Genome-on-Diet

Taming Large-Scale Genomic Analyses via Sparsified Genomics

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14 April 2023

ETH zürich

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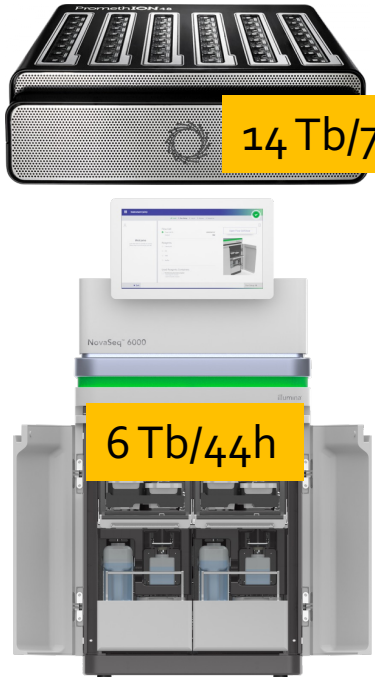
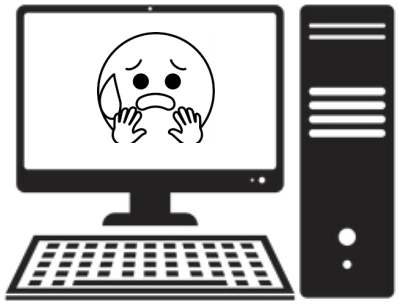
Genome Sequencing is Rapidly Growing

Specialized Machine
for Sequencing

Genome Sequencing is Rapidly Growing

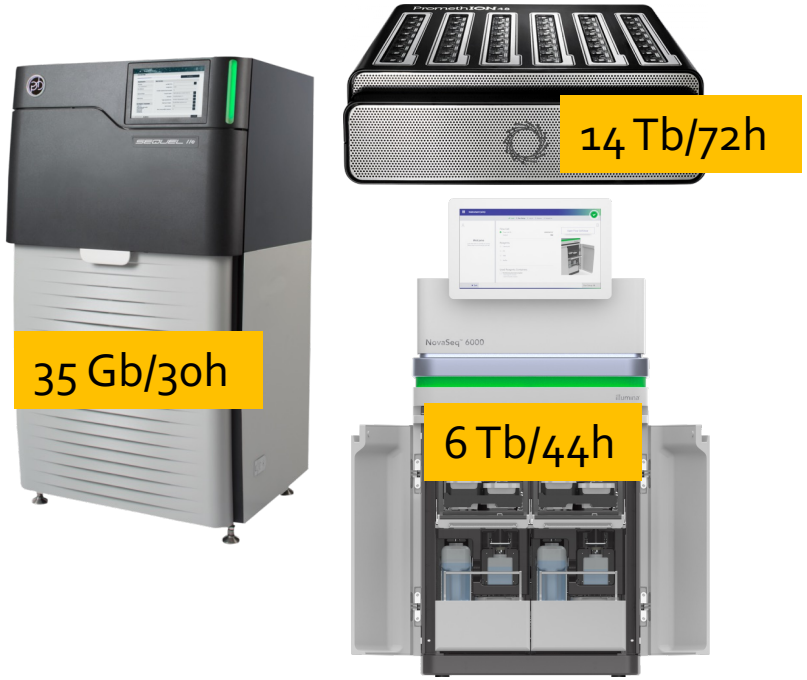


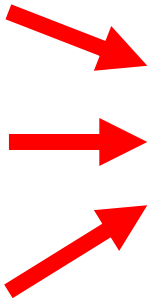
Specialized Machine
for Sequencing



General-Purpose Machine
for Analysis

Lack of Specialized Compute Capability





Specialized Machine for Sequencing

General-Purpose Machine for Analysis

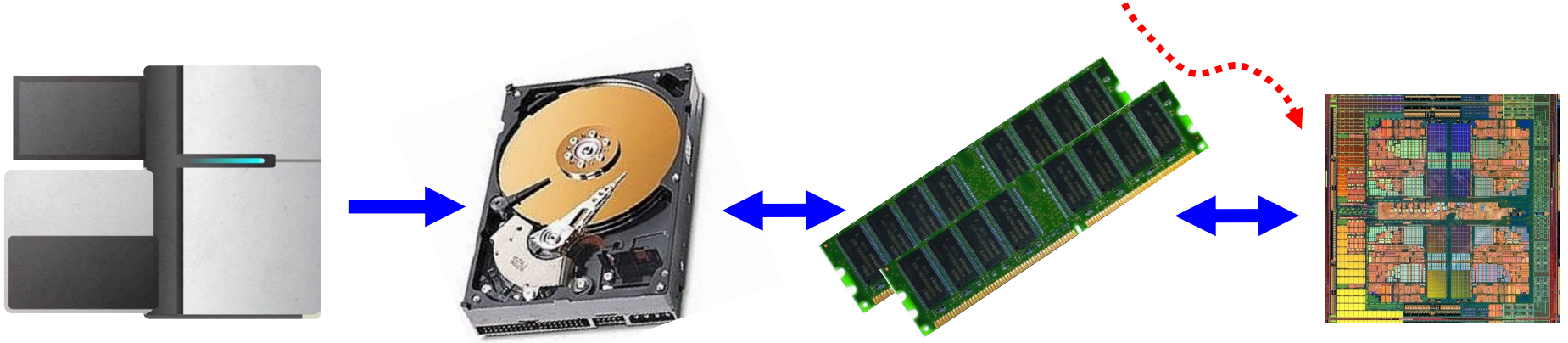
FAST

SLOW

Improving Processing via Accelerators

Specialized Genomic Accelerators (GPU, FPGA)

- **Scrooge [Bioinformatics 2023]**
- **RUBICON [arXiv 2022]**
- **GateKeeper-GPU [IPDPSW 2021]**
- **SneakySnake [Bioinformatics'20]**
- **Shouji [Bioinformatics 2019]**
- **MAGNET [AACBB 2018]**
- **GateKeeper [Bioinformatics 2017]**



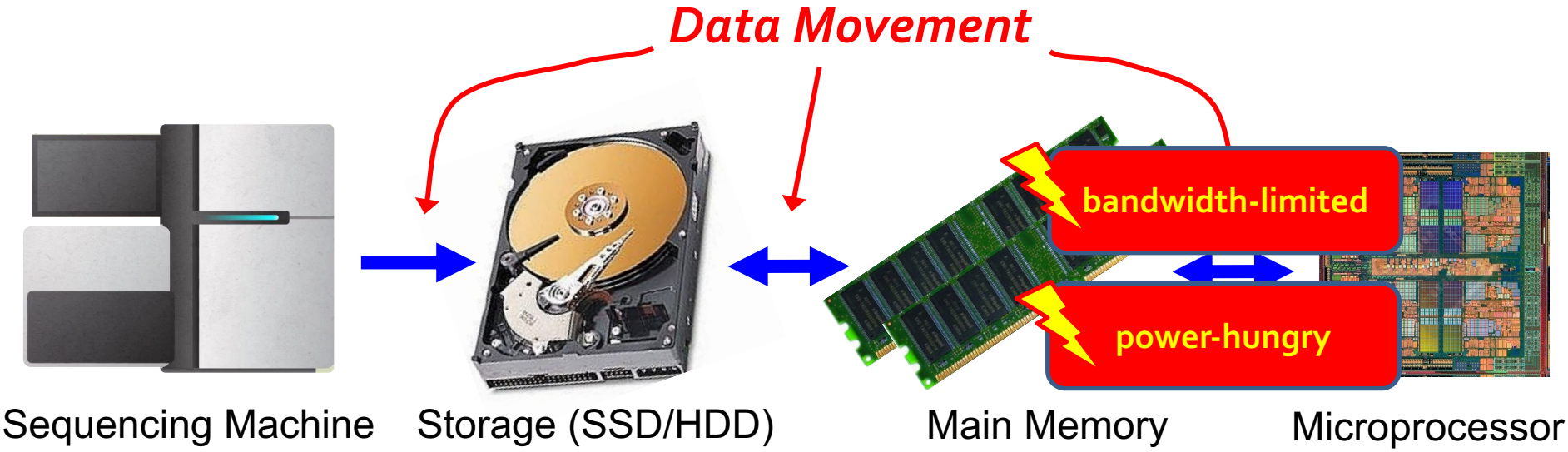
Sequencing Machine | Storage (SSD/HDD) | Main Memory | Microprocessor

Data Movement Bottleneck

Data movement is a major bottleneck
in modern computer architectures

Over 60% of the total system energy is spent on data movement

A. Boroumand et al., "Google Workloads for Consumer Devices: Mitigating Data Movement Bottlenecks," ASPLOS, 2018



Improving Processing via Paradigm Shift

Near-memory/In-memory Genomic Accelerators

AIM [Bioinformatics 2023]

SeGraM [ISCA 2022]

Specialized Genomic Accelerators (GPU, FPGA)

Scrooge [Bioinformatics 2023]

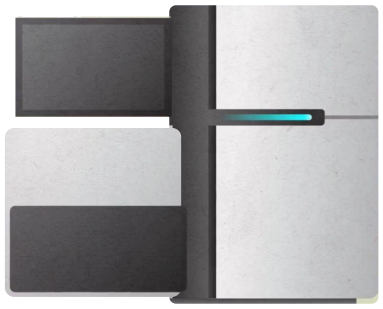
RUBICON [arXiv 2022]

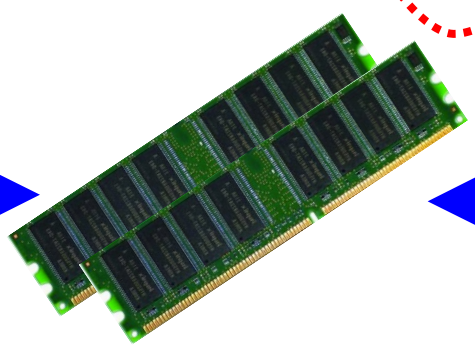
GateKeeper [Bioinformatics 2017]

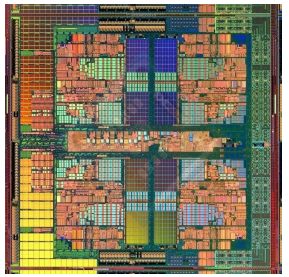
Improving **performance** and **energy efficiency** by 1-3 orders of magnitude

In-Storage Sequence Alignment

GenStore [ASPLOS 2022]







Sequencing Machine | Storage (SSD/HDD) | Main Memory | Microprocessor

Our Goal

To further reduce the execution time

and memory/storage footprint of genomic

analyses via **sparsified genomics**

Sparsifying Genomic Data

ACCCTAACCCTAACCCTAACCCTAACCCTAA

Exact Match

ACCCTAACCCTAACCCTAACCCTAACCCTAA

Sparsifying Genomic Data

ACCCTAACCCTAACCCTAACCCTAACCCTAA — N Bytes

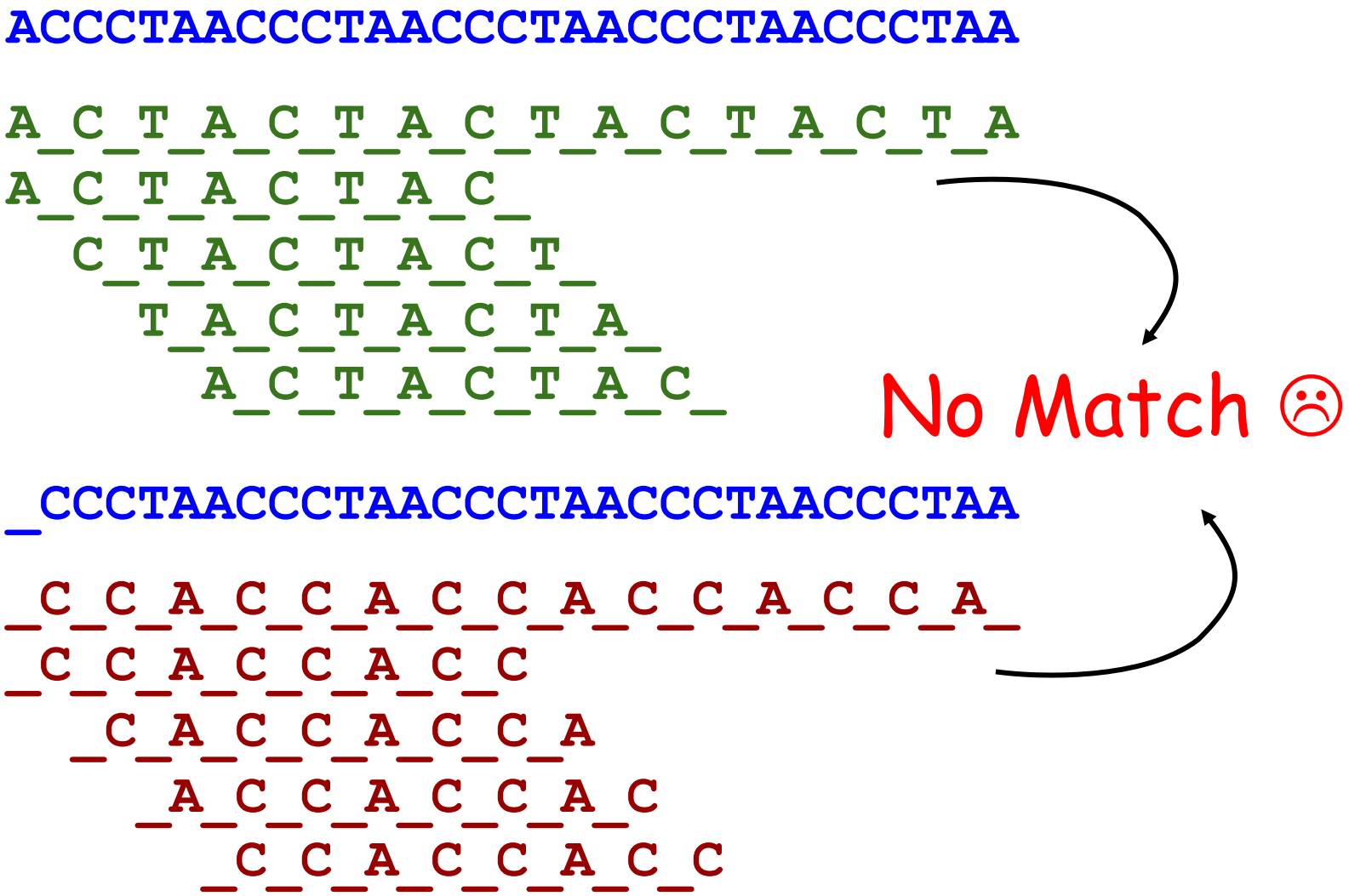
A_C_T_A_C_T_A_C_T_A_C_T_A_C_T_A — N/2 Bytes

Still Exact Match

ACCCTAACCCTAACCCTAACCCTAACCCTAA

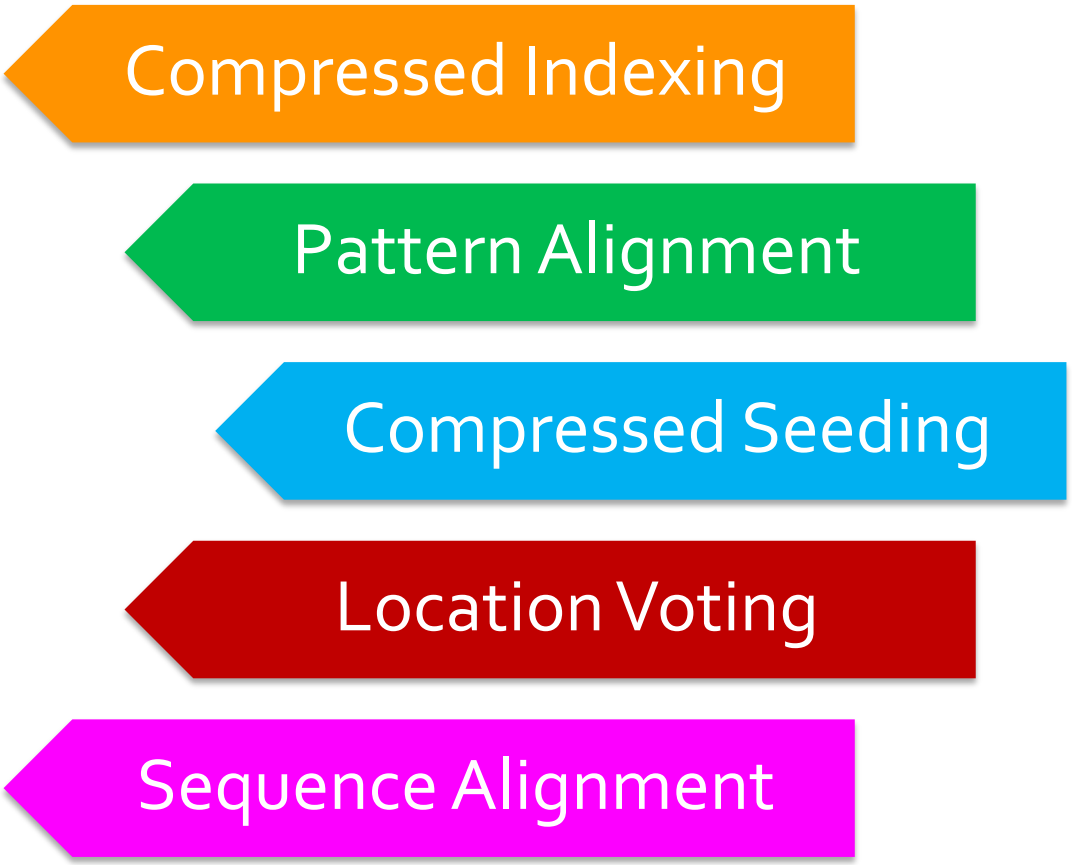
A_C_T_A_C_T_A_C_T_A_C_T_A_C_T_A

Sparsifying Genomic Data Is Challenging



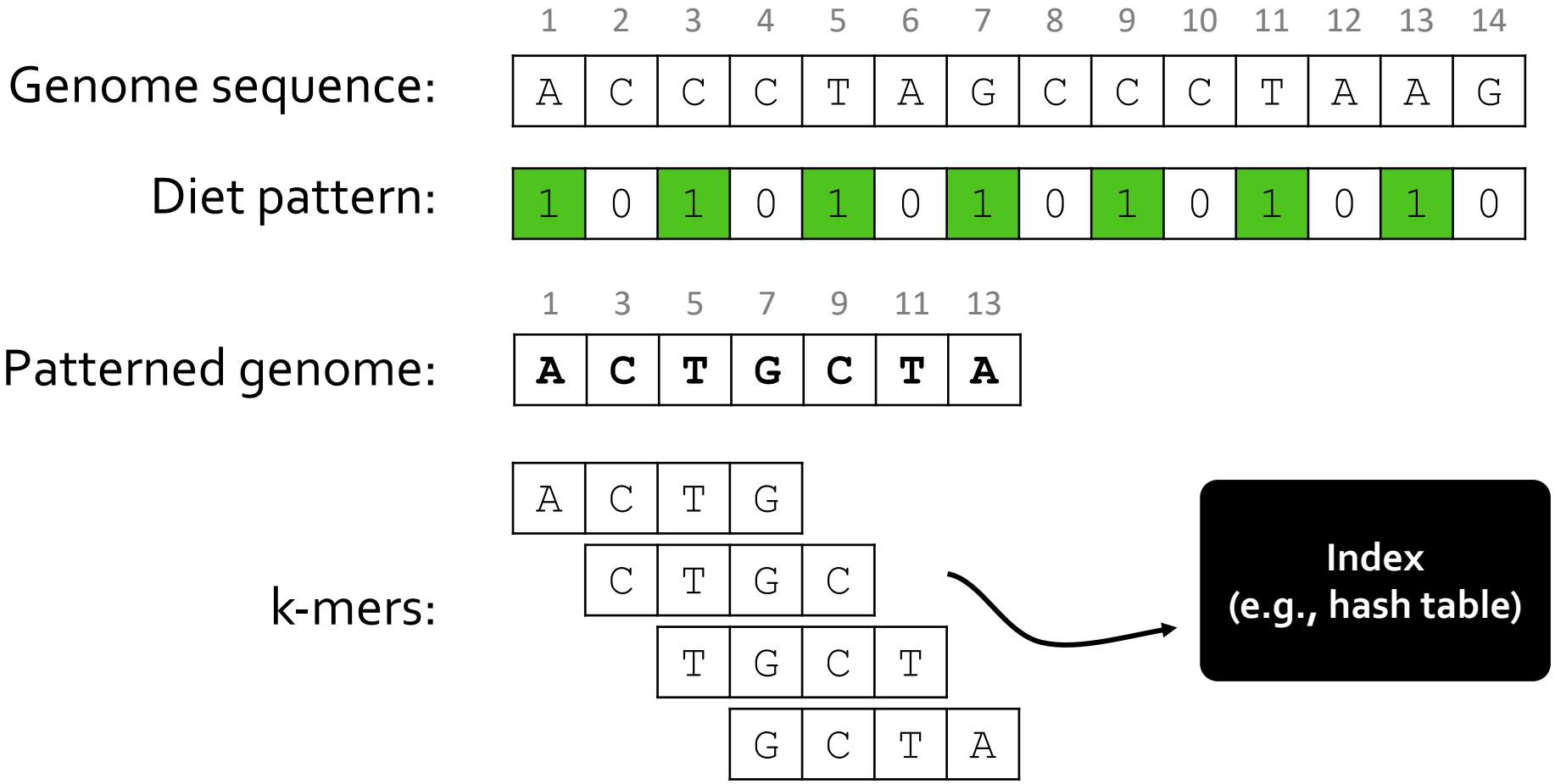
How It Works?

Genome-on-Diet Steps



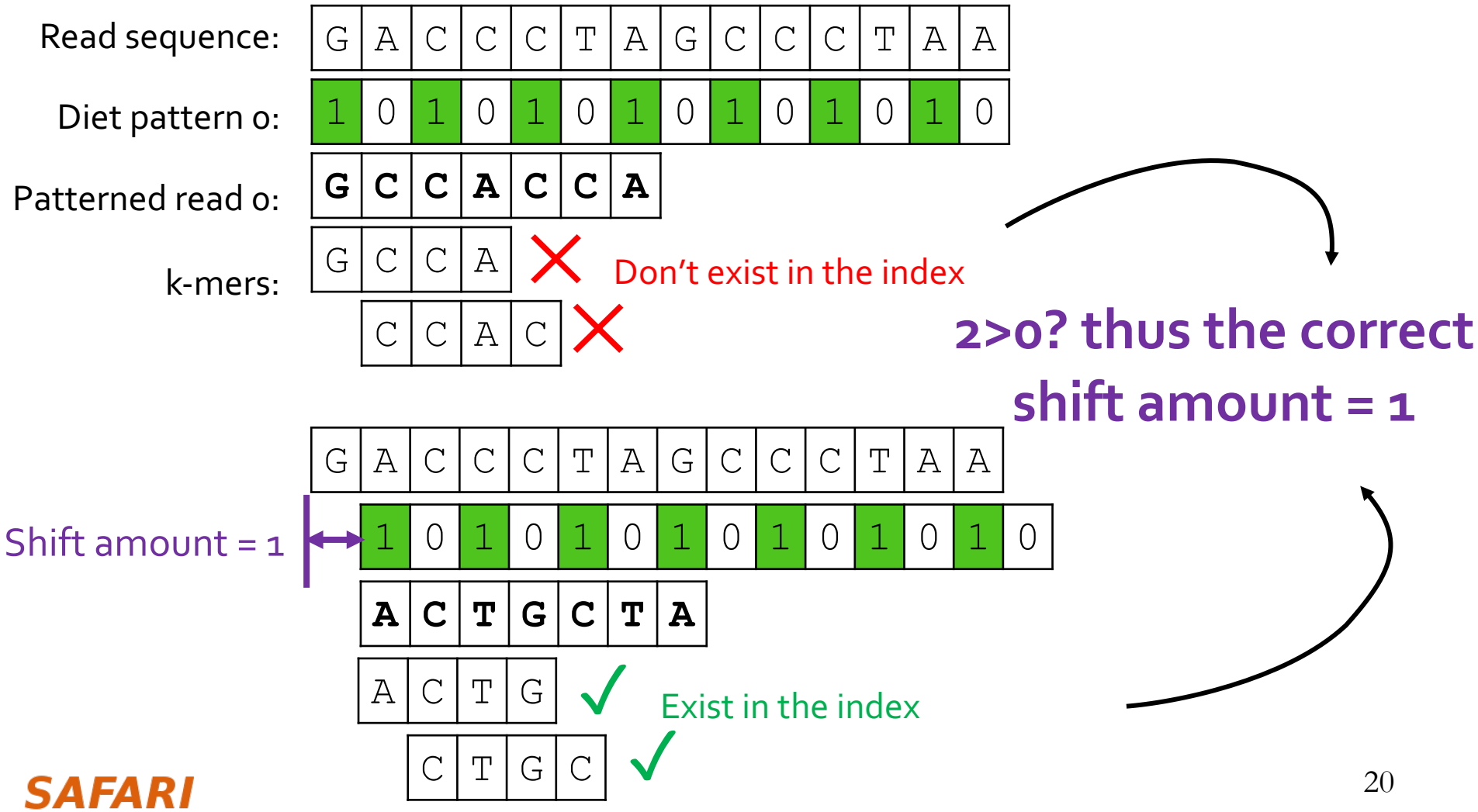
Step 1: Compressed Indexing

- We use a user-defined binary pattern to identify the location and number of the to-be-dropped bases.



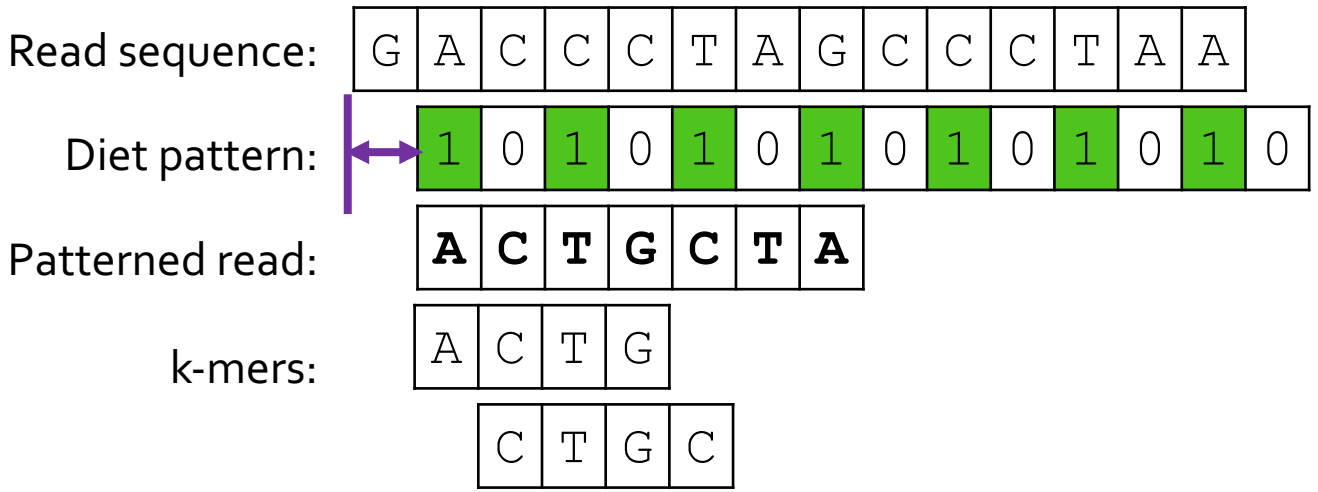
Step 2: Pattern Alignment

- Deciding where in the read to apply the pattern essential for the correctness of Genome-on-Diet



Step 3: Compressed Seeding

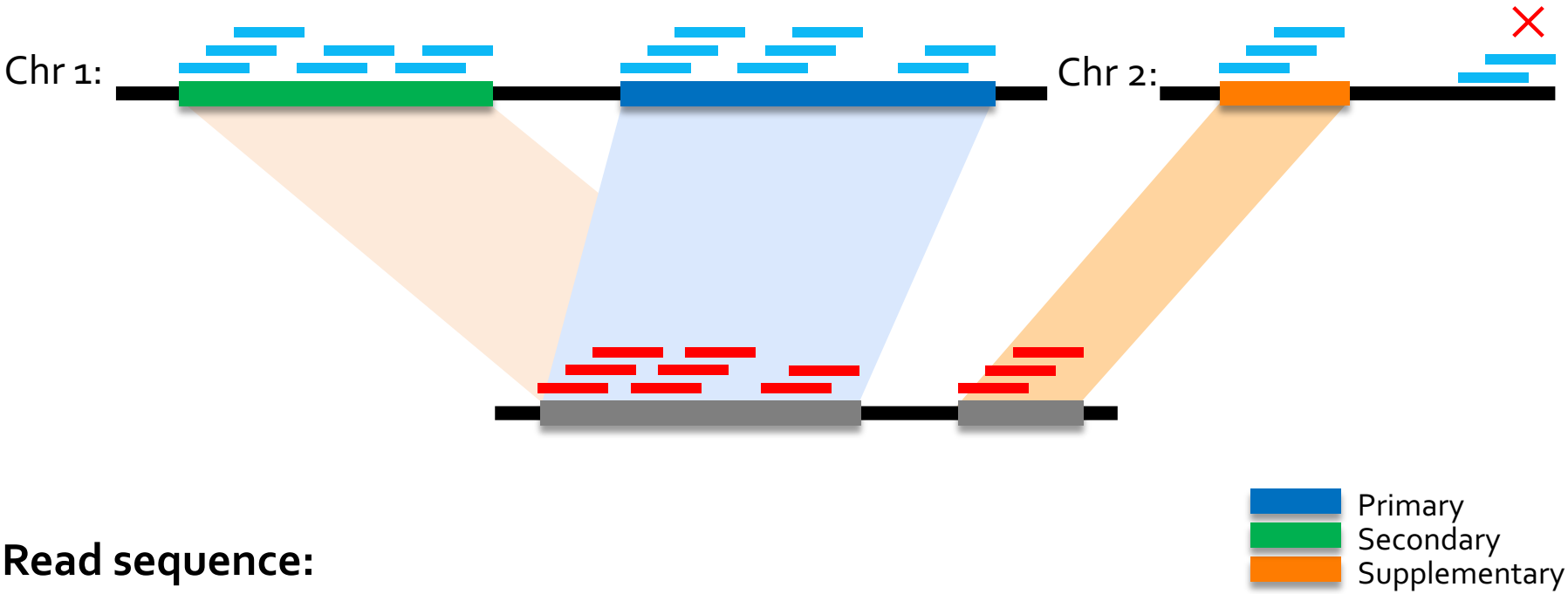
- Use the calculated shift amount to correctly extract seeds from the read sequence.
- Now both the reference genome and the read are half in length and their seeds can be still correctly matched



Step 4: Location Voting

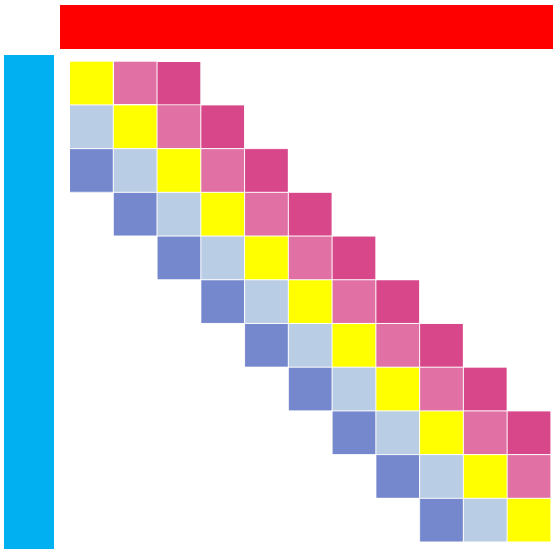
- Seeds are sparsified and thus cannot be directly chained, instead to detect mapping locations we use the number of matching seeds in a region

Genome sequence:



Read sequence:

Step 5: Sequence Alignment



Dynamic programming matrix

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Brief Communication | Published: 28 February 2022

Accelerating minimap2 for long-read sequencing applications on modern CPUs

Saurabh Kalikar ✉, Chirag Jain ✉, Md Vasimuddin ✉ & Sanchit Misra ✉

Nature Computational Science **2**, 78–83 (2022) | Cite this article

BMC Bioinformatics

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Methodology | Open Access | Published: 19 February 2018

Introducing difference recurrence relations for faster semi-global alignment of long sequences

Hajime Suzuki & Masahiro Kasahara ✉

BMC Bioinformatics **19**, Article number: 45 (2018) | Cite this article

CPU Implementation

Genome-on-Diet is implemented on top of minimiap2
(2.24-r1122 version as of 11 November 2022)

Introducing Four Optimization Strategies

- Accelerating Indexing & Seeding with **SIMD Instructions**
  - Calculating 8 (512/(32*2)) overlapping k-mers along with their hash values in parallel
- **Sorting** Seed Locations
  - Merge sort instead of Radix and Heap sort algorithms
- **Rescuing** Mapping Location
  - Based on two voting thresholds
- Handling **Exactly-Matching** Short Reads
  - It is observed that 80% of short reads usually exactly match to the reference genome

Applications of Sparsified Genomics

- Applications that compare sequences for similarity
  - Genome similarity & genomic distance
  - Prealignment filtering
  - Containment search

They may or may not require building index

- Applications that generate huge index
  - Taxonomic profiling
  - Pangenomics

Index can be up to 21.25x larger in size than a single (2-bit encoded) indexed genome

- Applications that require building index during the analysis
  - Read mapping for many assembly ve
  - Identifying *de novo* variations by con members
  - Identifying somatic variations by con healthy and tumor cells of the same patient

Indexing and seeding time account for

97% Taxonomic Profiling

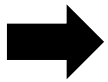
10%-27% Read Mapping

- And many more …

Genome-on-Diet vs. Spaced Seeding?

Spaced Seeding:

```
ACCCTAACCCTAACCCTAACCCTAA..
ACCCTAACCC
 CCCTAACCCT
  CCTAACCCTA
   CTAACCCTAA
    TAACCCTAAC
     AACCCTAACC
```



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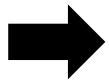


```
A___T_A__C
 C___A_C__T
  C___A_C__A
   C___C_C__A
    T___C_T__C
     A___C_A__C
```

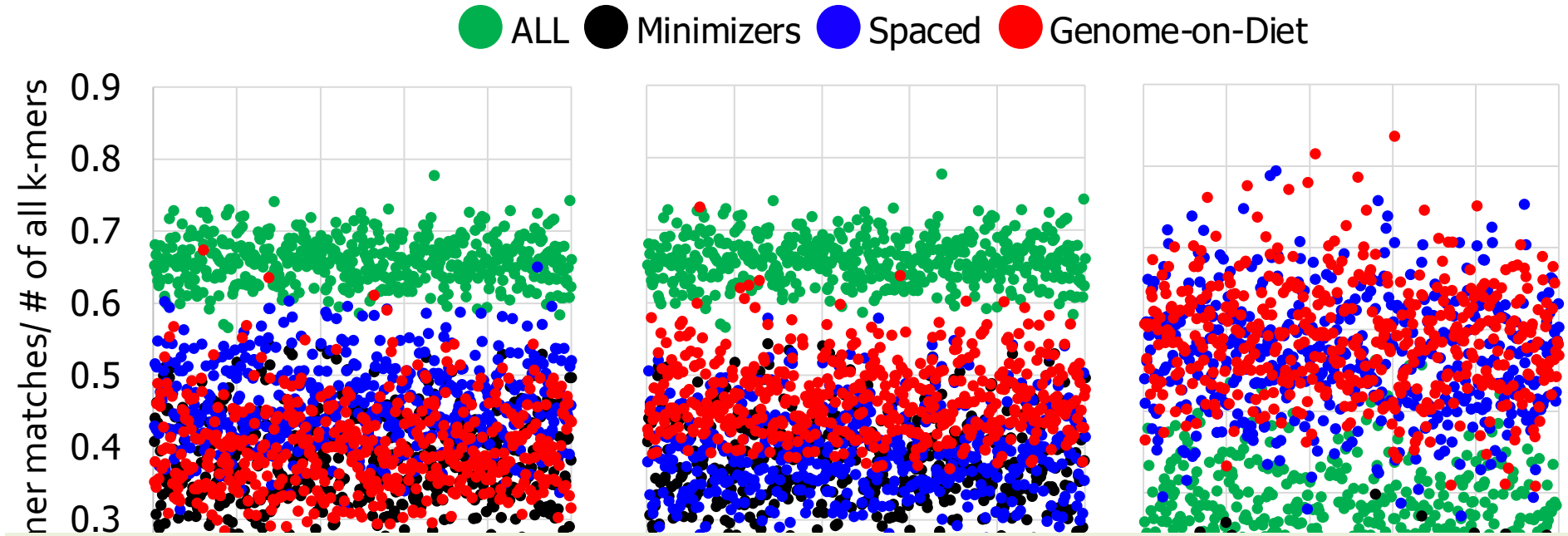
Increased execution time
No effect on peak memory footprint
No effect on the number of seeds
All seeds have the same pattern

Genome-on-Diet:

```
ACCCTAACCCTAACCCTAACCCTAA..
10001010011000101001000101001
A___T_A__CT___C_T__CC___A..
A___T_A__C
   T_A__CT
     A__CT___C
```

Reduced execution time
Reduced peak memory footprint
Reduced number of seeds
Each seed may have its own pattern

Increasing Common k-mers Rate



Genome-on-Diet provides the same or higher sensitivity compared to spaced seeding, while Genome-on-Diet is always faster and more memory efficient

Evaluation Results

Great Benefits by Sparsified Genomics

Read Mapping

- Genome-on-Diet is 1.13-6.28x faster and has 2.1x smaller memory footprint, and 2x smaller index size compared to minimap2, for performing read mapping.

Containment Search

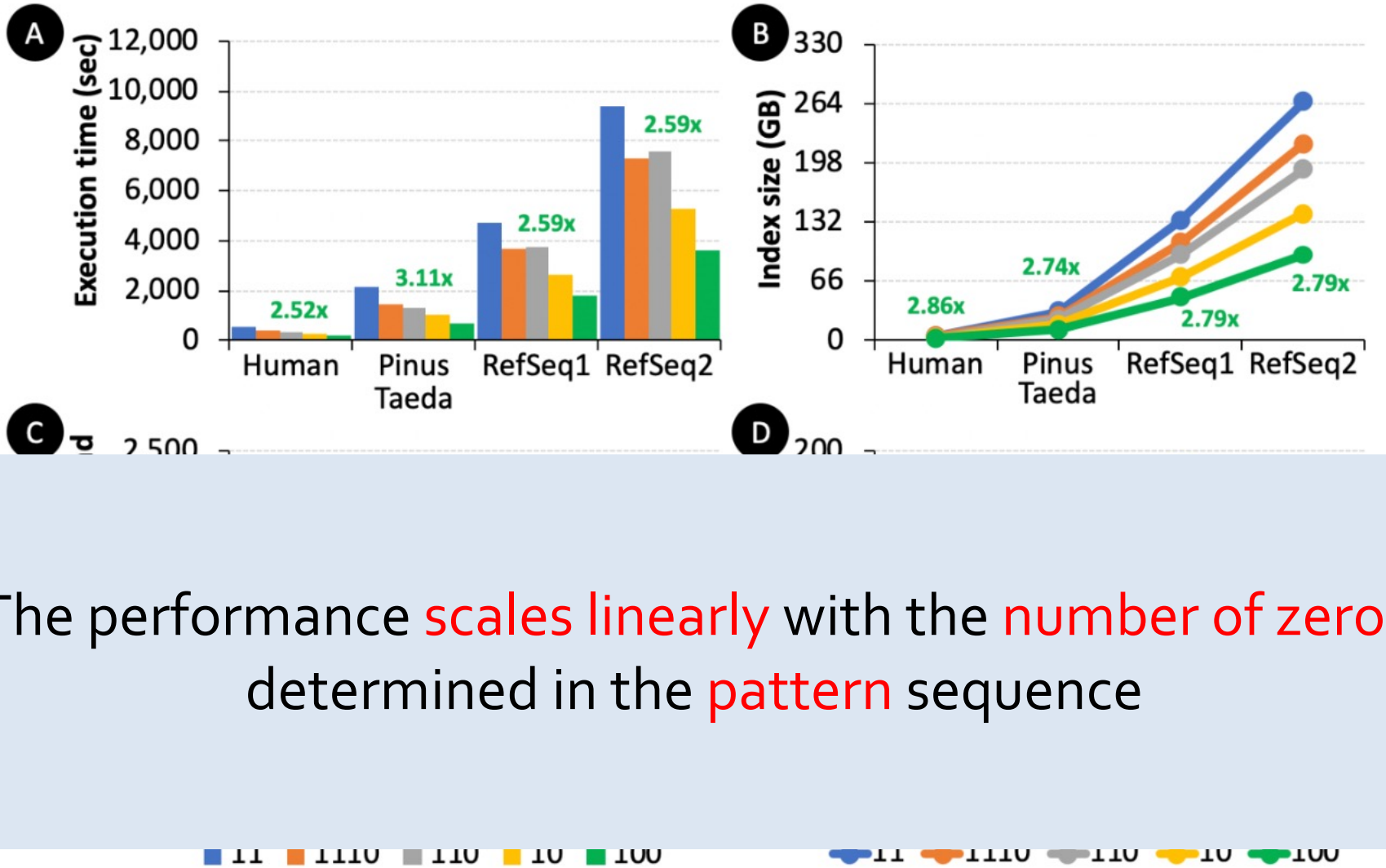
- Genome-on-Diet is 72.7-75.88x faster and 723.3x more storage-efficient than KMC3 combined with CMash, for performing containment search.

Metagenomic Profiling

- Genome-on-Diet is 54.15-61.88x faster and 720x more storage-efficient than Metalign, for performing taxonomic profiling of metagenomic samples.

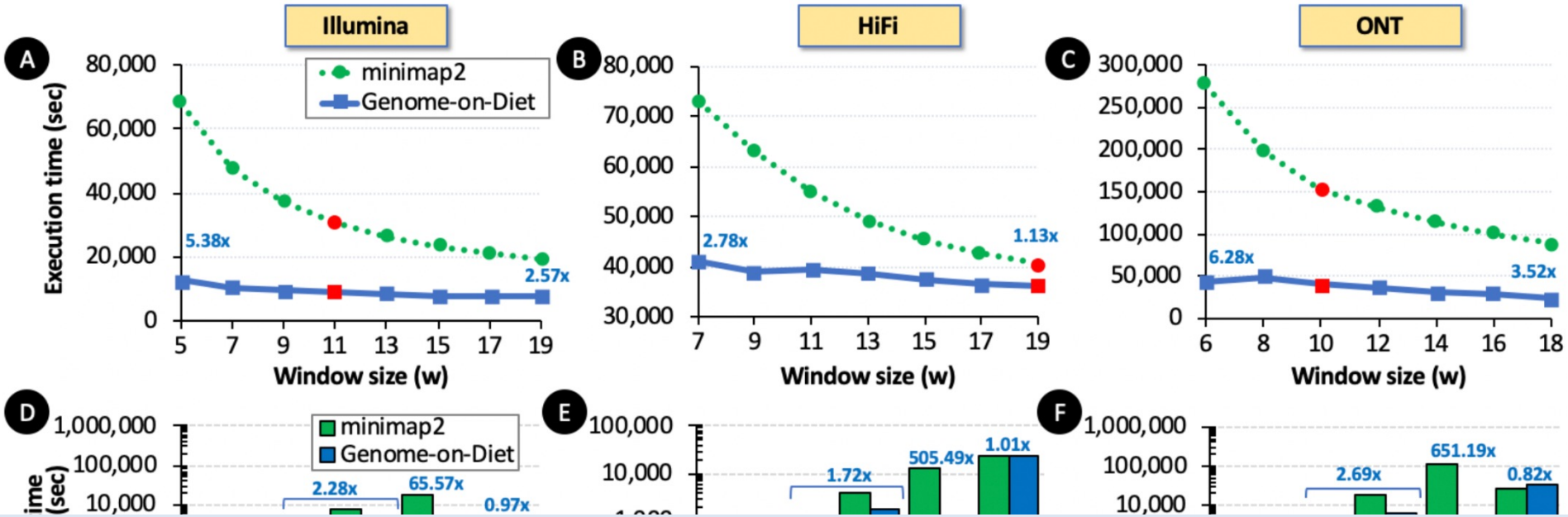
Effect of Using Different Patterns

For performing both containment indexing and k-mer intersection



The performance scales linearly with the number of zeros determined in the pattern sequence

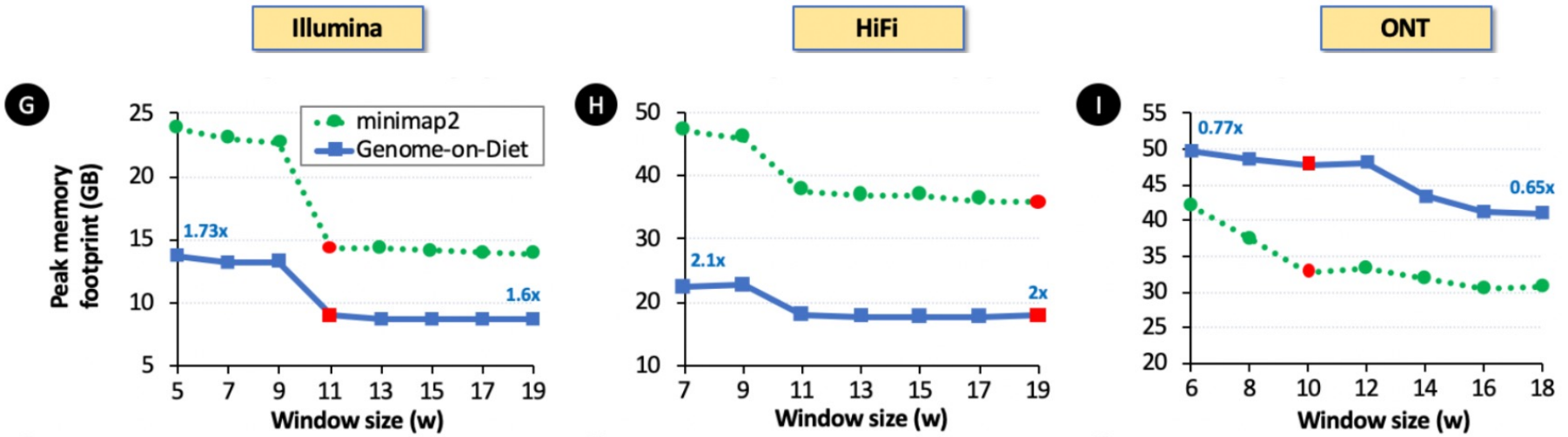
See Our Paper for Many More Analyses and Results



Genome-on-Diet performance is not affected by the value of minimizer window.

Location voting step is much faster than seed chaining

See Our Paper for Many More Analyses and Results



J

		G-on-Diet	minimap2
Indels / SNPs	Correctly detected	**19,105**	18,178
	Incorrectly detected	787	**14**
	Missed	**2,119**	3,046
Execution time (sec)		**9,178.78**	31,358.75
Peak memory (GB)		**8.62**	14.38

K

		G-on-Diet	minimap2
Indels / SNPs	Correctly detected	**17,795**	17,297
	Incorrectly detected	2,028	**938**
	Missed	**3,429**	3,927
SVs	Correctly detected	**193**	185
	Incorrectly detected	57	**11**
	Missed	**23**	31
Execution time (sec)		**37,787.72**	41,016.12

L

		G-on-Diet	minimap2
Indels / SNPs	Correctly detected	**13,432**	5,717
	Incorrectly detected	5,620	**3,862**
	Missed	**7,792**	15,507
SVs	Correctly detected	**147**	41
	Incorrectly detected	**61**	226
	Missed	**69**	175
Execution time (sec)		**40,348.88**	161,545.61

Genome-on-Diet leads to the detection of a higher number of SNPs, indels, and SVs compared to minimap2

Preprint and Source Code

Computer Science > Data Structures and Algorithms

[Submitted on 15 Nov 2022 (v1), last revised 18 Jan 2023 (this version, v2)]

Genome-on-Diet: Taming Large-Scale Genomic Analyses via Sparsified Genomics

Mohammed Alser, Julien Eudine, Onur Mutlu

https://arxiv.org/abs/2211.08157

https://github.com/CMU-SAFARI/Genome-on-Diet

Contributors

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Genome-on-Diet

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