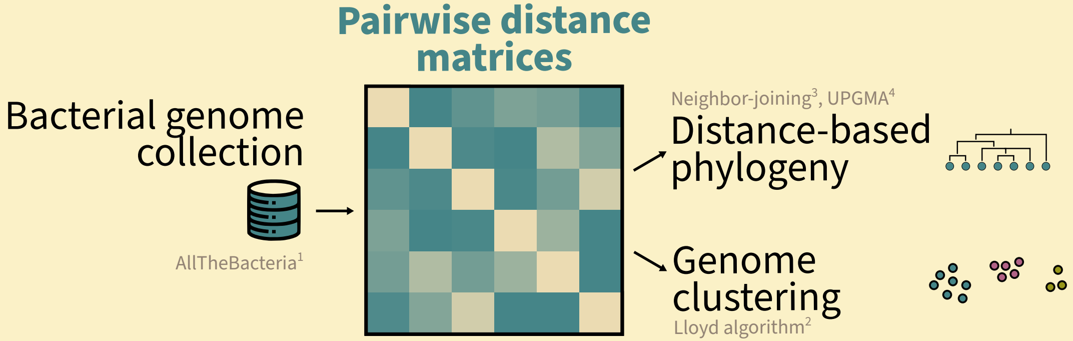
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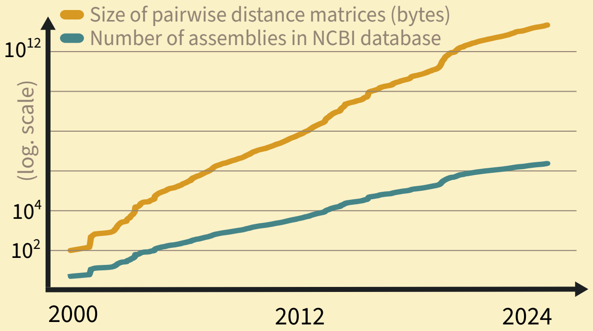
Efficient computation of distance matrices

Sketching (e.g., Mash[5], Dashing[6]) and **parallel computing** make it tractable

Storage of genome distances is challenging

Size of bacterial collections increases exponentially



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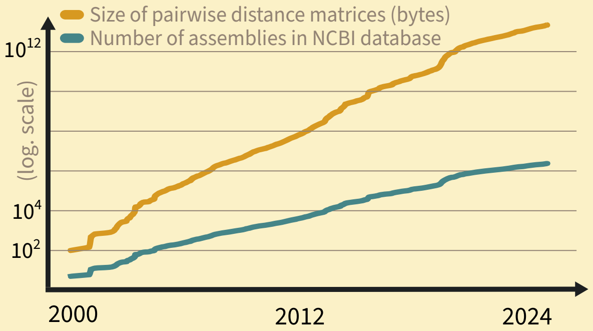

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Generic matrix compression techniques

Matrix-specific compression techniques are restricted to sparse and low-rank matrices, and are **not directly applicable**

Problem formulation

This work focuses on the **subquadratic storage of pairwise distance matrices**

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Many variants can be framed

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  e.g., random access, sequencial access, nothing, . . .

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Focus of our preliminary work (this talk)

I. Restricted to a simplified model of evolution

1. **Lossless static** data structure for pairwise distances with **constant time random access**

II. On a 10k collection of *Streptococcus pneumoniae*

2. **Lossless static** data structure for pairwise distances (without specific operation)
3. **Lossy static** data structure for pairwise distances (without specific operation)

Contrib 1. Method for a simple evolutionary model

ISM: a simple evolutionary model

∞ The infinite site model[7]

It **postulates** that mutations always arise during **vertical descent**, and on a **novel locus**

(because genomes are of *infinite* size)

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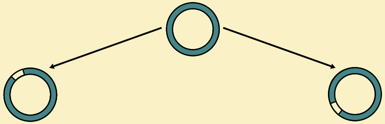

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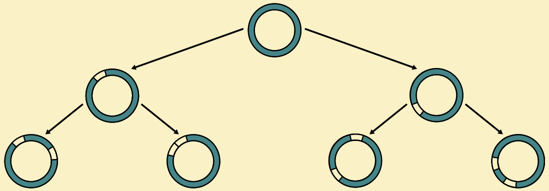

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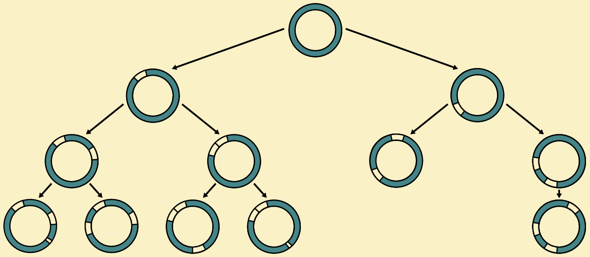

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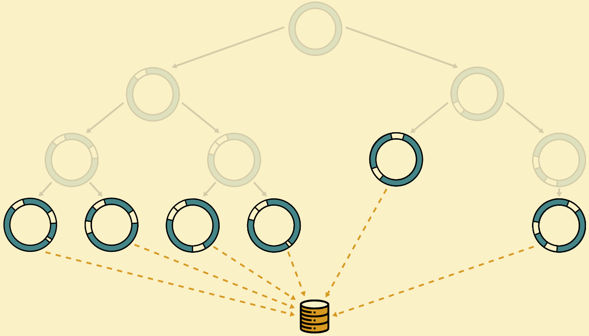

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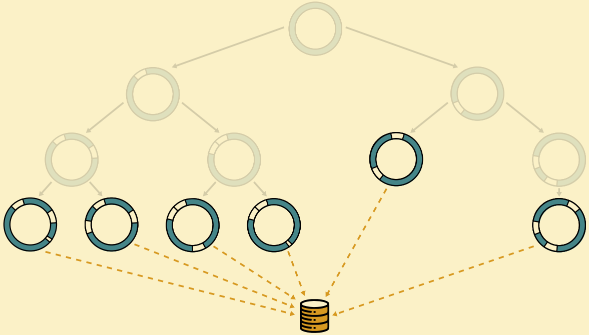

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(the number of loci where the genomes differ)

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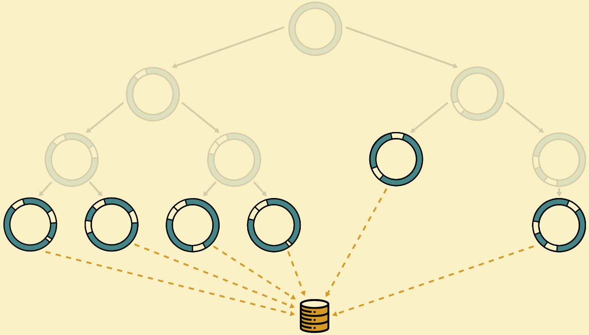

A simplistic model, really?

At **small time scale**, real data almost follows such model

(eg. clinical outbreak)

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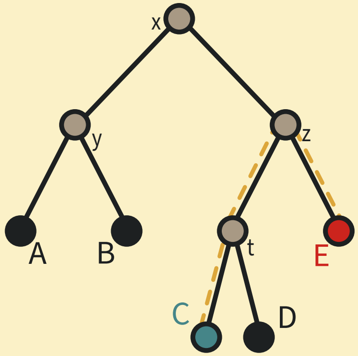
Tree distance in constant-time (with precomputation)[8]



Objective. Compute $\delta(C, E)$
(naive algo. in linear time)

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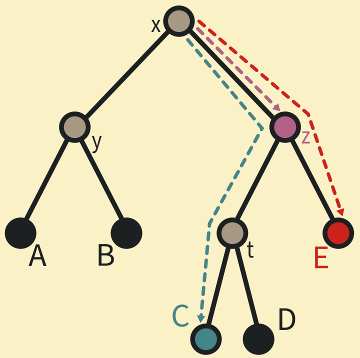

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1. Expressing $\delta(C, E)$ with root-to-node distances

$$\delta_T(C, E) = \mathrm{rtn}(C) + \mathrm{rtn}(E) - 2 * \mathrm{rtn}(\mathrm{lca}(C, E))$$

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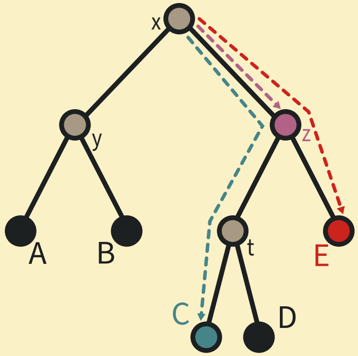

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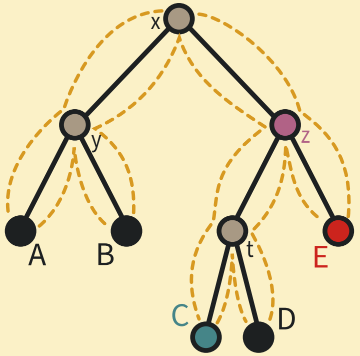

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2.a Lowest Common Ancestors are range minima

Eulerian path	xyAyByxzt	CtDtzE	zx
Eulerian depth	012121012	323212	10

$$\mathrm{lca}(C,E) = \mathtt{Path}\left[\mathrm{argmin}_{k \in [\mathtt{index}(C), \mathtt{index}(E)]} \mathtt{Depth}[k]\right]$$

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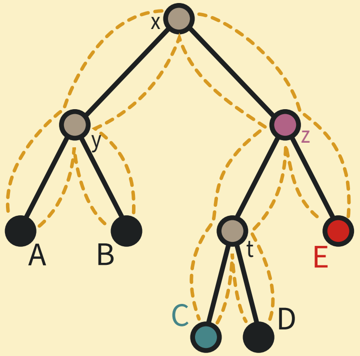

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2.b Range-Minimun Queries on `Depth` in constant-time

- Store every query in a lookup table $O(n^2)$ space
- LUT + LUT for block RMQs $O(n)$ space

Contrib 1. $O(n)$-space lossless storage with $O(1)$-random access for ISM data

Lemma

There exists a linear space data structure that can statically store Hamming pairwise distances of genomes following the *infinite site model* while providing constant time random access

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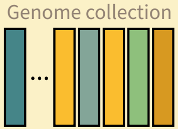
We **store this tree** using the data structure explained earlier ■

Contrib 2. Methods for real data *(lossless)*

Phylogenetic compression

A phylogeny guided reordering for improved local compressibility



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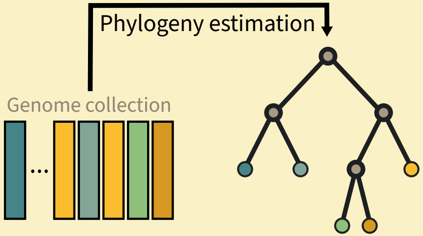

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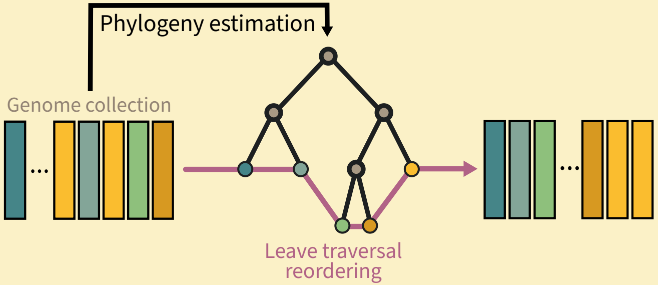

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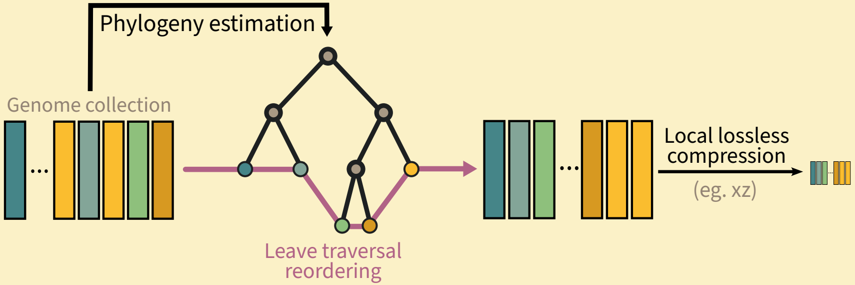

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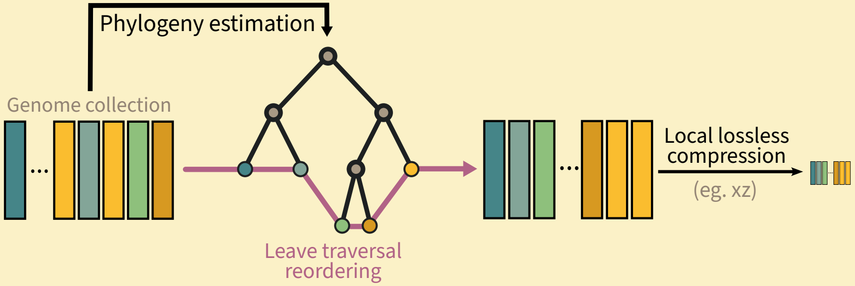
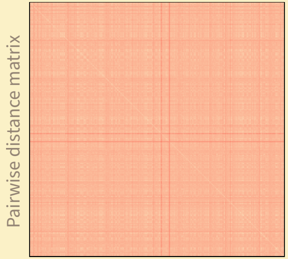


Phylogenetic compression saves orders of magnitude

Running `xz` on reordered genome collections (BIGSIdata, 661k, AllTheBacteria) **saves about two orders of magnitude**[9]

CONTRIB 2. Lossless compression of pairwise genome distances

Phylogenetic compression of pairwise distance matrices



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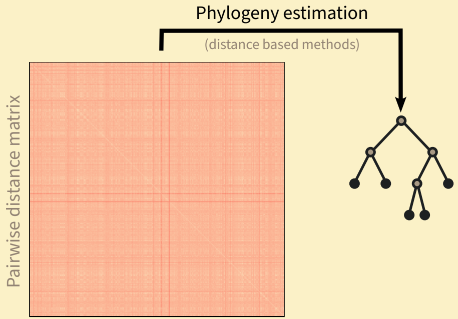

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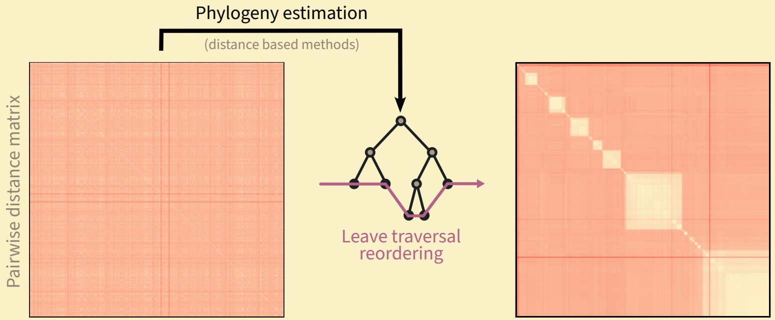

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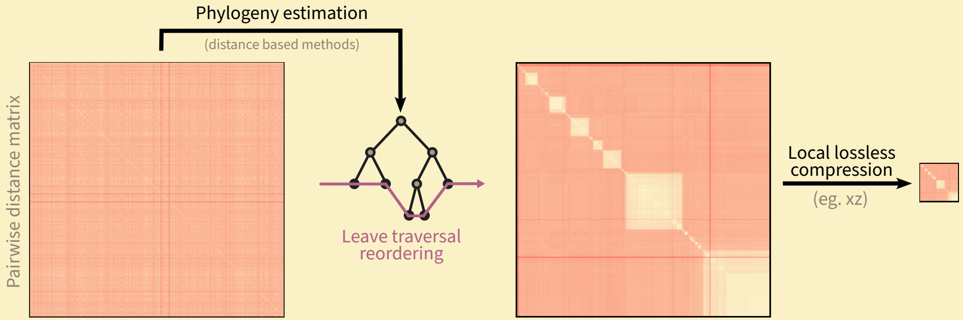

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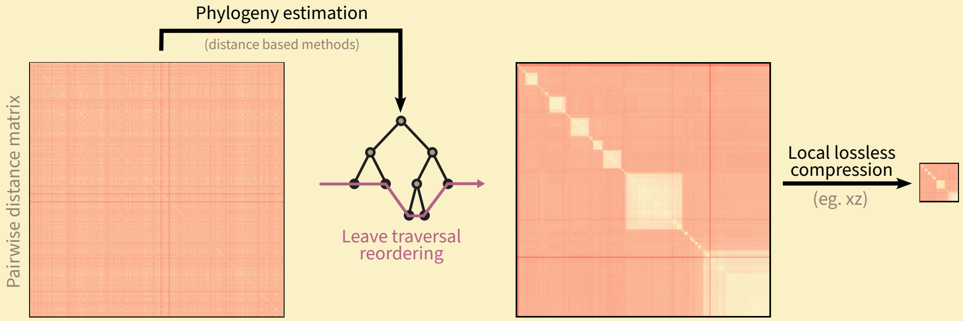


→ Phylogenetic compression can be **applied beyond the scope** of [9]

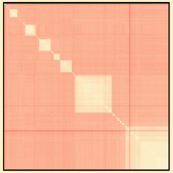
Contrib 3. Methods for real data *(lossy)*

Tree decomposition of distance matrices

⏮ The *infinite site model*, simplistic, really?

At small time scale, real data almost follows such model

$\rightarrow$ Most of the distance signal is explainable by the tree distance



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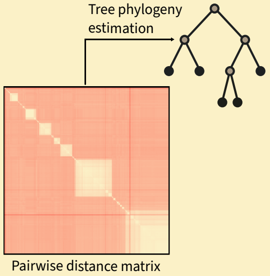

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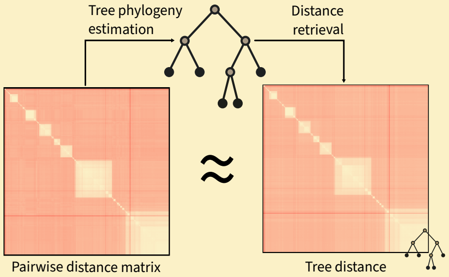

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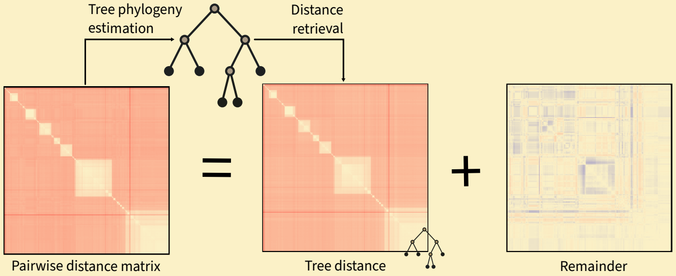

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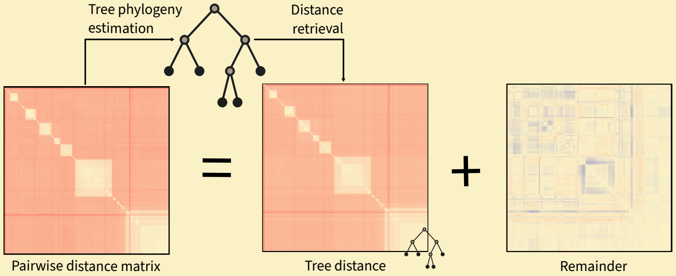


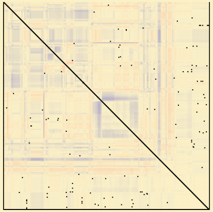
This approach cannot work for lossless compression

The **remainder has a size similar to the original distance**, and does not exhibit strong structure

Biology-informed thresholding

⓪ Thresholding small values of the reminder matrix based on ANI

All values below a threshold are set to zero → from 8 to 1 char in the .phylip format



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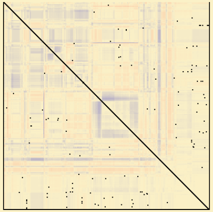

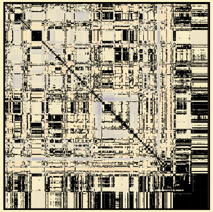

Increasing threshold = increasing sparsity

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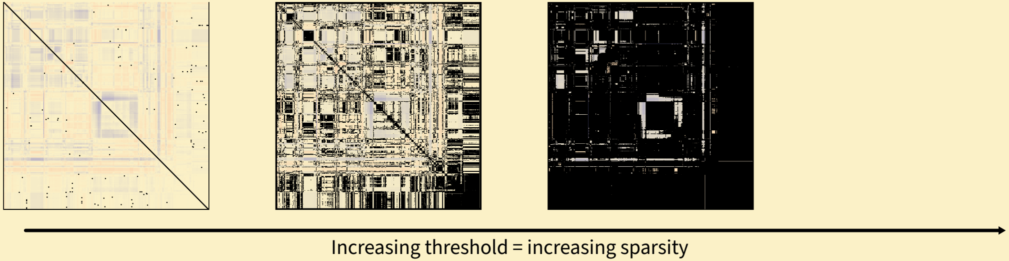

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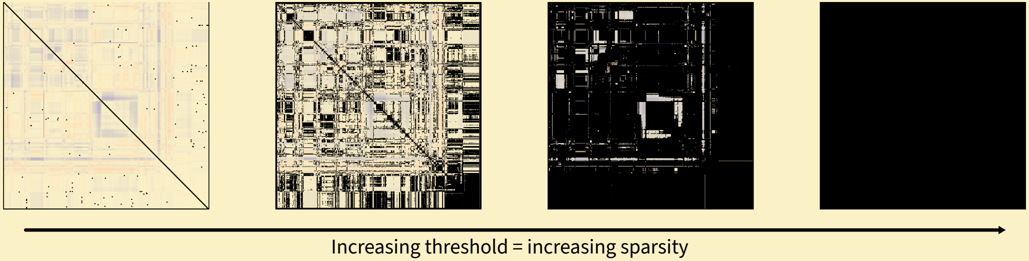

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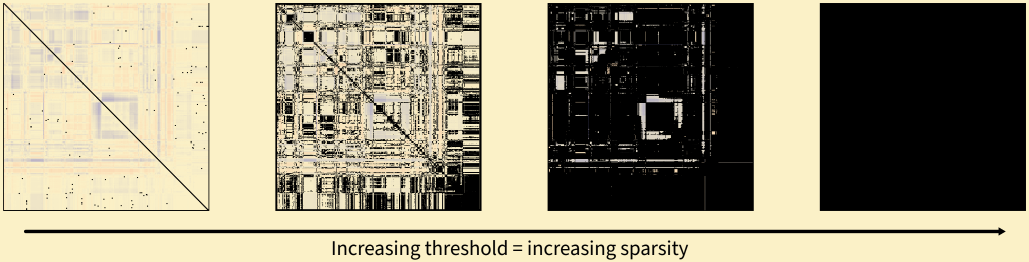
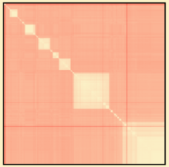


Biological meaning of thresholds (for future work)

For similar enough genomes, **taxonomy can be defined with distance thresholds**[10]

e.g., Specie $\equiv$ >90% ANI $\equiv$ <0.05 Mash dist. or Strain $\equiv$ >99.99% ANI $\equiv$ <0.0001 Mash dist.

CONTRIB 3. Loss-monitored compression of pairwise genome distances


Pairwise distance matrix

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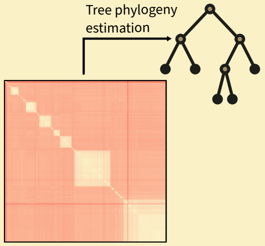

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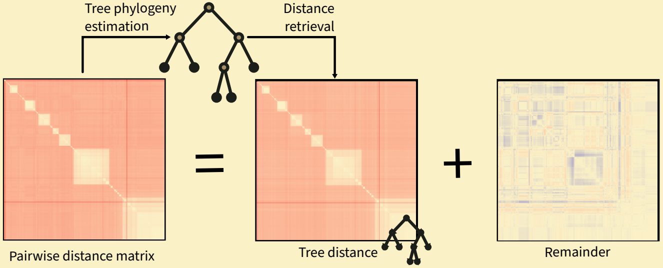
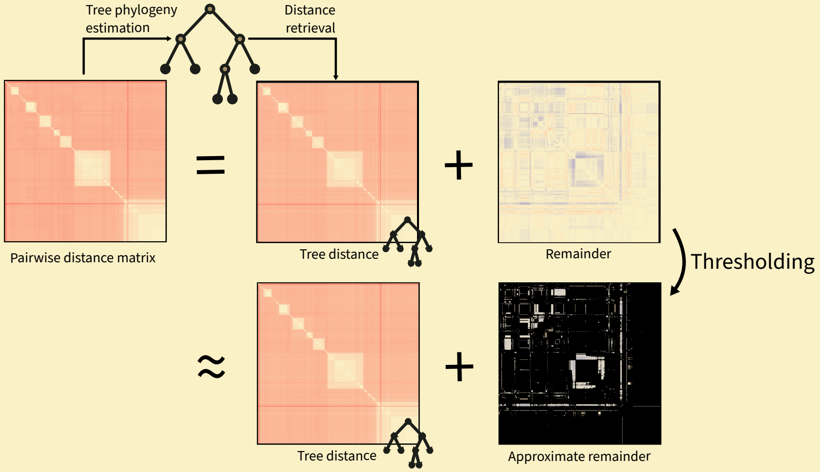
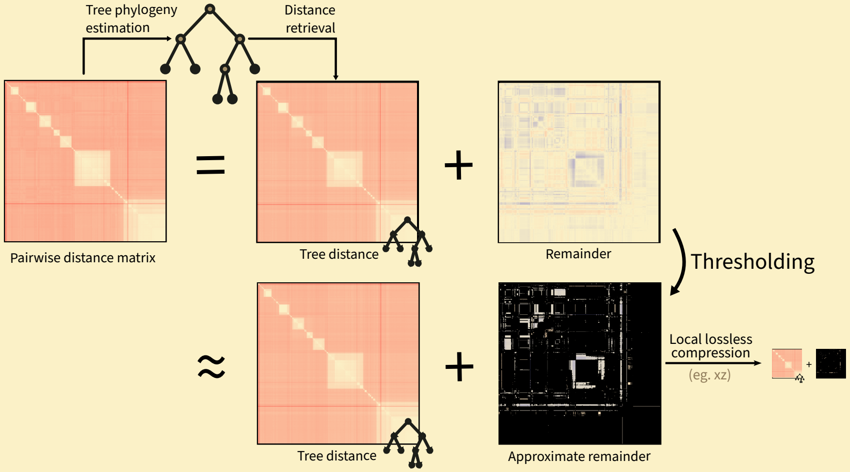


CONTRIB 3. Loss-monitored compression of pairwise genome distances



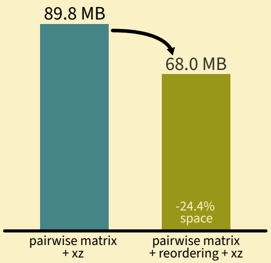
CONTRIB 3. Loss-monitored compression of pairwise genome distances



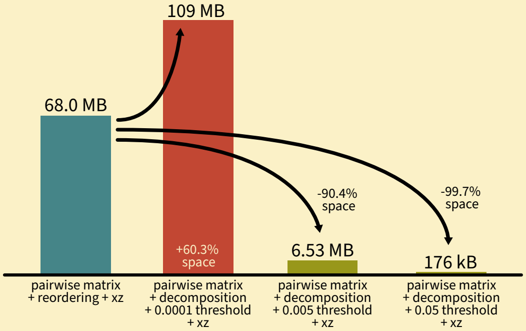
Results

Exploiting phylogeny pushes compressibility bundaries

Data	10k *Streptococcus pneumoniae* genomes from the AllTheBacteria[1] collection
Distance estimator	Mash
Phylogeny estimator	NJ algorithm, with quicktree[11]
Distance retrieval	**new tool** nwk2phy[12] (implements constant-time tree distance retrieval)
Compression scheme	xz



Lossless compression



Lossy compression

Conclusion

Conclusion

Context

Many **downstream analyses** rely on **pairwise distance matrices**, that are already challenging to store due to their **quadratic size**

Approach

We aim to leverage the **specific structure** of genomic data, that can extensively be **explained by the underlying phylogeny**

First results

- **Theory.** Pairwise matrices of genome collections following the *infinite site model* can be stored in **linear space** supporting **constant time** queries
- **Practice.** Phylogeny-aware (lossy) compression of *10k s.-pneumo.* pairwise matrices **saves over 90% space** compared to xz

Future work

- Better compressing of the remainder

  iterative decomposition, compression techniques for sparse matrices
- Theoretical guarantees via tracking of distortion

  e.g., $\forall \tau, \forall (x,y), \quad \delta(x,y) \leq \tau \Rightarrow \tilde{\delta}_\tau(x,y) \leq \tau$
- Exploring alternative phylogenetic backbones and distances

  phylogenetic networks, phylogenetic splits ; dashing, symetrical difference of kmer sets
- Generalisation to many-species collections

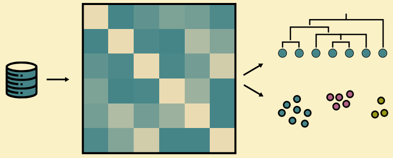
Eventually, distance data structures for **all bacterial genomes** with **monitored distortion**

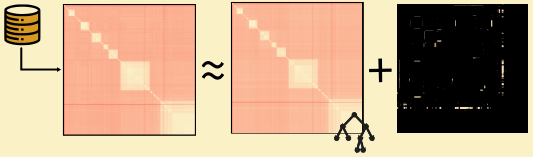
Thank you for your attention!

Léo Ackermann
Pierre Peterlongo
Karel Břinda

Towards space-efficient

data structures for large genome-distance matrices with quick retrieval





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