Scalable indexing and mapping of long seqs through locally consistent phrases

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DSB 2026, February 19th, Venice

Context: accurate long reads enable new methods

Sequencing data keeps getting longer and more accurate

Recent trend: working on sequence of “minimizers”
(smaller sequences on a bigger alphabet)

- Minimizer-space dBG (Ekim et al. 21)
- Mapquik (Ekim et al. 23)
- U-index (Ayad et al. 25)

Can we adapt these ideas into a lossless framework?

From sampling anchors to parsing phrases

Start by sampling anchors (e.g. minimizers) in your sequence

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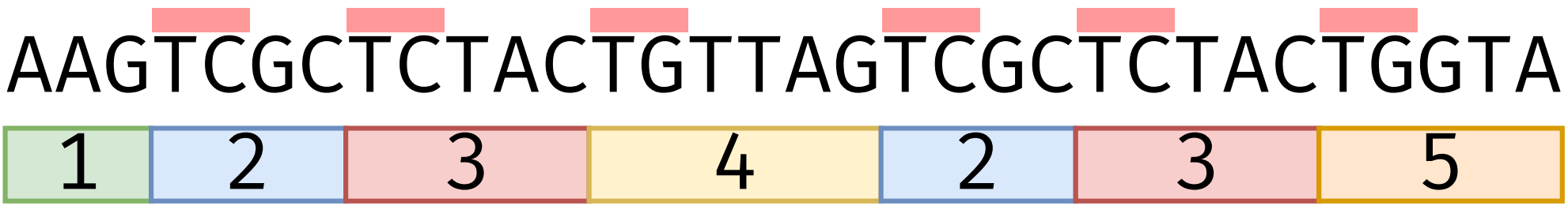

then look at the phrases *between* anchors

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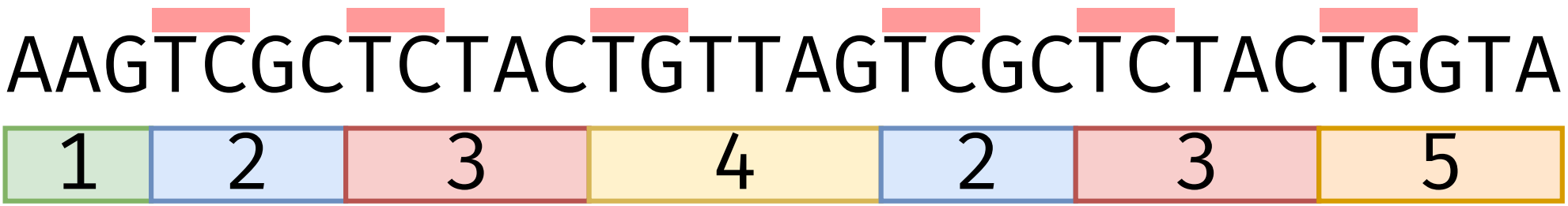

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Local consistency

same context ⇒ same anchors ⇒ same phrases

A global framework based on consistent phrases

1. **parse** the sequence into locally consistent phrases
2. **fingerprint** the phrases (e.g. with their lex. rank, hash...)
3. **index** the sequence of fingerprints

the sequence of fingerprints is much shorter (# phrases),
but has a larger alphabet (# distinct fingerprints)

Parsing

Fingerprinting

Indexing

Querying

Different ways to select the anchors

We'll focus on sampling *k*-mers based on their (canonical) **hash**

Sampling parameter *p*

Expected distance between selected *k*-mers

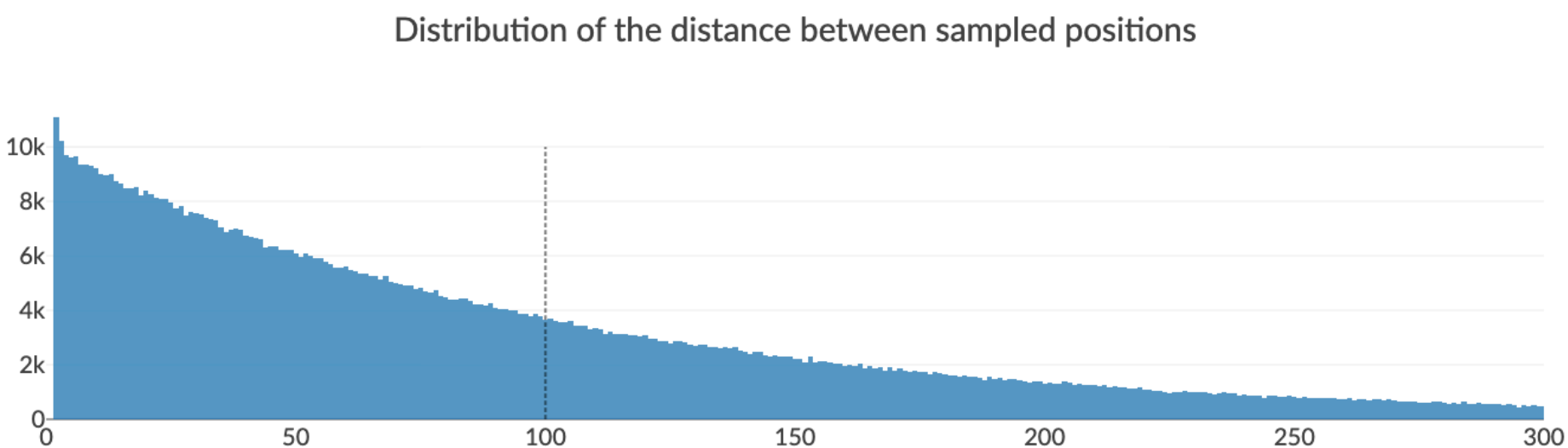
- **context-free**: e.g. $h = 0 \bmod p$ or $h \leq \frac{\texttt{maxint}}{p}$ (prefix-free parsing)

$\rightarrow$ simple and fast, but the distance is *unbounded*

- **context-based**: e.g. minimizer schemes, syncmers...

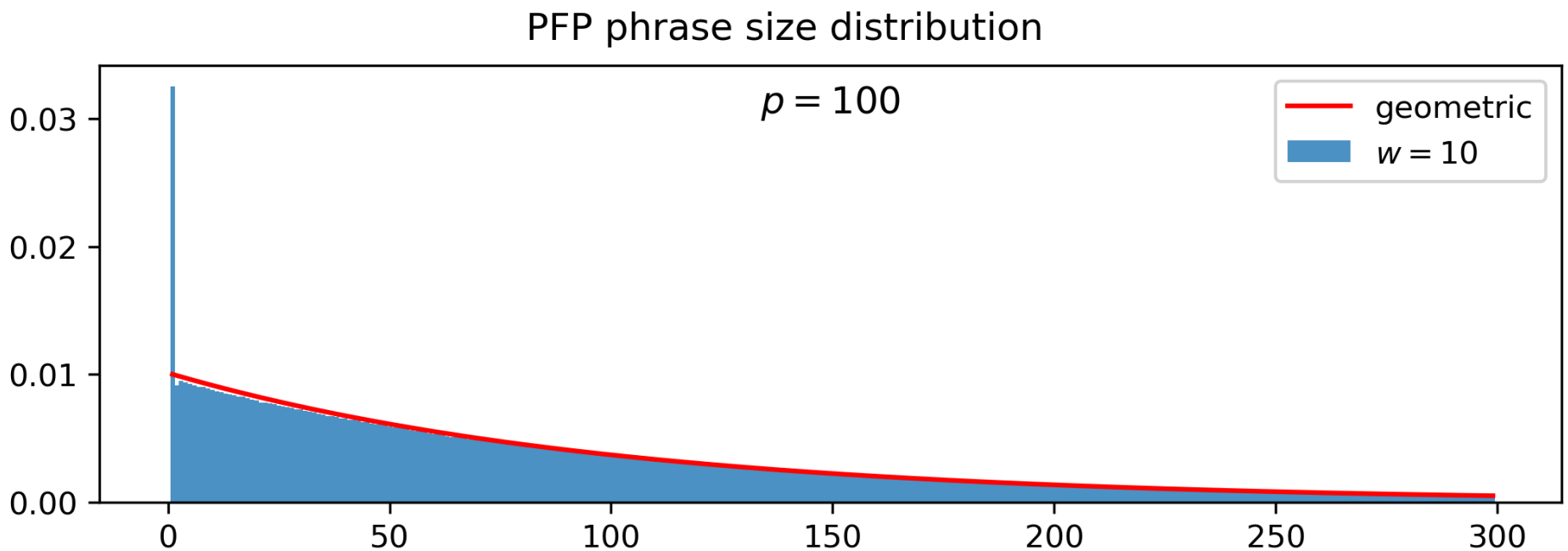
$\rightarrow$ more involved, but ensure a *window guarantee*

A look at prefix-free parsing (PFP)



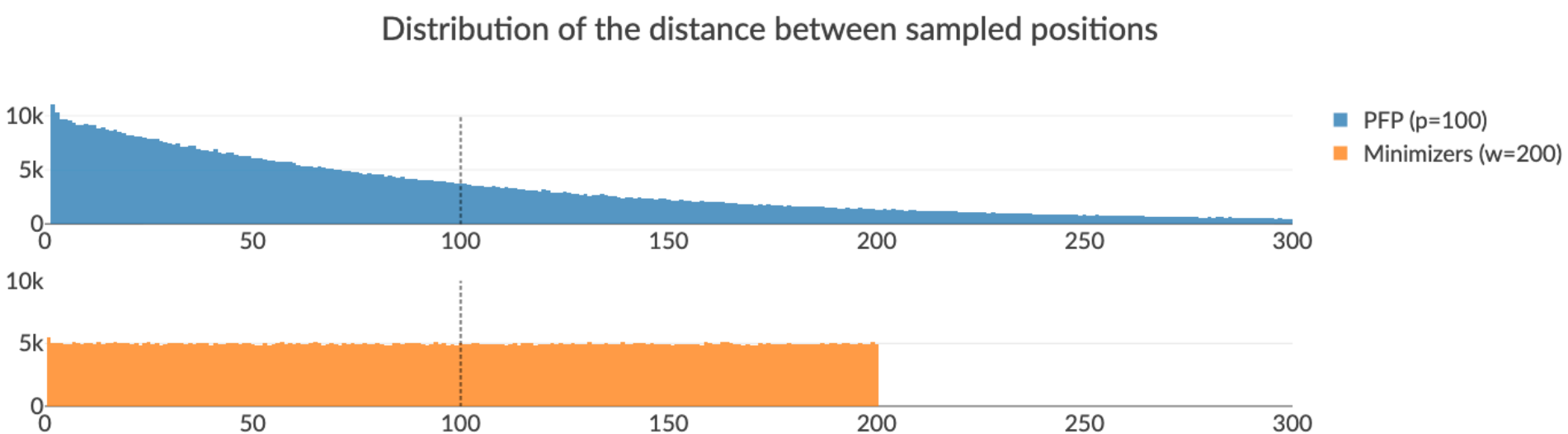
Context-free anchors produce a ~geometric distribution

Sidenote: Biased hash (NtHash) → biased distribution



Experiments available at github.com/imartayan/pfp-distribution

Enforcing an upper-bound with minimizers

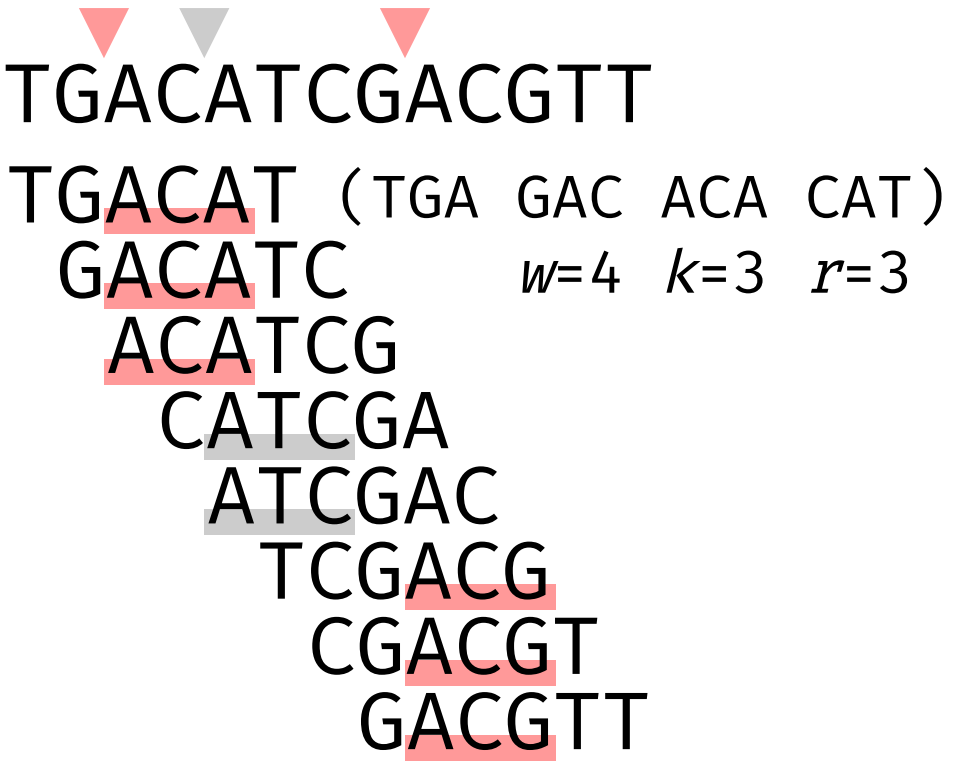


Random minimizers produce a ~uniform distribution

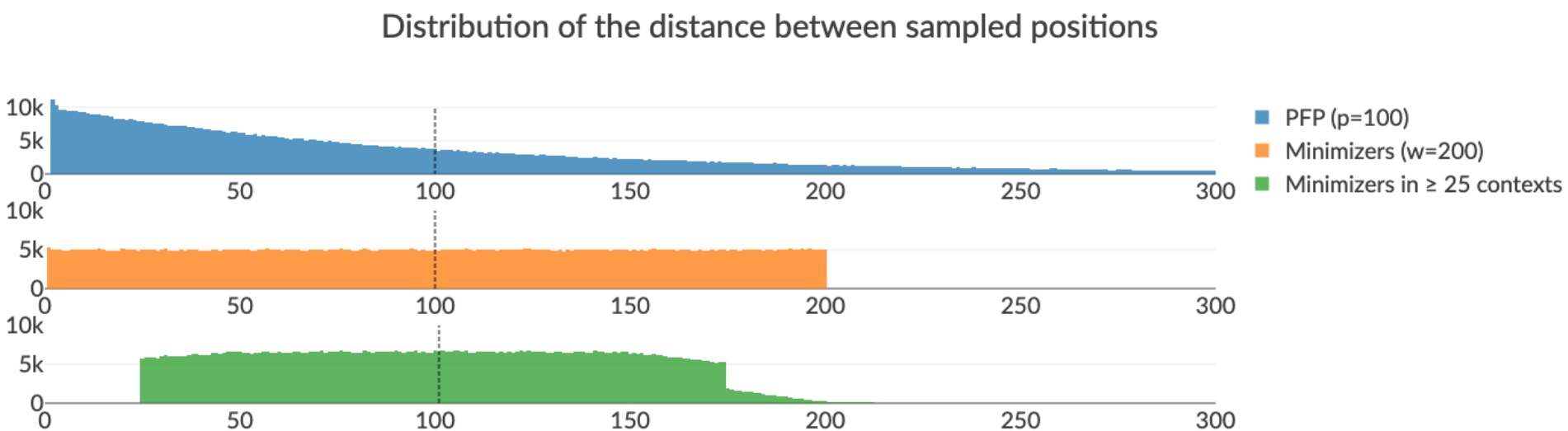
Enforcing a lower bound with *robust* minimizers

Given a robustness factor r, only keep minimizers that are selected in a least r windows.

$\Rightarrow$ at least r positions apart



Enforcing a lower bound with *robust* minimizers



Open question: can we enforce a lower *and* an upper bound?

Parsing

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Querying

Representing phrases by their fingerprints

- Instead of storing the raw sequences of each phrase, we can represent them by small fingerprints (e.g. 64-bit hashes)
- If we use a rolling hash, this step can be merged with parsing!
- Enables fast exact matches, but not fine-grained comparison

What if we want to match phrases within small edit distance?

Using small sketches for approximate matching

Idea: compute sketches for each phrase to estimate similarity

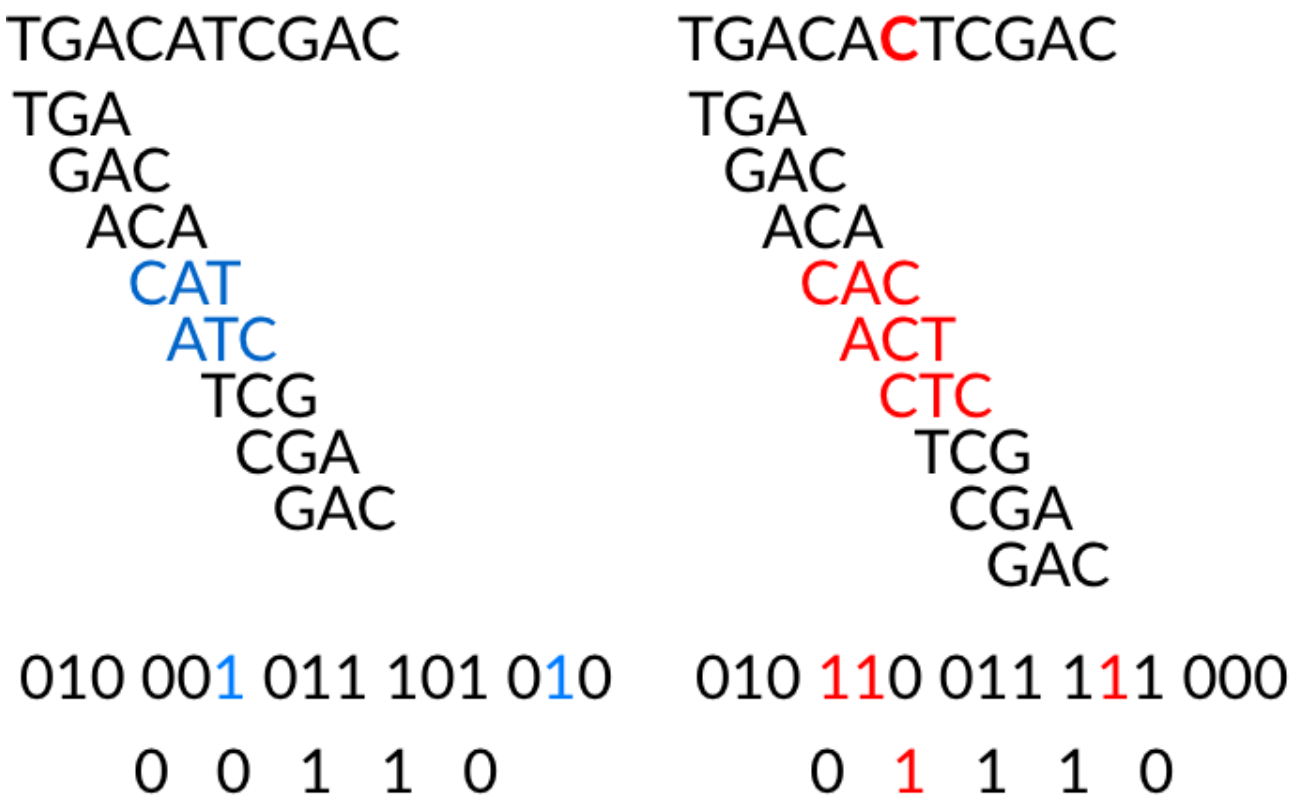
One approach:

- store the k-mers of a phrase Bloom filter (k should be small!)
- build a small sketch by averaging blocks from the Bloom filter

quantized BF of similar phrases have a low Hamming distance

(other ideas worth exploring: MinHash, DotHash)

Quantized Bloom Filter



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Overview of the (uncompressed) index

Component	Data structure	Size estimation (on CHM13v2, p=100)
Phrase positions	Elias-Fano	5 MB
Phrase orientations	Bitvector	0.5 MB
Phrase fingerprints	Array	15 MB
Index	Suffix array	15 MB

Total size: ~35 MB for a human genome (3.2 Gbp)

How fast is it? (on my laptop, using 8 threads)

	Incremental steps	Throughput
1.	Hashing k-mers	15 Gbp/s
2.	Sampling minimizers*	5 Gbp/s
3.	Hashing phrases	5 Gbp/s
4.	Indexing fingerprints	1.5 Gbp/s

$\rightarrow$ indexing a human genome takes ~2s

*using github.com/rust-seq/simd-minimizers

Towards a compressed version of the index (not implemented yet)

If the text is repetitive, we can store the index in $O(\#\text{BWT runs})$ using different data structures:

- any compressed representation of the phrases supporting random access, e.g. **relative Lempel-Ziv** (Kuruppu et al. 10)
- the **suffixient array** of the fingerprints (Cenzato et al. 24)

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Using this index for mapping (WIP)

Heuristics:

1. look for exact matches on the fingerprints
   using the suffix(ient) array (similar to STAR)

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2. try to extend them as much as possible
   with approximate matches (with few errors)
3. chain close matches that have the same orientation

Take-home messages

- very flexible framework (parse / fingerprint / index)
- supports both exact and approximate queries
- vectorized implementation
- (optional) compressed space

What's next?

- finish the mapper
- experiment with the different parameters (p, r, k...)
- implement compressed index

Take-home messages

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Thank you!

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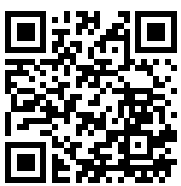
Rust crates for vectorized sequence processing 🦀

Helicase: vectorized parsing & bitpacking

github.com/imartayan/helicase

Seq-hash: vectorized rolling hash

github.com/rust-seq/seq-hash



SIMD minimizers & syncmers

github.com/rust-seq/simd-minimizers