Storage-Centric Computing for Genomics and Metagenomics

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SAFARI

Brief Self Introduction

- A PhD student at the SAFARI Research Group @ ETH Zurich, advised by Professor Onur Mutlu

- **Research interests:**
  - Computer architecture
  - Large-scale bioinformatics applications
  - Storage systems
  - Near data processing
  - Emerging technologies such as ultra-dense 3D integrated systems

- **Contact information**
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  - **Personal website:** https://bit.ly/nikamgh

Outline

- Brief Intro to (Meta)Genomics

- Storage-Centric Designs for (Meta)Genomics
  - GenStore
  - MegIS

- Conclusion

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- *Brief Intro to (Meta)Genomics*

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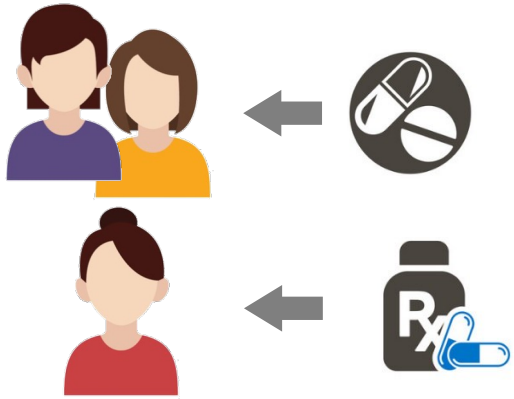
- Conclusion

Genomics and Metagenomics are Critical for Many Applications



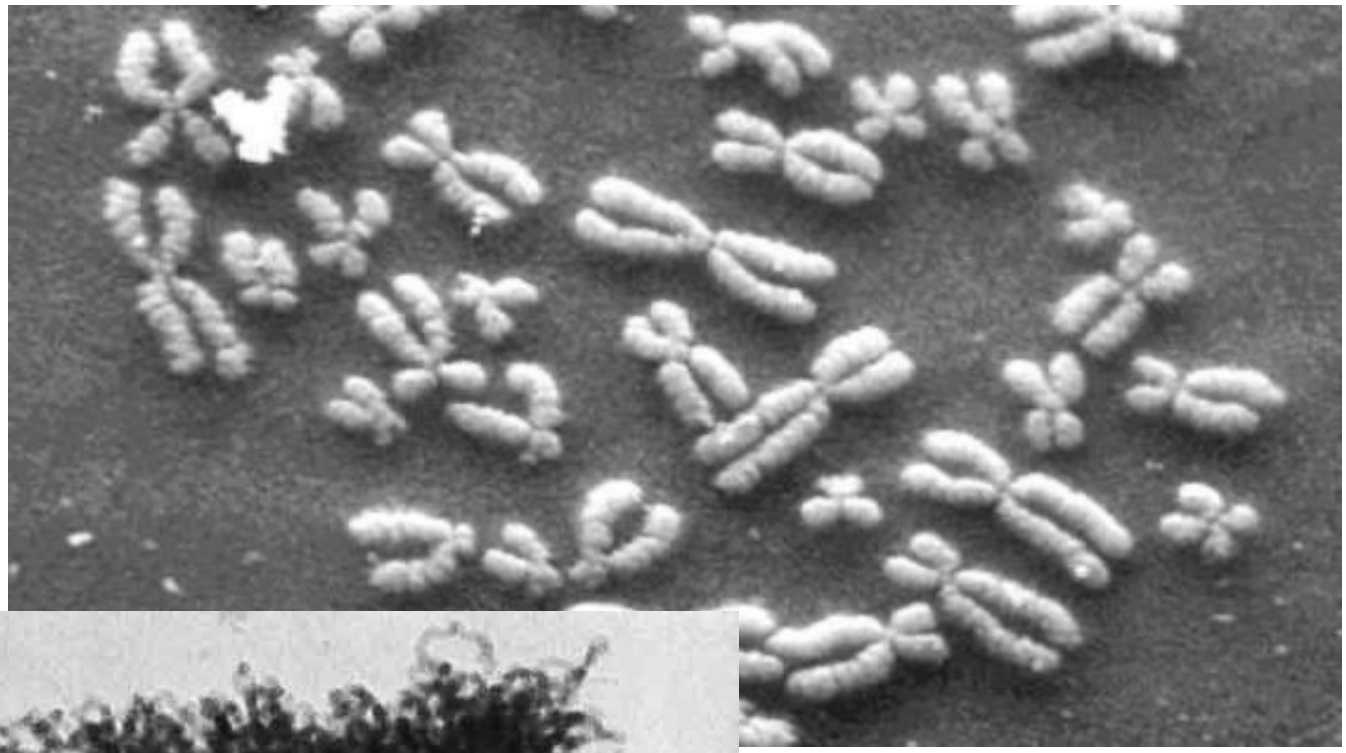
Developing **personalized medicine**

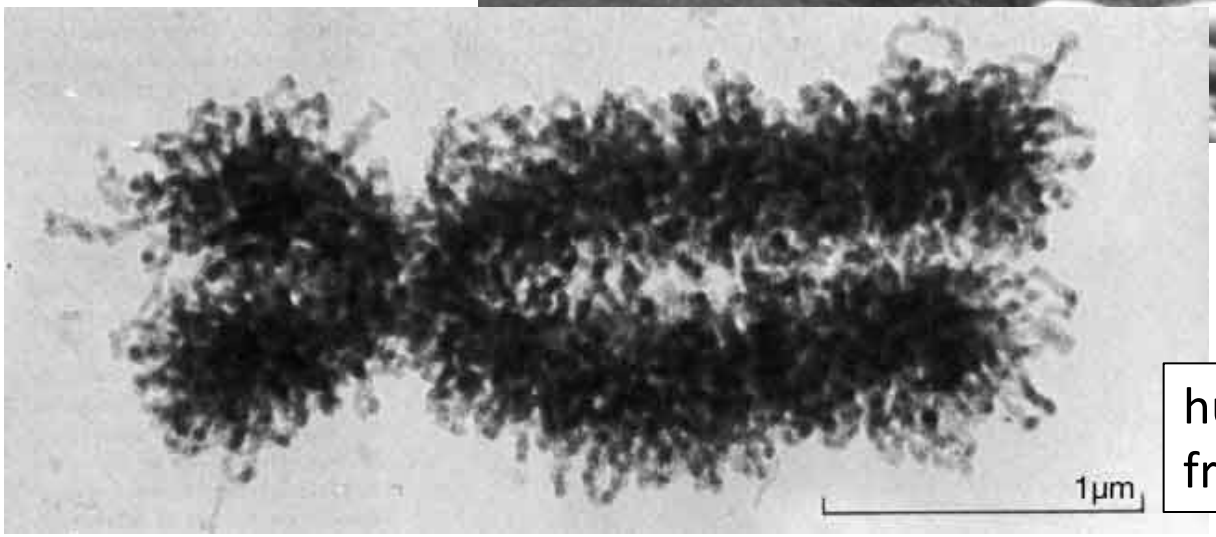
Predicting the presence and relative abundance of **microbes** in a sample

Rapid surveillance of **disease outbreaks**

Understanding **genetic variations, species, evolution, …**

DNA Under Electron Microscope



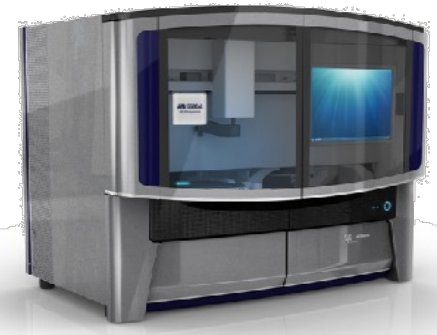


human chromosome #12
from HeLa's cell

CCTCCTCAGTGCCACCCAGCCCACTGGCAGCTCCCAAACA
GGCTCTTATTAAAACACCCTGTTCCCTGCCCCTTGGAGTG
AGGTGTCAAGGACCTAAACTAAAAAAAAAAAAAGAAAA
AGAAAAGAAAAAGAATTTAAAATTTAAGTAATTCTTTGAA
AAAAACTAATTTCTAAGCTTCTTCATGTCAAGGACCTAATG
TGCTAAACAGCACTTTT**TTGACCATTAT**TTTGGATCTGAAA
GAAATCAAGAATAAATGAAGGACTTGATACATTGGAAGA
GGAGAGTCAAGGACCTACAGAAAAAAAAAAAAAAGAAA
AAGAAAAGAAAAAGA**A**TTTAAAATTTAAGTAATTCTTTGA
AAAAAACTAATTTCTAAGCTTCTT**C**ATGTCAAGGACCTAAT
GTCTGTGTTGCAGGTCTTCTTGCATTTCCCTGTCAAAAGA
AAAAGAATTTAAAATTTAAGTAATTCTTTGAAAAAAACTA
ATTTCTAAGCTTCTTCATGTCAAGGACCTAATGTCAGGCC
GGCTCTTATTAAAACACCCTGTTCCCTGCCCCTTGGAGTG

Genome Sequencers

Roche/454



AB SOLiD

Illumina MiSeq

Complete Genomics

Oxford Nanopore MinION

Illumina NovaSeq 6000

Illumina HiSeq2000

Pacific Biosciences RS

Oxford Nanopore GridION

Ion Torrent PGM

Ion Torrent Proton

… and more! All produce data with different properties.

High-Throughput Sequencers

Illumina MiSeq

Pacific Biosciences Sequel II

Oxford Nanopore PromethION

Oxford Nanopore MinION

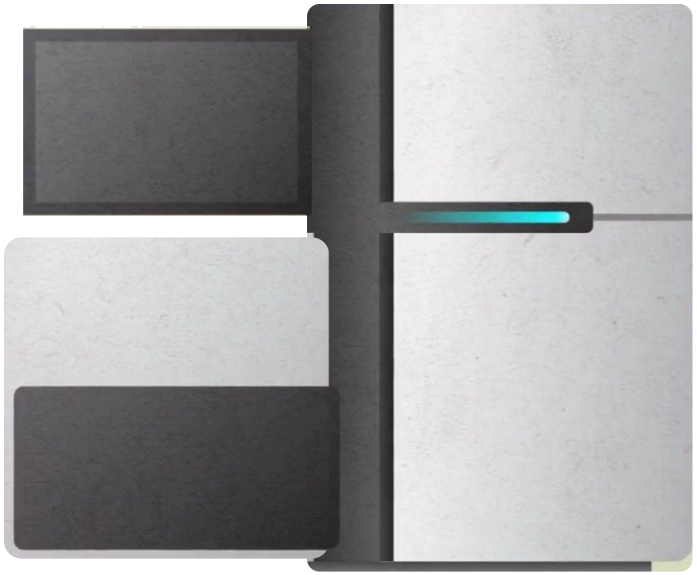
Illumina NovaSeq 6000

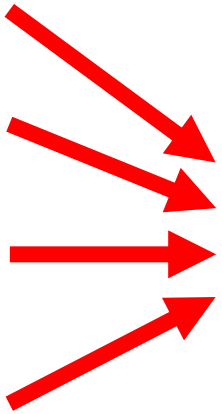
Pacific Biosciences RS II

Oxford Nanopore SmidgION

… and more! All produce data with different properties.

Problems with (Meta)Genome Analysis Today





Special-Purpose Machine
for **Data Generation**

FAST

General-Purpose Machine
for **Data Analysis**

SLOW

Genome Sequence Analysis

Storage System

Main Memory

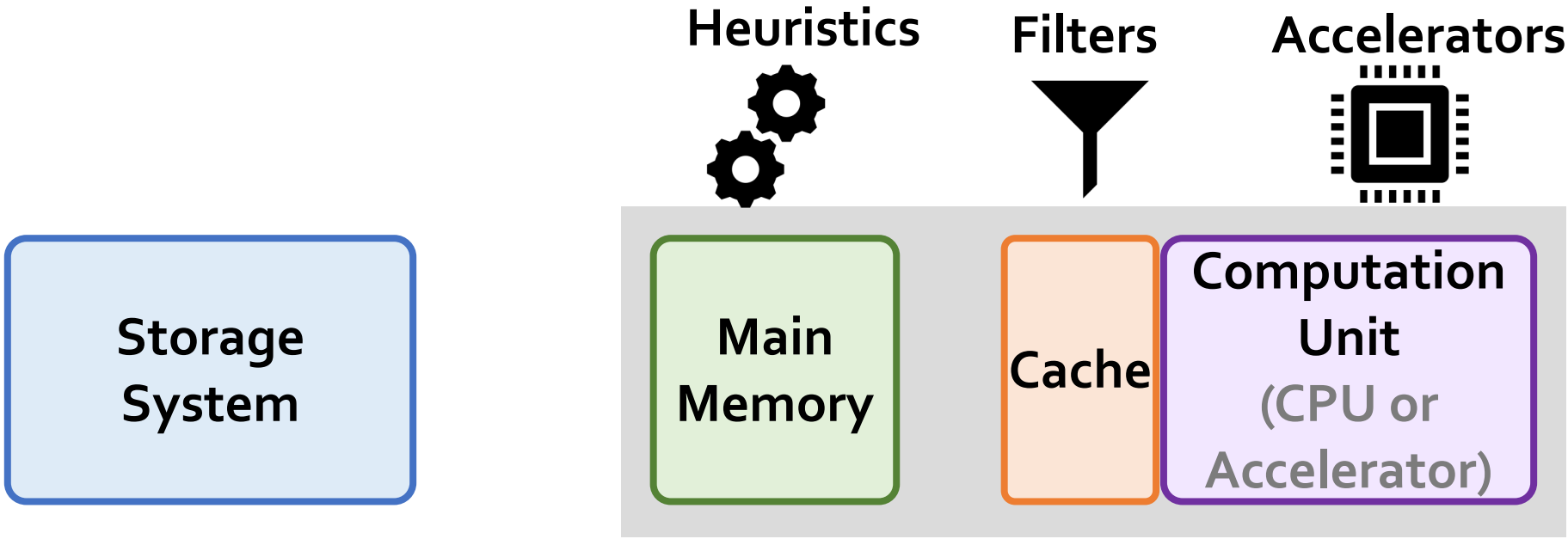
Cache

Computation Unit (CPU or Accelerator)

Computation overhead

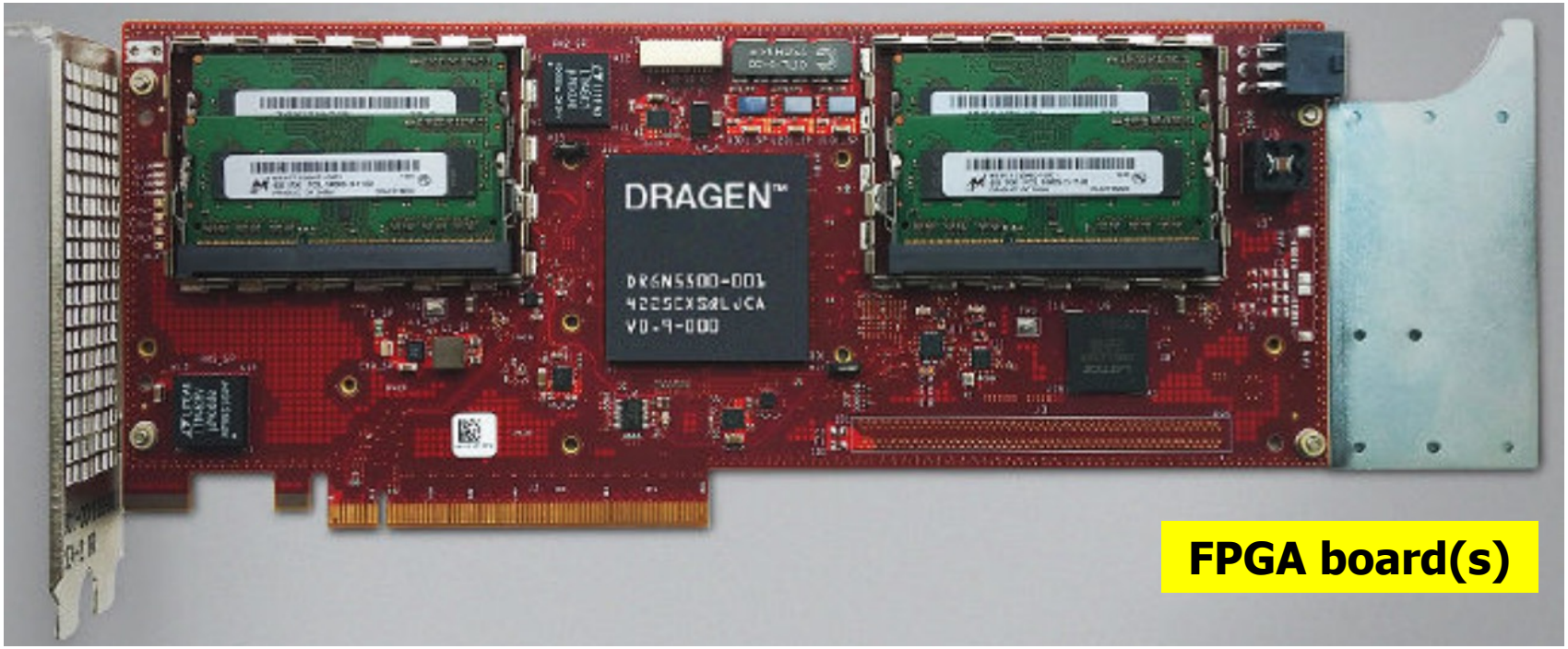
Data movement overhead

Accelerating Genome Analysis



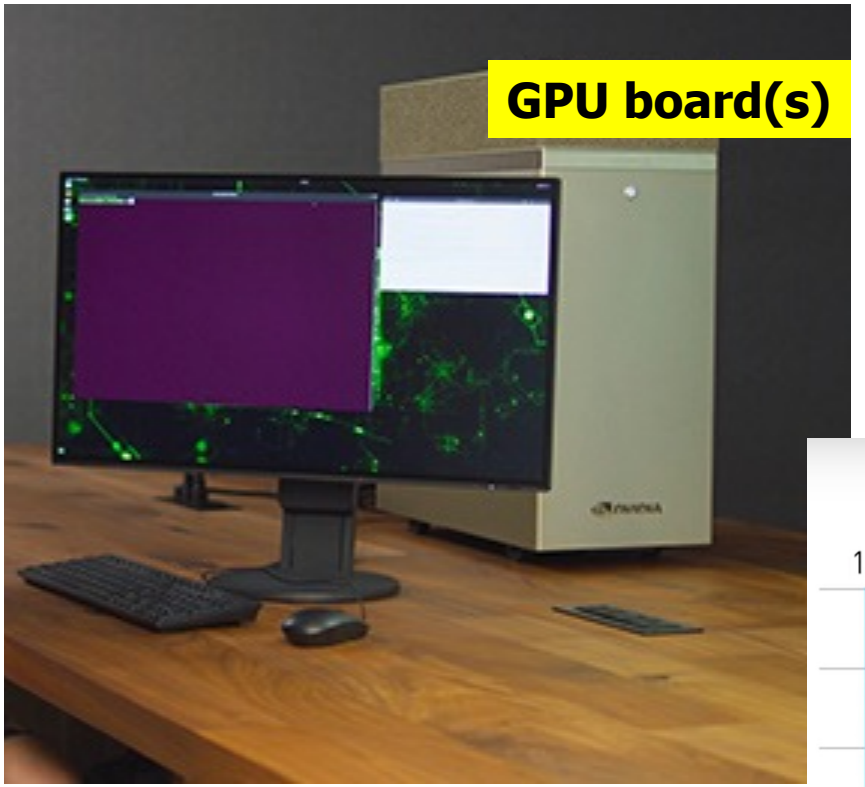
Illumina DRAGEN Bio-IT Platform (2018)

- Processes whole genome at 30x coverage in ~25 minutes with hardware support for data compression

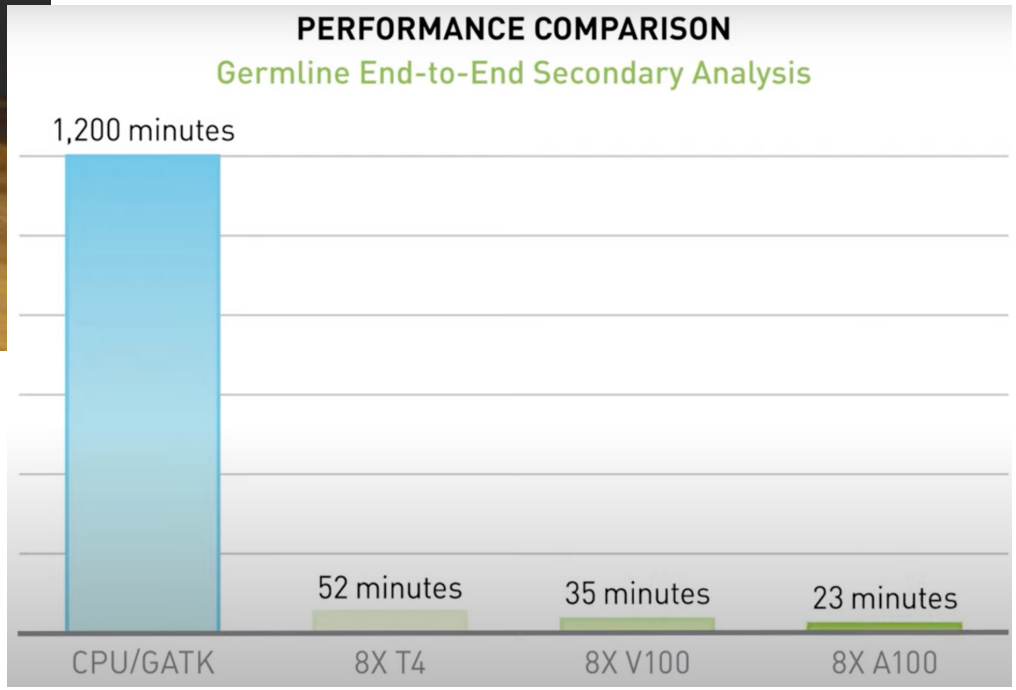


emea.illumina.com/products/by-type/informatics-products/dragen-bio-it-platform.html
emea.illumina.com/company/news-center/press-releases/2018/2349147.html

NVIDIA Clara Parabricks (2020)



A University of Michigan startup in 2018 joined NVIDIA in 2020



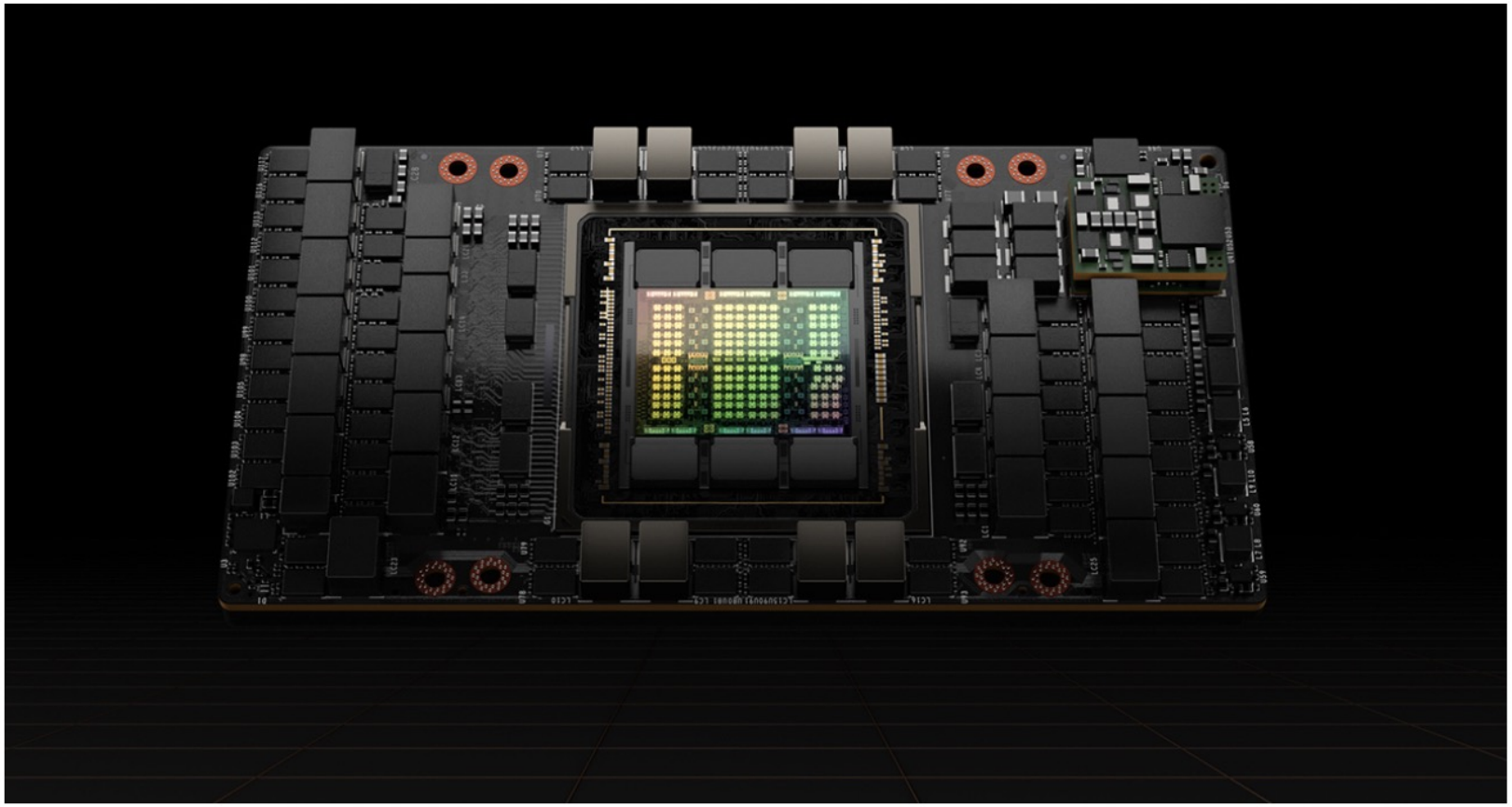
https://developer.nvidia.com/clara-parabricks

NVIDIA Hopper DPX Instructions (2022)

NVIDIA Hopper GPU Architecture Accelerates Dynamic Programming Up to 40x Using New DPX Instructions

Dynamic programming algorithms are used in healthcare, robotics, quantum computing, data science and more.

March 22, 2022 by DION HARRIS



https://blogs.nvidia.com/blog/2022/03/22/nvidia-hopper-accelerates-dynamic-programming-using-dpx-instructions/

- We are accelerating the transformation in how we analyze the human genome!

Bionano & NVIDIA:
Accelerating Analysis for Fast Time to Results

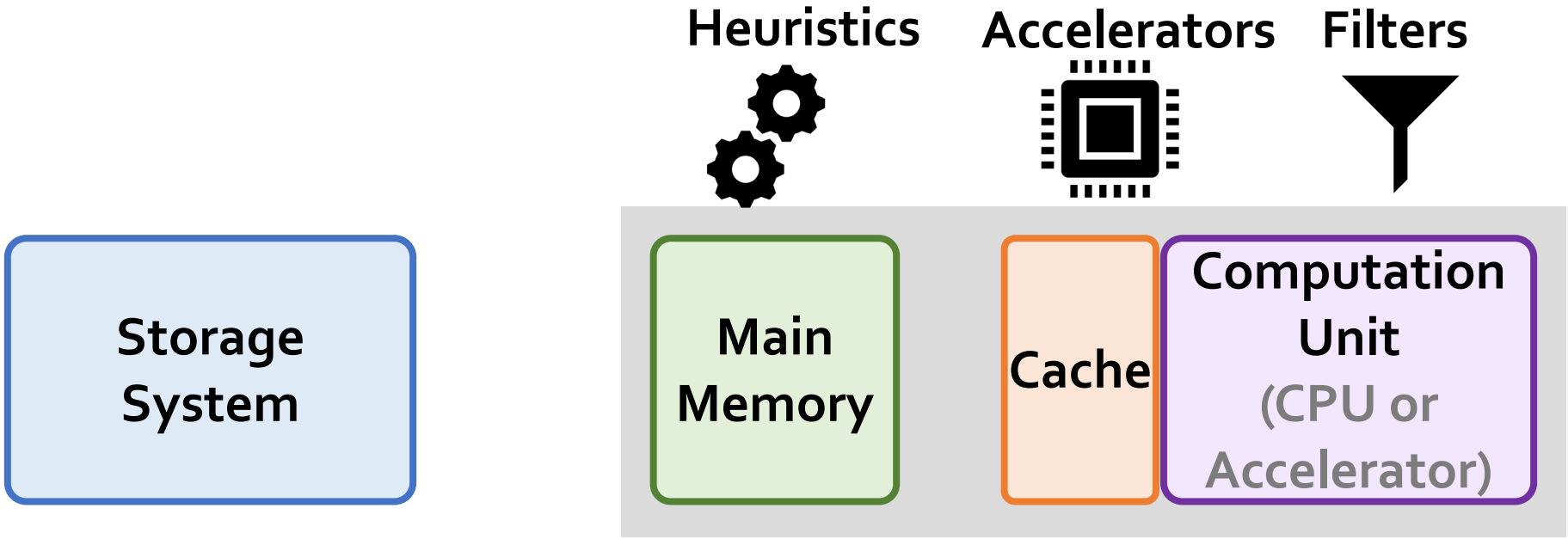
Technological solution to **support higher throughput**

New high-performance algorithms from Bionano

Powered by NVIDIA RTX™ 6000 Ada Generation GPUs

Workflow tailored for a **small lab and IT footprint**

Accelerating Genome Sequence Analysis

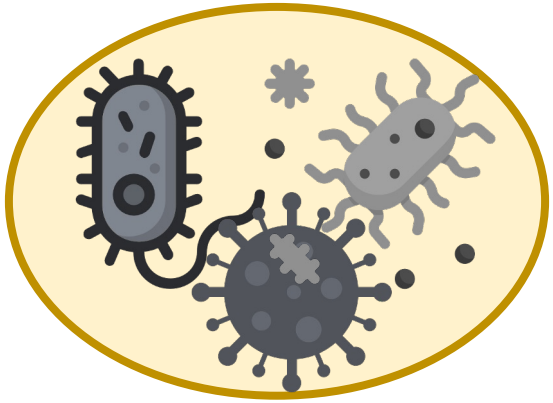


✓ Computation overhead

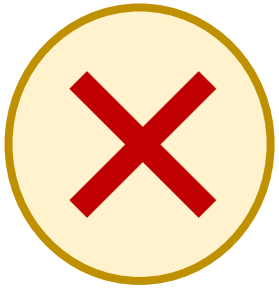
✗ Data movement overhead

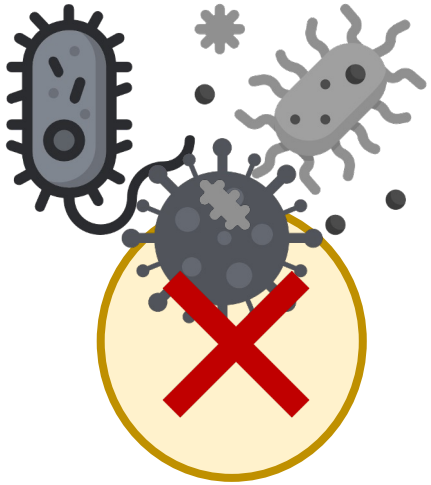
What is Metagenomics?

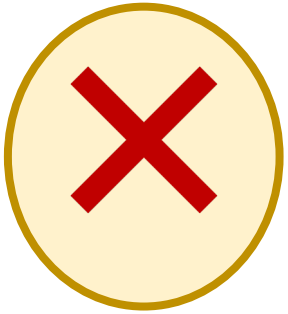
- ***Metagenomics:*** Study of genome sequences of **diverse organisms** within a **shared environment** (e.g., blood, ocean, soil)



- **Overcomes the limitations of traditional genomics**
  - Bypasses the need for analyzing individual species in isolation







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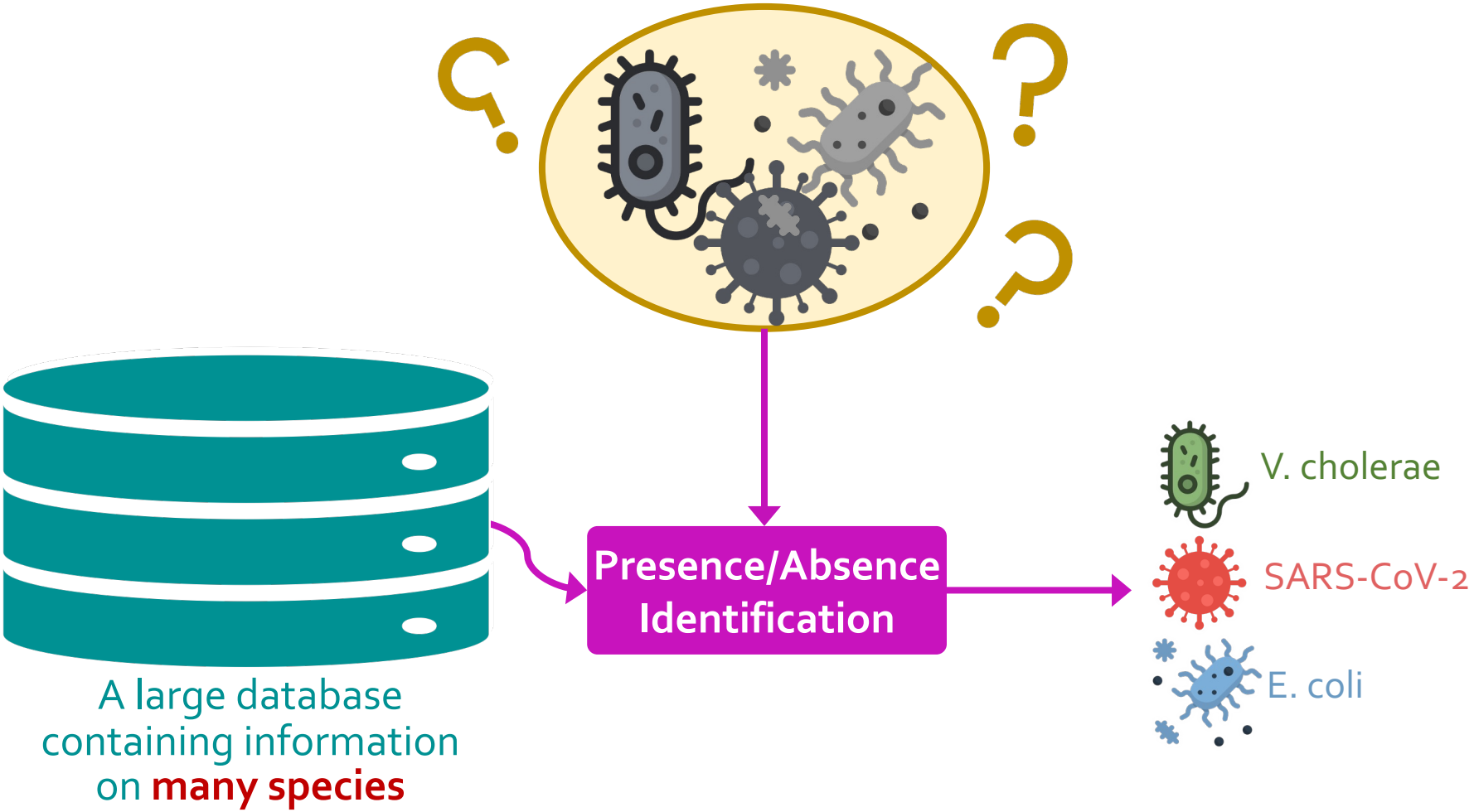

(e.g., > 100 TBs in emerging databases)

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- **Brief Intro to (Meta)Genomics**

- ***Storage-Centric Designs for (Meta)Genomics***
  - ***GenStore***
  - **MegIS**

- **Conclusion**

GenStore *[ASPLOS'22]*

GenStore: A High-Performance and Energy-Efficient In-Storage Computing System for Genome Sequence Analysis

Nika Mansouri Ghiasi[1] Jisung Park[1] Harun Mustafa[1] Jeremie Kim[1] Ataberk Olgun[1]
Arvid Gollwitzer[1] Damla Senol Cali[2] Can Firtina[1] Haiyu Mao[1] Nour Almadhoun Alserr[1]
Rachata Ausavarungnirun[3] Nandita Vijaykumar[4] Mohammed Alser[1] Onur Mutlu[1]

[1]ETH Zürich [2]Bionano Genomics [3]KMUTNB [4]University of Toronto

GenStore

A High-Performance In-Storage Processing System for Genome Sequence Analysis

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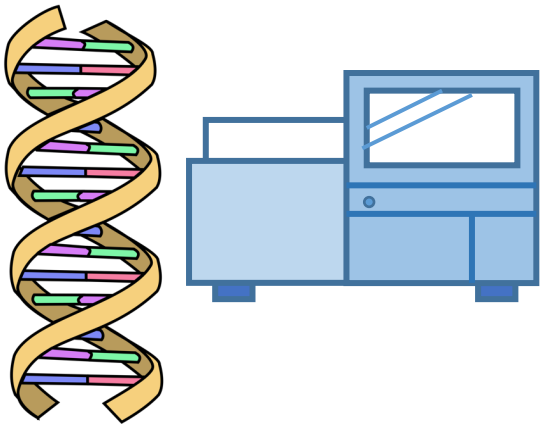
bionano GENOMICS

UNIVERSITY OF TORONTO

Genome Sequence Analysis

- Genome sequence analysis is critical for many applications
  - Personalized medicine
  - Outbreak tracing
  - Evolutionary studies

- Genome sequencing machines extract smaller fragments of the original DNA sequence, known as reads



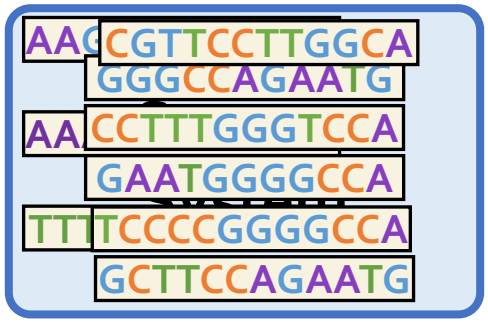
Genome Sequence Analysis

- **Read mapping:** first key step in genome sequence analysis
  - Aligns reads to potential matching locations in the reference genome
  - For each matching location, the alignment step finds the degree of similarity (alignment score)

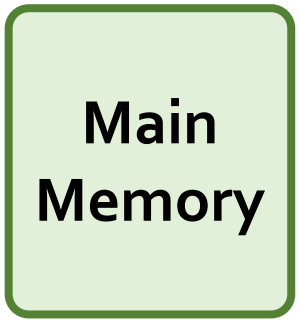
- Calculating the alignment score requires computationally-expensive approximate string matching (ASM) to account for differences between reads and the reference genome due to:
  - Sequencing errors
  - Genetic variation

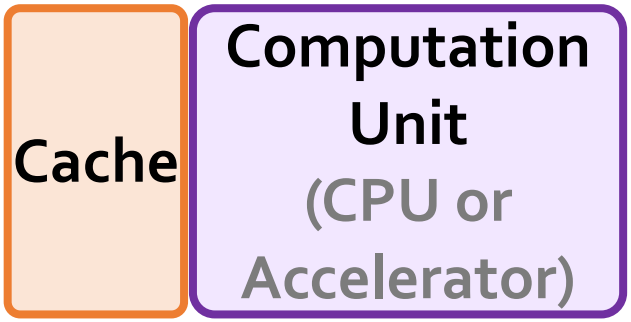
Key Idea

Filter* reads that do *not* require alignment *inside the storage system



Filtered Reads





Exactly-matching reads

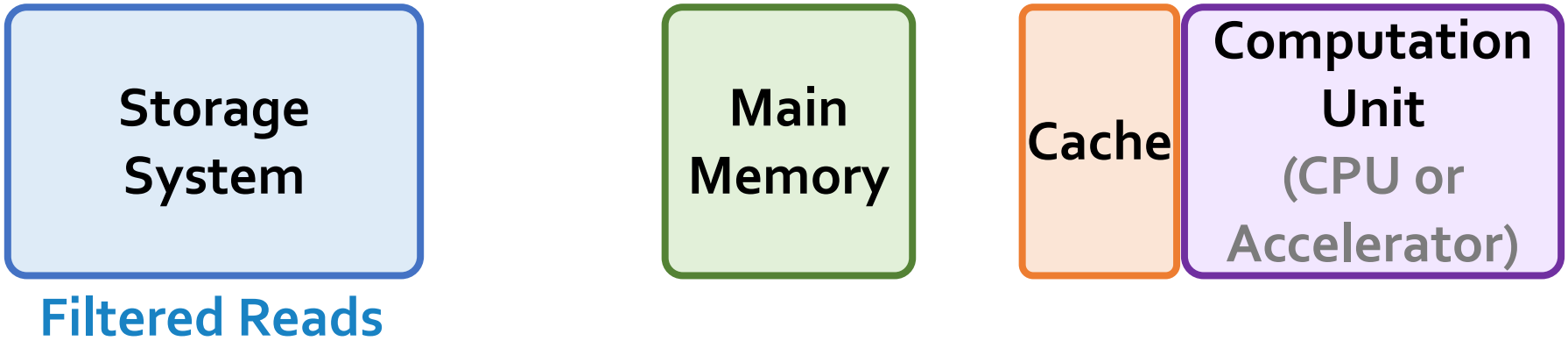
Do not need expensive approximate string matching during alignment

Non-matching reads

Do not have potential matching locations and can skip alignment

Challenges

Filter reads that do *not* require alignment *inside the storage system*

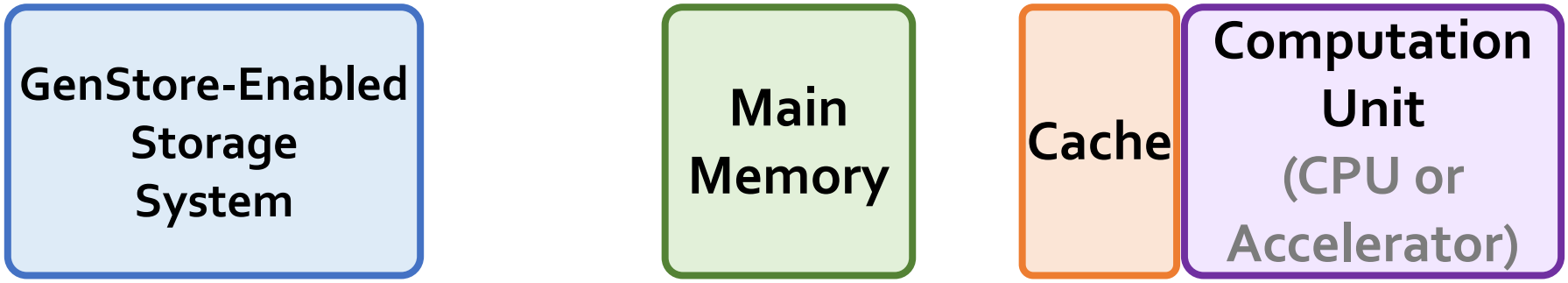


Read mapping workloads can exhibit different behavior

There are limited hardware resources in the storage system

GenStore

Filter reads that do *not* require alignment *inside the storage system*



Computation overhead

Data movement overhead

GenStore provides significant speedup (1.4x - 33.6x) and energy reduction (3.9x – 29.2x) at low cost

Outline

Background

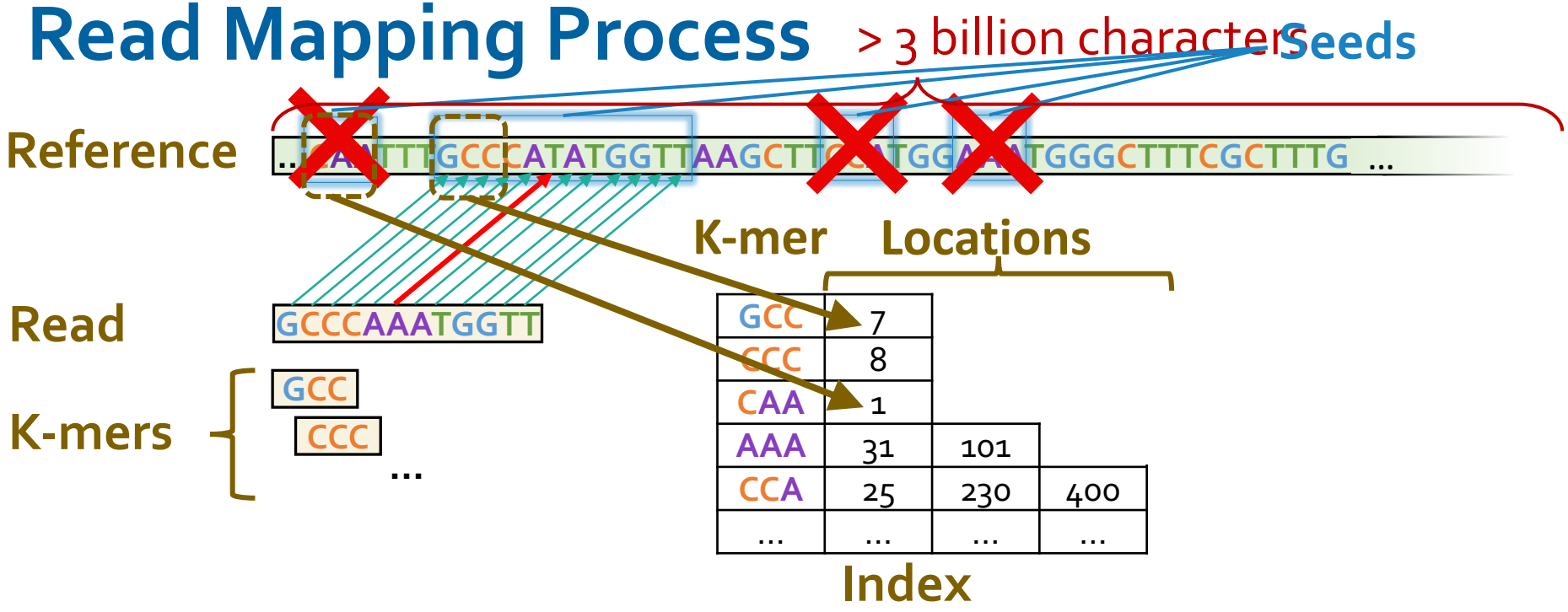
Motivation and Goal

GenStore

Evaluation

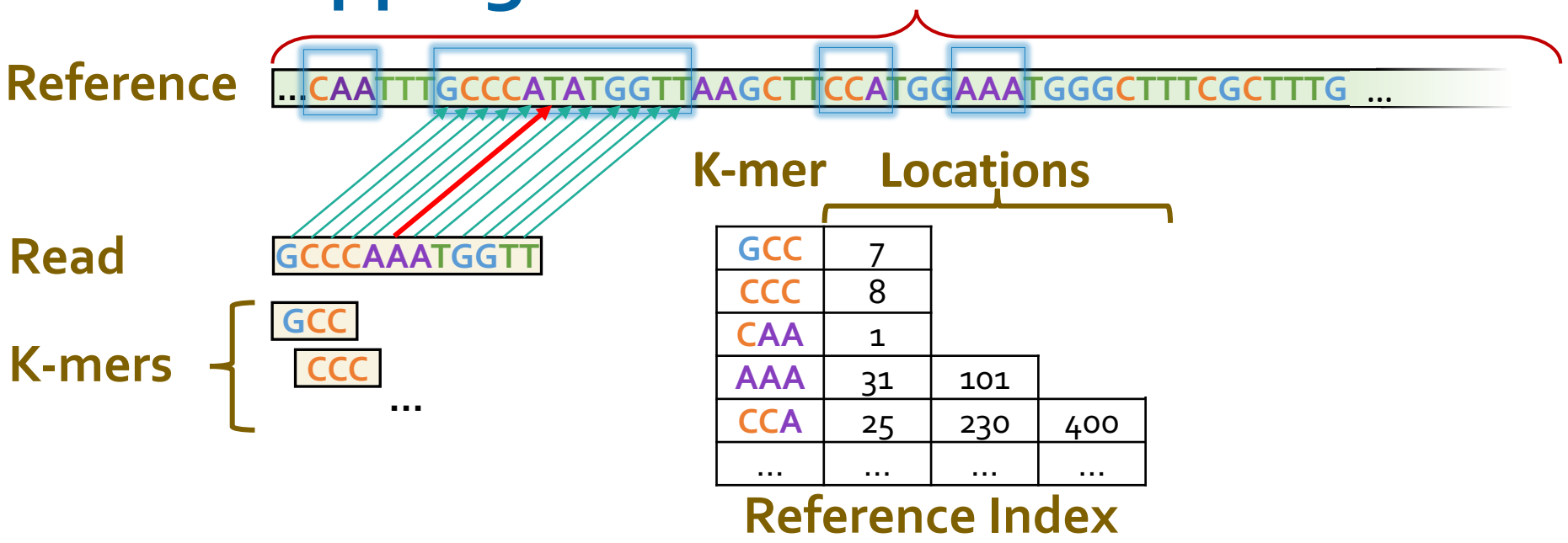
Conclusions

Read Mapping Process



Seeding	Determine potential matching locations (seeds) in the reference genome
Seed Filtering (e.g., Chaining)	Prune some seeds in the reference genome
Alignment	Determine the exact differences between the read and the reference genome

Read Mapping Process



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Motivation

- Case study on a real-world genomic read dataset
  - Various read mapping systems
  - Various state-of-the-art SSD configurations

The ideal in-storage filter significantly improves performance by

1) reducing the computation overhead

2) reducing the data movement overhead

Motivation

- Case study on a real-world genomic read dataset
  - Various read mapping systems
  - Various state-of-the-art SSD configurations

Filtering outside SSD provides lower performance benefit since it

1) does not reduce the data movement overhead

2) must compete with read mapping for system resources

A HW accelerator reduces the computation bottleneck,

which makes I/O a larger bottleneck in the system

Our Goal

Design an in-storage filter for genome sequence analysis in a cost-effective manner

Design Objectives:

Performance

Provide high in-storage filtering performance to overlap the filtering with the read mapping of unfiltered data

Applicability

Support reads with 1) different properties and 2) different degrees of genetic variation in the compared genomes

Low-cost

Do not require significant hardware overhead

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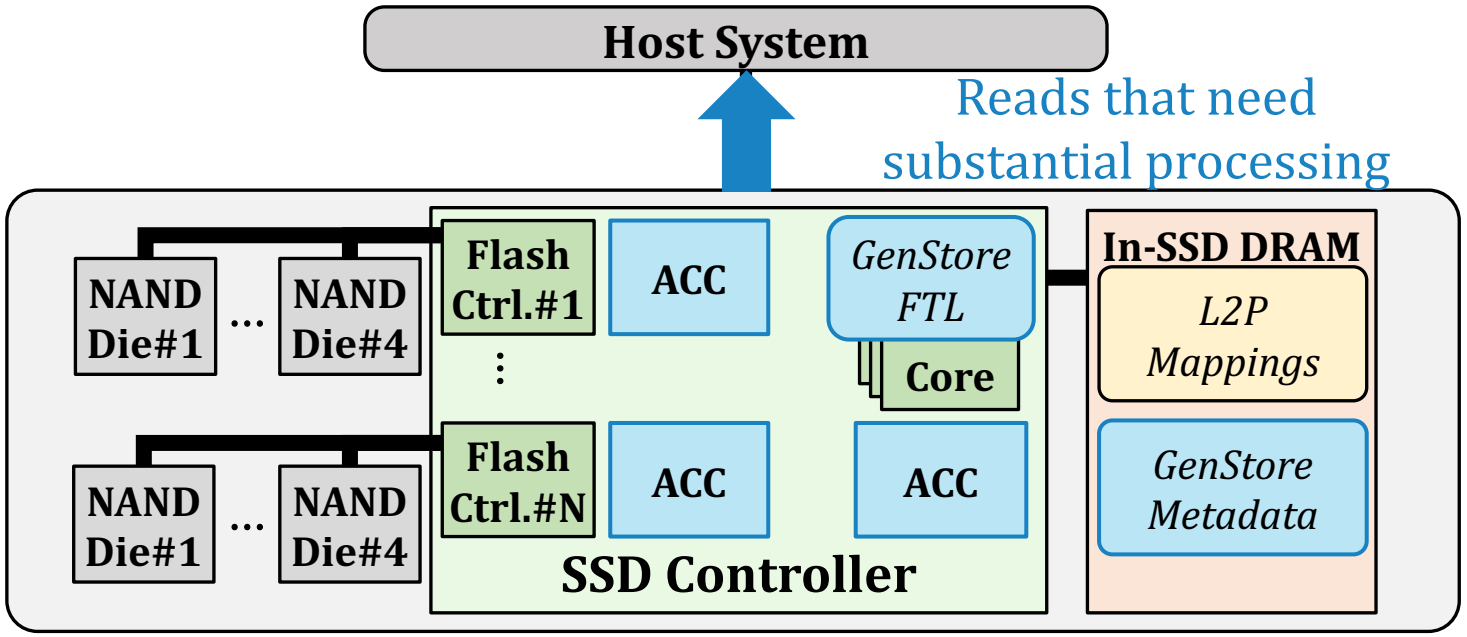
GenStore

- **Key idea:** Filter reads that do not require alignment inside the storage system

- **Challenges**
  - Different behavior across read mapping workloads
  - Limited hardware resources in the SSD



Filtering Opportunities

- Sequencing machines produce one of two kinds of reads
  - **Short reads:** highly accurate and short
  - **Long reads:** less accurate and long

Reads that do not require the expensive alignment step:

Exactly-matching reads

Do not need expensive approximate string matching during alignment

- Low sequencing error rates (short reads) combined with
- Low genetic variation

Non-matching reads

Do not have potential matching locations, so they skip alignment

- High sequencing error rates (long reads) or
- High genetic variation (short or long reads)

GenStore

GenStore-EM for Exactly-Matching Reads

GenStore-NM for Non-Matching Reads

GenStore

GenStore-EM for Exactly-Matching Reads

GenStore-NM for Non-Matching Reads

GenStore-EM

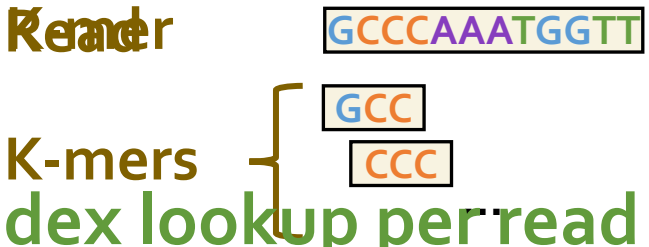
- Efficient in-storage filter for reads with at least one exact match in the reference genome
- Uses simple operations, without requiring alignment
- **Challenge:** large number of random accesses per read to the reference genome and its index

Expensive random accesses to flash chips

Limited DRAM capacity inside the SSD

GenStore-EM: Data Structures

- **Read-sized k-mers:** to reduce the number of accesses per each read



✓ Only one index lookup per read

- **Sorted read-sized k-mers:** to avoid random accesses to the index

✓ Sequential scan of the read set and the index

GenStore-EM: Data Structures

Sorted Read Table

	Read
	AAAAAAAAAA
	AAAAAAAAAG
	AAAAAAAACT
	…

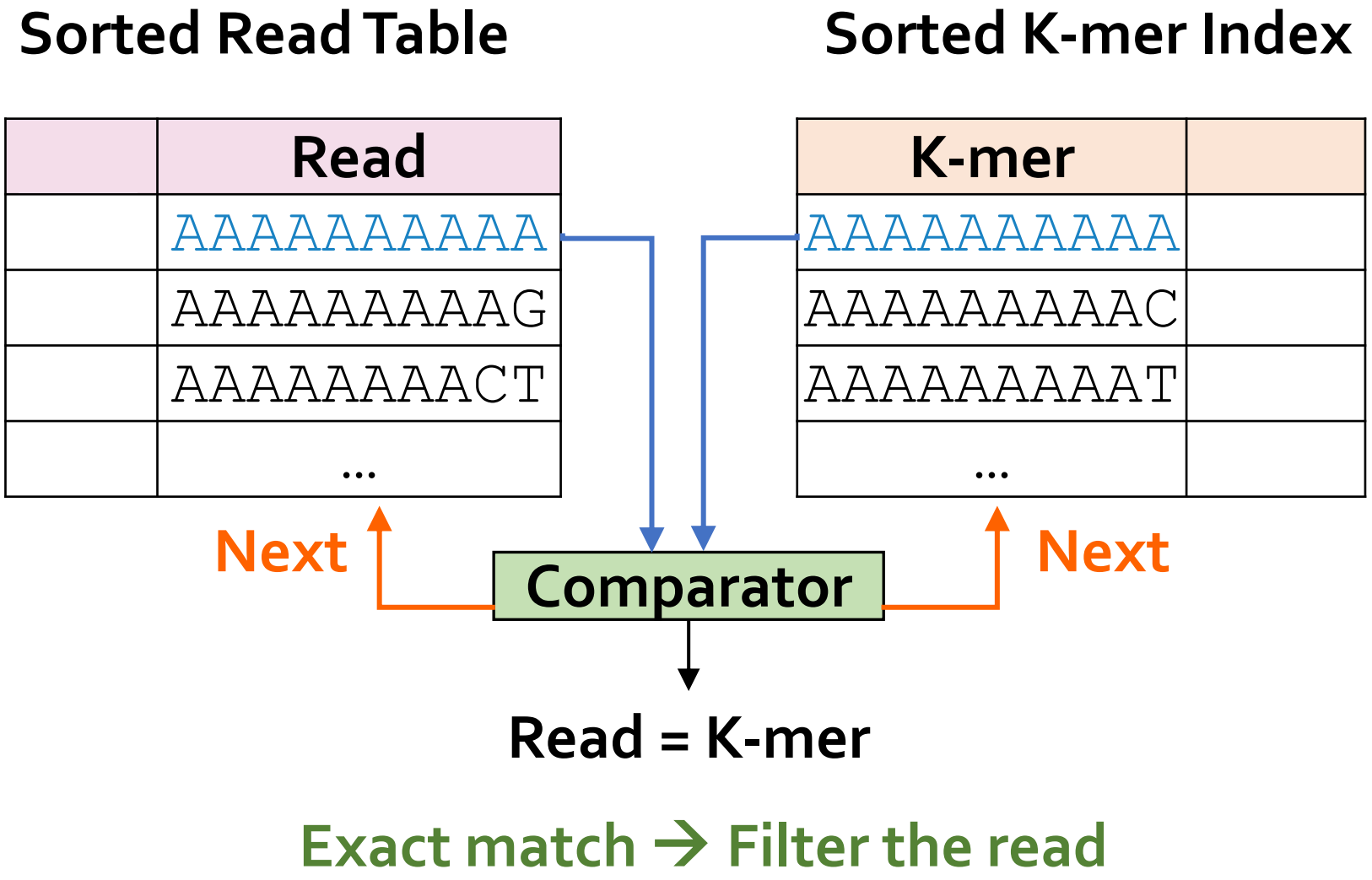
Sorted

Sorted K-mer Index

K-mer	
AAAAAAAAAA	
AAAAAAAAAC	
AAAAAAAAAT	
…	

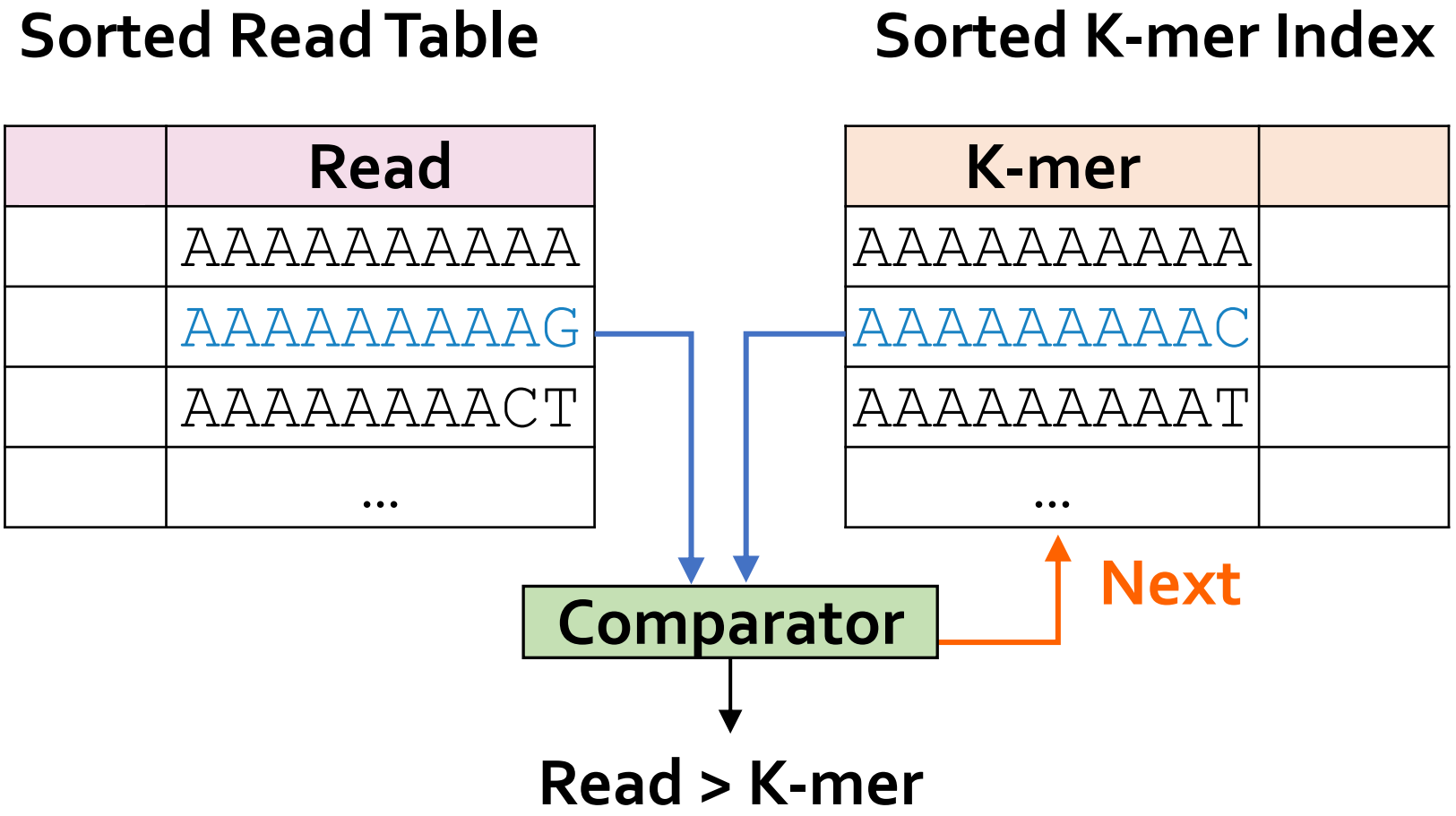
Read-sized K-mers

GenStore-EM: Finding a Match

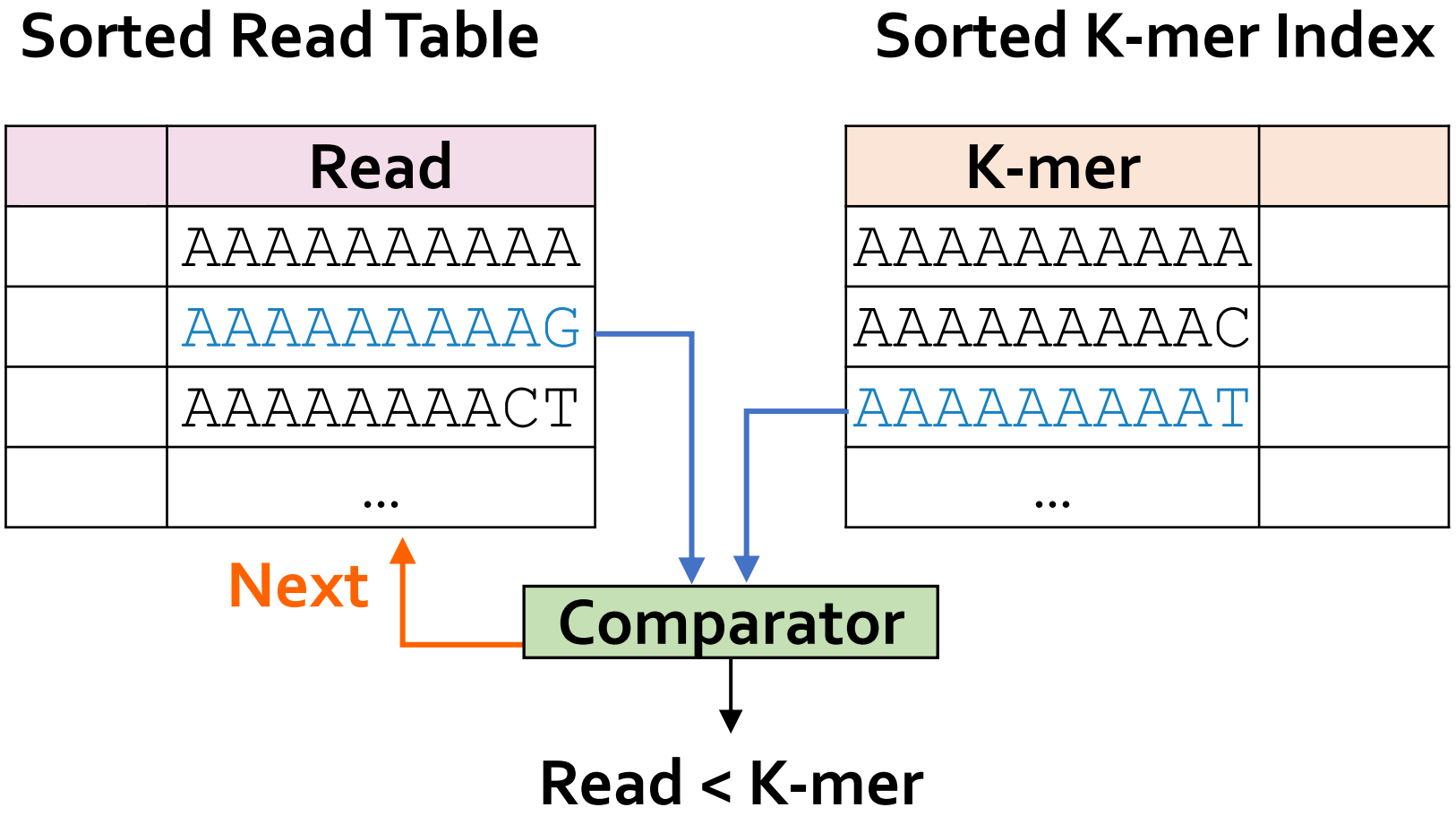


Exact match → Filter the read

GenStore-EM: Not Finding a Match

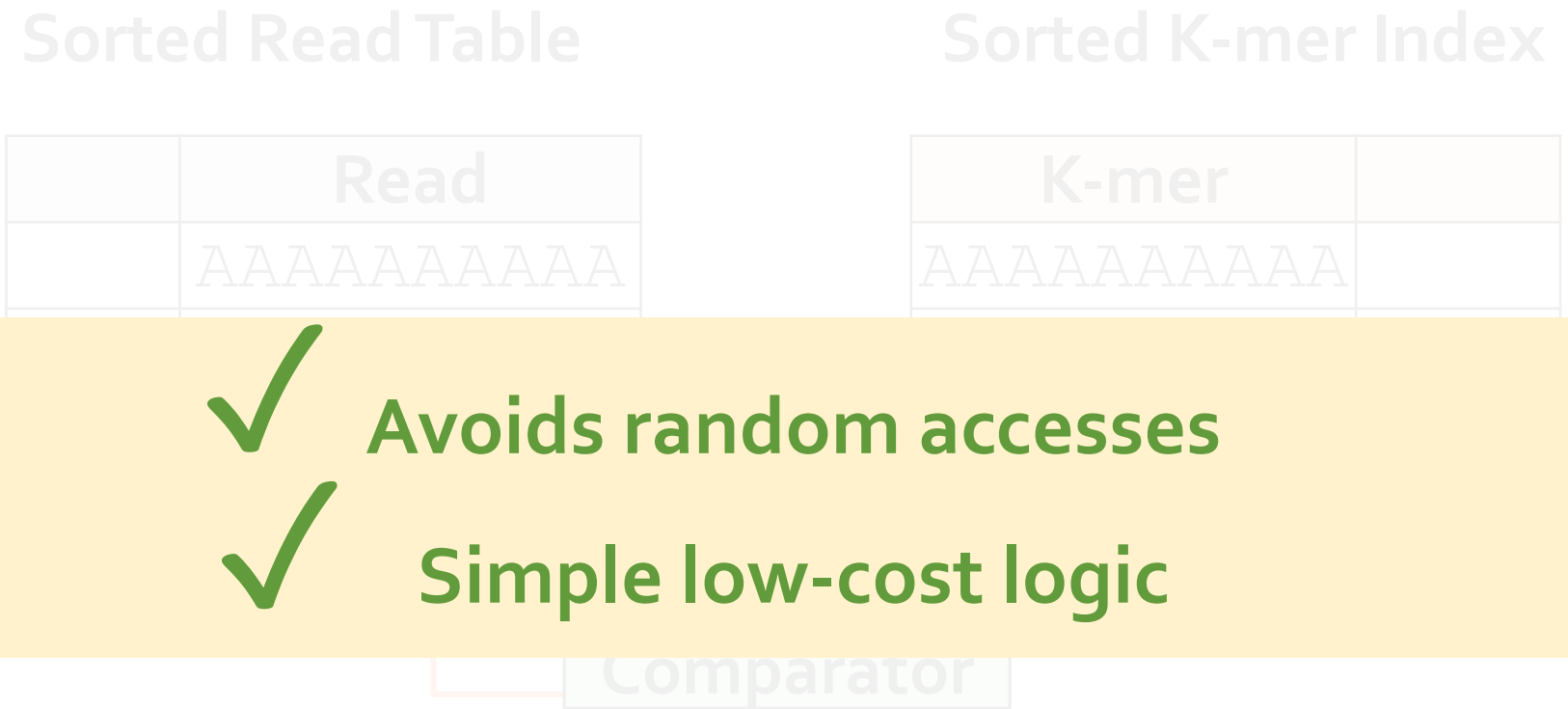


GenStore-EM: Not Finding a Match



Not an exact match → Send to read mapper

GenStore-EM: Not Finding a Match



✓ Avoids random accesses

✓ Simple low-cost logic

GenStore-EM: Optimization

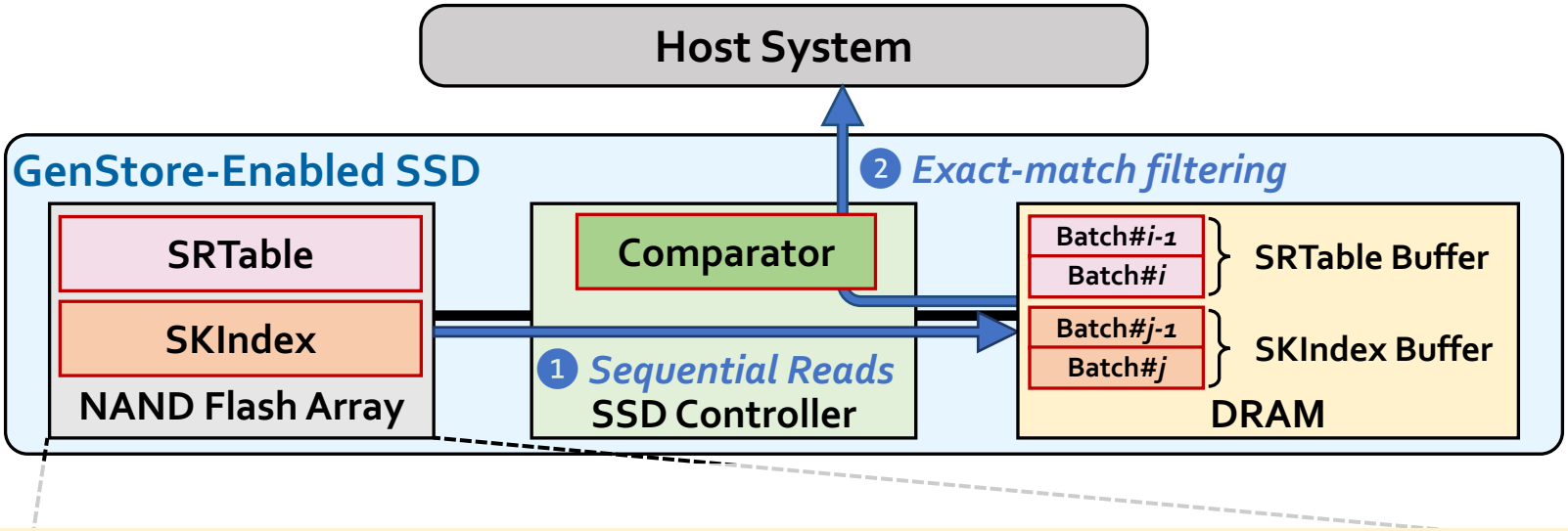
- Read-sized k-mer index takes up a large amount of space (126 GB for human index) due to the larger number of unique k-mers

Sorted K-mer Index

Strong Hash Value	Loc.
1	1, 8, …
4	51
7	23, 37
16	…

Using strong hash values instead of read-sized k-mers reduces the size of the index by 3.9x

GenStore-EM: Design



Steps 1 and 2 are pipelined.
During filtering, GenStore-EM sends the unfiltered reads to the host system.

Data is evenly distributed between channels, dies, and planes to leverage the full internal bandwidth of the SSD

GenStore

GenStore-EM for Exactly-Matching Reads

GenStore-NM for Non-Matching Reads

Details on GenStore-NM's design are in the paper

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Evaluation Methodology

Read Mappers

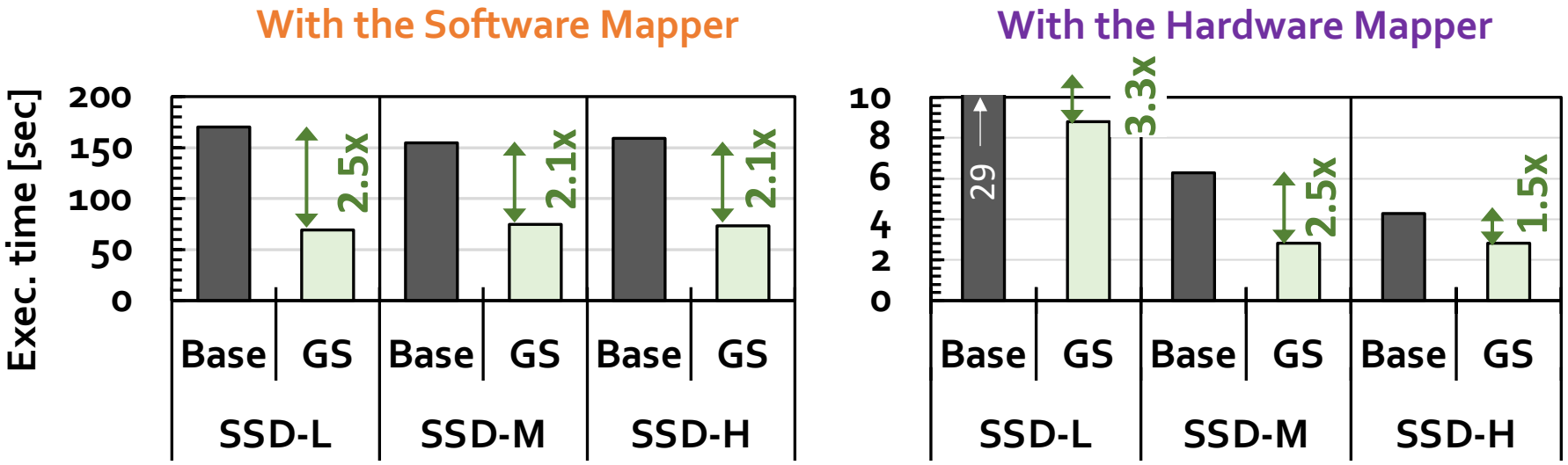
- **Base:** state-of-the-art software or hardware read mappers
  - Minimap2 [Bioinformatics'18]: software mapper for short and long reads
  - GenCache [MICRO'19]: hardware mapper for short reads
  - Darwin [ASPLOS'18]: hardware mapper for long reads
- **GS:** Base integrated with GenStore

SSD Configurations

- **SSD-L:** with SATA3 interface (0.5 GB/s sequential read bandwidth)
- **SSD-M:** with PCIe Gen3 interface (3.5 GB/s sequential read bandwidth)
- **SSD-H:** with PCIe Gen4 interface (7 GB/s sequential read bandwidth)

Performance – GenStore-EM

For a read set with 80% exactly-matching reads



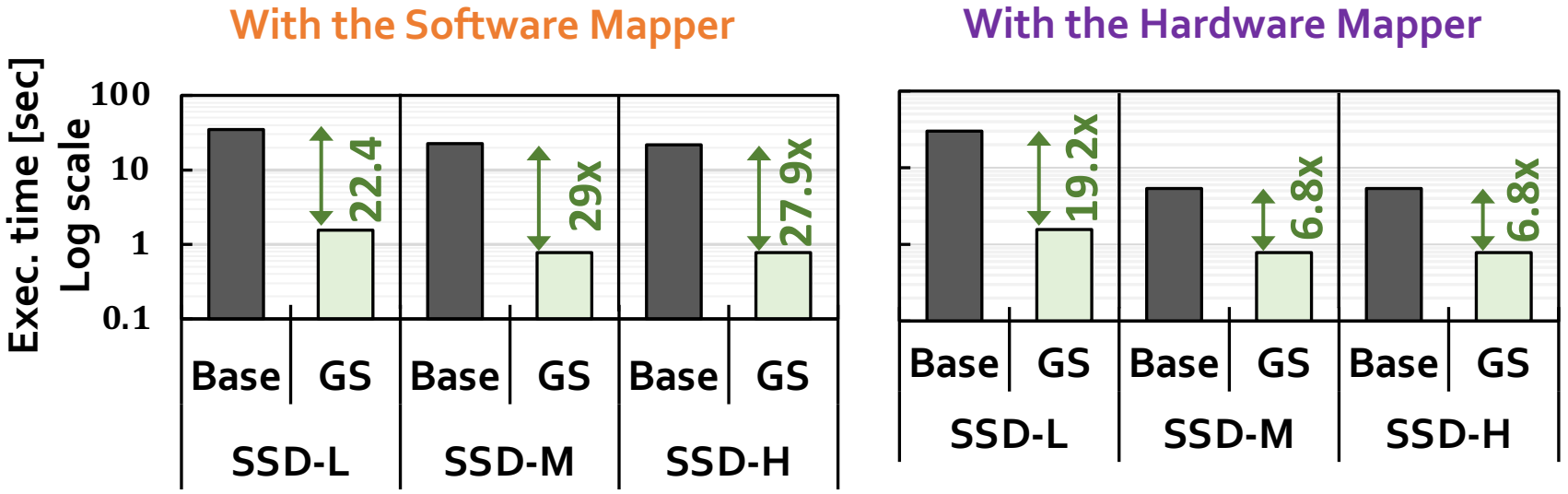
2.1× - 2.5× speedup compared to the software Base

1.5× – 3.3× speedup compared to the hardware Base

On average 3.92× energy reduction

Performance – GenStore-NM

For a read set with 99.7% non-matching reads



22.4× – 27.9× speedup compared to the software Base

6.8× – 19.2× speedup compared to the hardware Base

On average 27.2× energy reduction

More in the Paper

- Effect of read set features on performance
  - Data size (up to 440 GB)
  - Filter ratio
- Performance benefit of an implementation of GenStore outside the SSD
  - In some cases, it provides performance benefits due more efficient streaming accesses
  - Provides significantly lower benefit compared to GenStore
- More detailed characterization of non-matching reads across different read mapping use cases and species

GenStore

A High-Performance In-Storage Processing System for Genome Sequence Analysis

Nika Mansouri Ghiasi, Jisung Park, Harun Mustafa, Jeremie Kim, Ataberk Olgun, Arvid Gollwitzer, Damla Senol Cali, Can Firtina, Haiyu Mao, Nour Almadhoun Alserr, Rachata Ausavarungnirun, Nandita Vijaykumar, Mohammed Alser, and Onur Mutlu

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ETH zürich

bionano GENOMICS

UNIVERSITY OF TORONTO

Outline

- **Brief Intro to (Meta)Genomics**

- ***Storage-Centric Designs for (Meta)Genomics***
  - **GenStore**
  - ***MegIS***

- **Conclusion**

MegIS *[ISCA'24]*

MegIS: High-Performance, Energy-Efficient, and Low-Cost Metagenomic Analysis with In-Storage Processing

Nika Mansouri Ghiasi[1] Mohammad Sadrosadati[1] Harun Mustafa[1] Arvid Gollwitzer[1]
Can Firtina[1] Julien Eudine[1] Haiyu Mao[1] Joël Lindegger[1] Meryem Banu Cavlak[1]
Mohammed Alser[1] Jisung Park[2] Onur Mutlu[1]
[1]ETH Zürich [2]POSTECH

MegIS

High-Performance, Energy-Efficient, and Low-Cost Metagenomic Analysis with In-Storage Processing

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Outline

Background

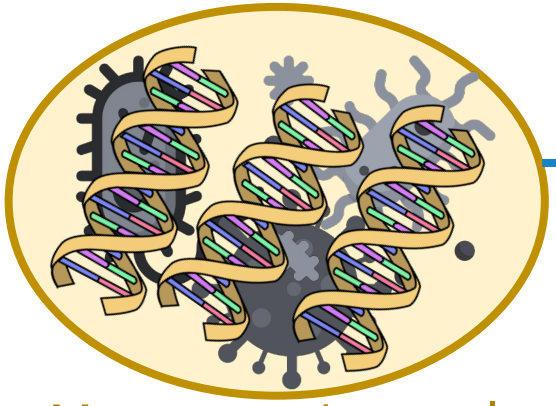
Motivation and Goal

MegIS

Evaluation

Conclusion

Metagenomic Analysis



Metagenomic sample with species that are **not known** in advance

A large database containing information on **many species**

Preparation of Input Queries

Query K-mers: GCTCA, CTCAT, TCATG, ...

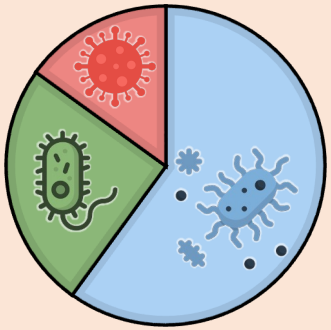
Presence/Absence Identification

V. cholerae

SARS-CoV-2

E. coli

Abundance Estimation



(e.g., > 100 TBs in emerging databases)

Outline

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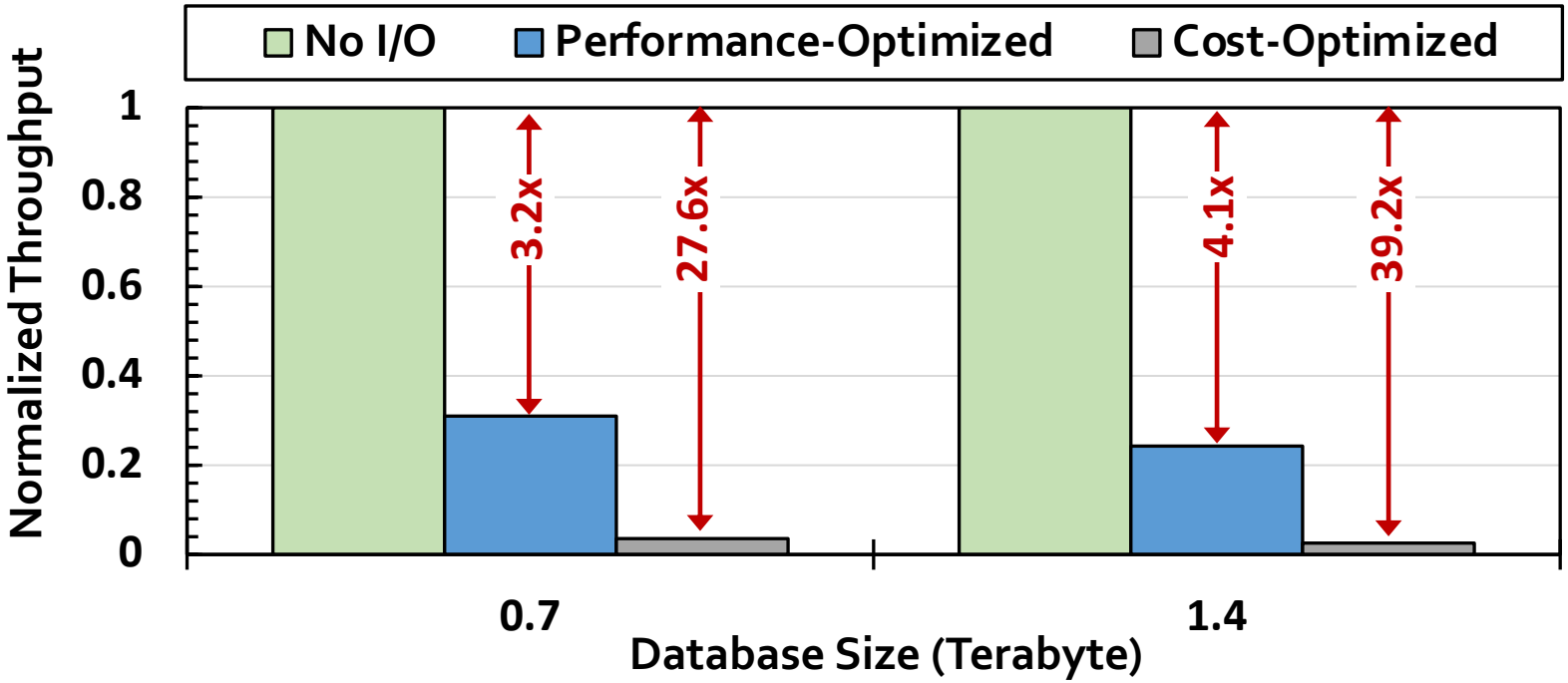
Motivation

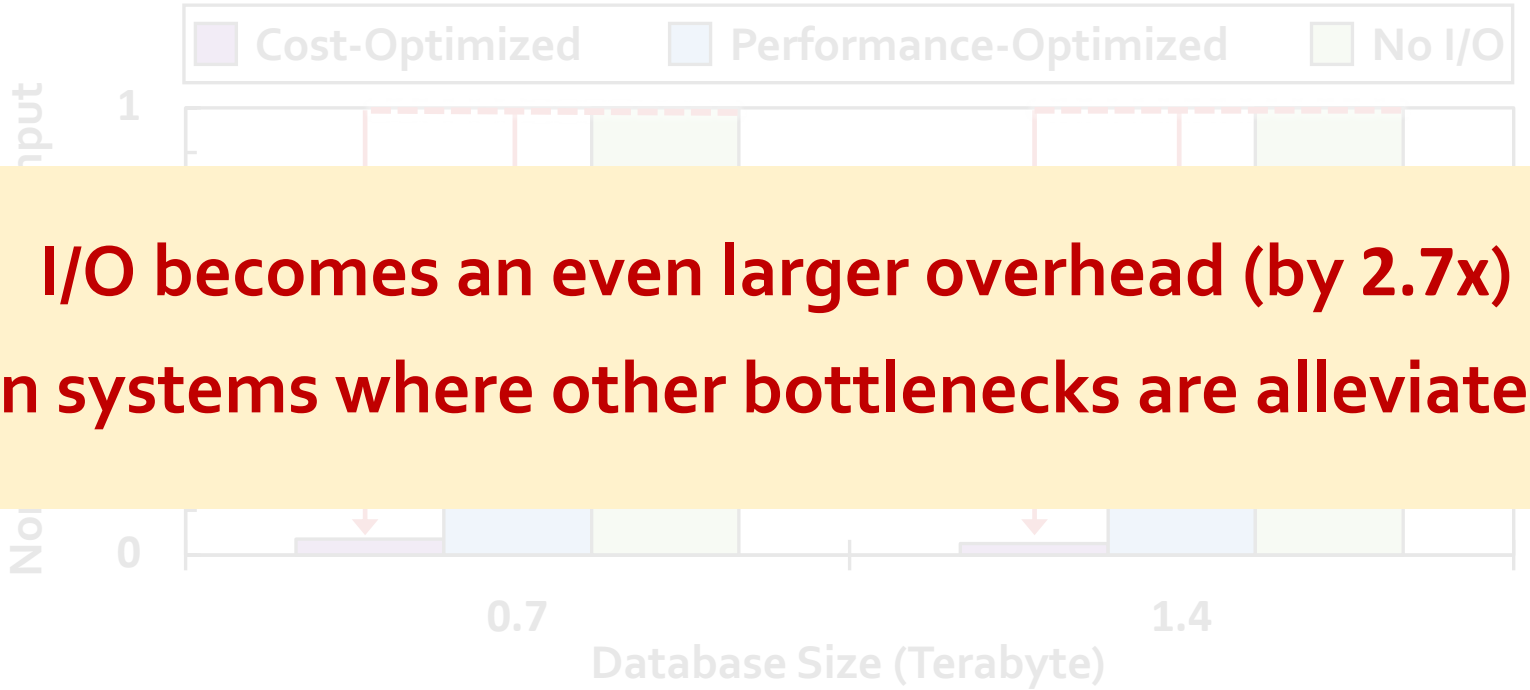
- Case study of the performance of metagenomic analysis tools
- With various state-of-the-art SSD configurations



I/O data movement causes significant performance overhead

Motivation

- Case study on the throughput of metagenomic analysis tools
- With Various state-of-the-art SSD configurations



I/O becomes an even larger overhead (by 2.7x) in systems where other bottlenecks are alleviated

I/O data movement causes significant performance overhead

I/O Overhead is Hard to Avoid

I/O overhead due to accessing **large**, **low-reuse** data is hard to avoid

Sampling techniques to shrink database sizes

[Wood+, Genome Biology'19], [Ounit+, BMC Genomics'15], [Kim+, Genome Research'16], …

✗ *Reduce accuracy to levels unacceptable for many use cases*

Keeping all data required by metagenomic analysis completely and always resident in main memory

✗ *Energy inefficient, costly, unscalable, and unsustainable*

- Database sizes **increase rapidly** (doubling every few months)
- Different analyses need **different databases**

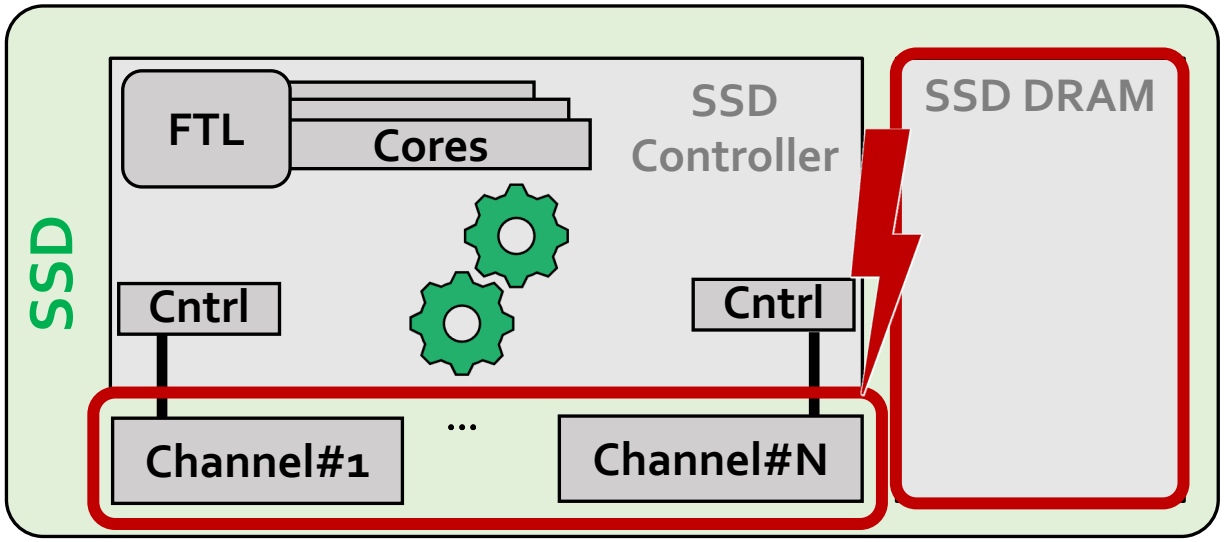
Our Goal

Improve metagenomic analysis ***performance***
by reducing large ***data movement overhead***
from the storage system
in a ***cost-effective*** *manner and with* ***high accuracy***

Challenges of In-Storage Processing

No metagenomic analysis tools can run in-storage due to SSD limits

- Long **latency of NAND flash** chips
- Limited **DRAM capacity** inside the SSD
- Limited **DRAM bandwidth** inside the SSD



Outline

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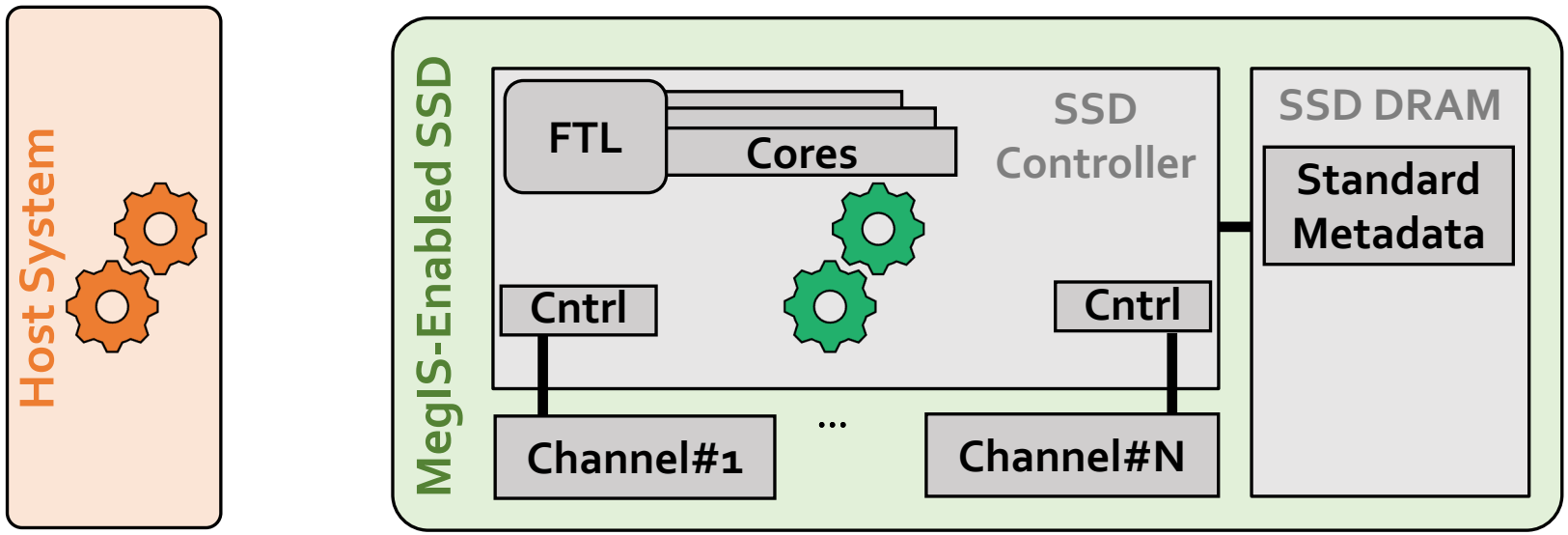
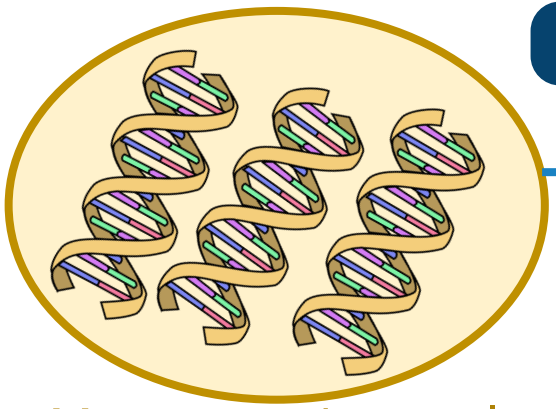
MegIS: Metagenomics In-Storage

- First in-storage system for *end-to-end* metagenomic analysis
- **Idea:** Cooperative in-storage processing for metagenomic analysis
  - Hardware/software co-design between



MegIS's Steps



Metagenomic sample with species that are **not known** in advance

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Step 1

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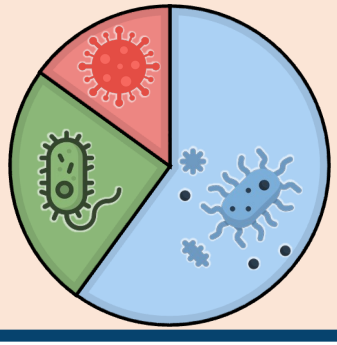
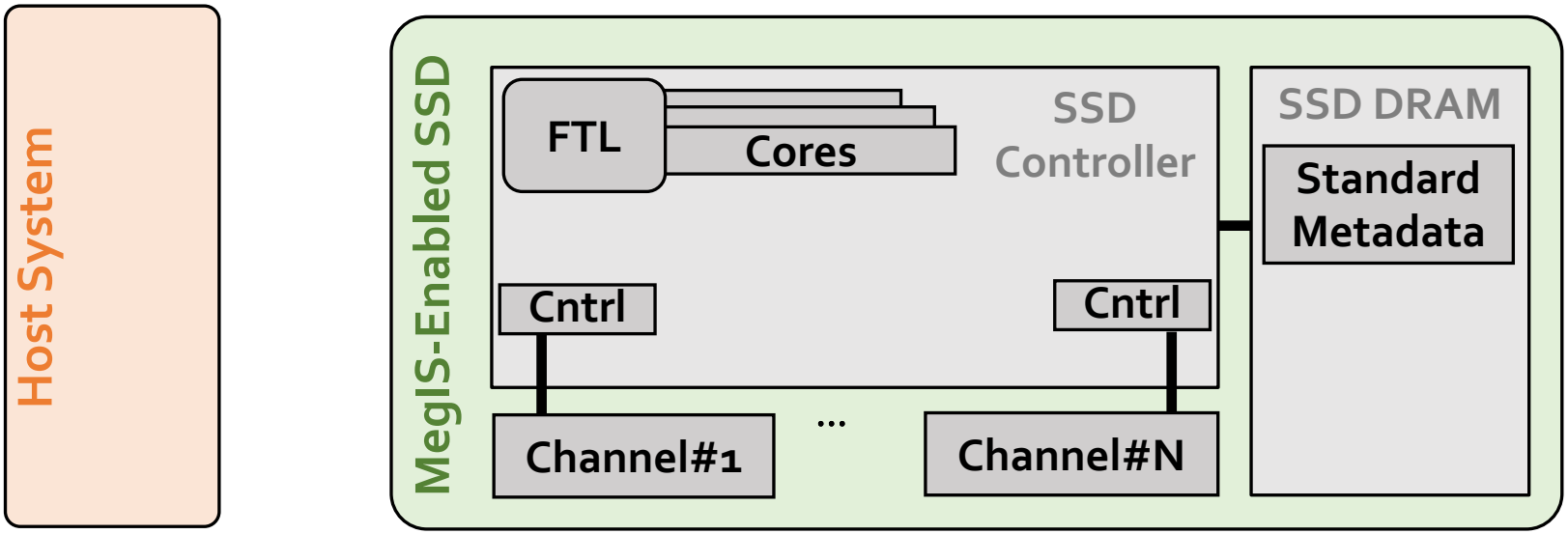
E. coli

Step 3

Abundance Estimation



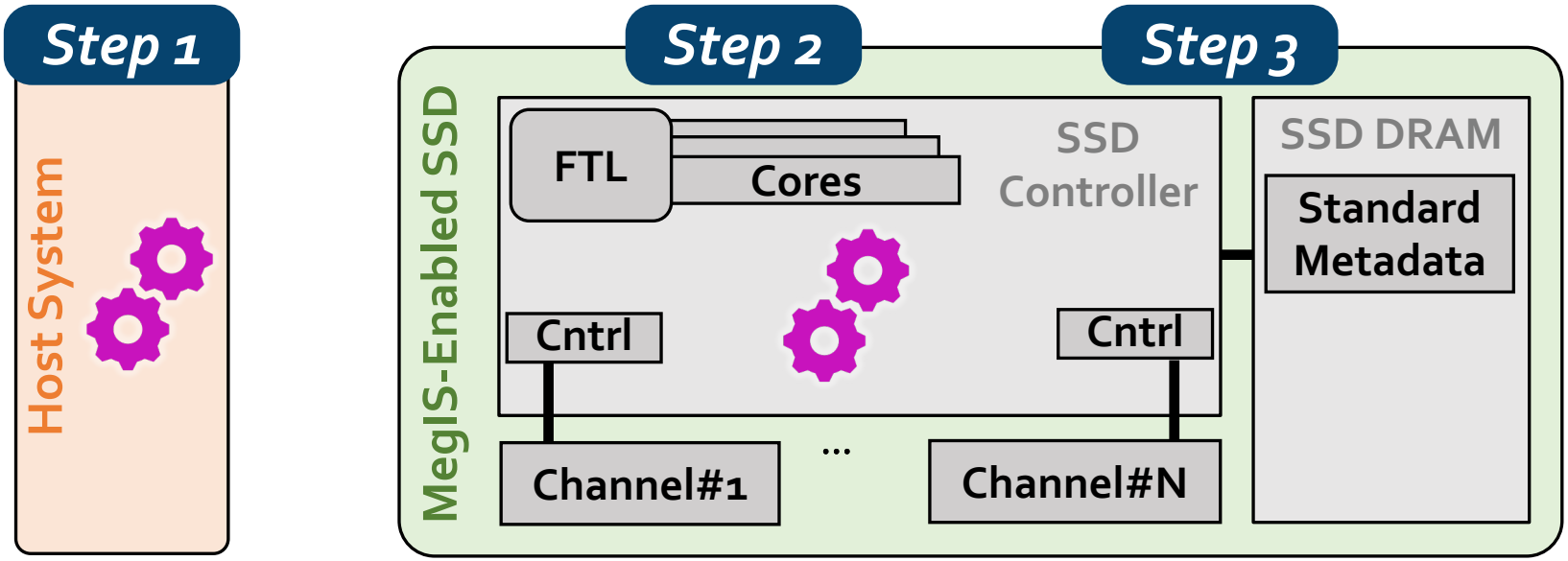
MegIS Hardware-Software Co-Design



MegIS Hardware-Software Co-Design

Task partitioning and mapping

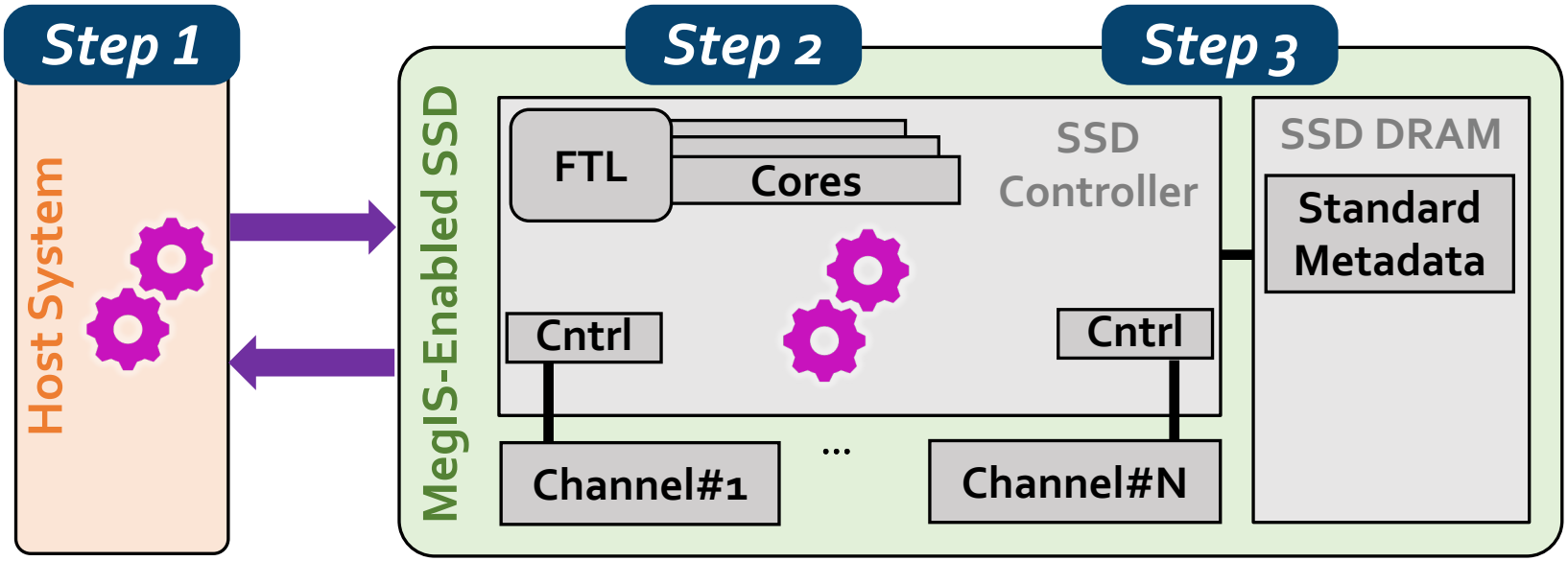
- *Each step executes in its most suitable system*



MegIS Hardware-Software Co-Design

Task partitioning and mapping
- *Each step executes in its most suitable system*

Data/computation flow coordination
- *Reduce communication overhead*
- *Reduce #writes to flash chips*



MegIS Hardware-Software Co-Design

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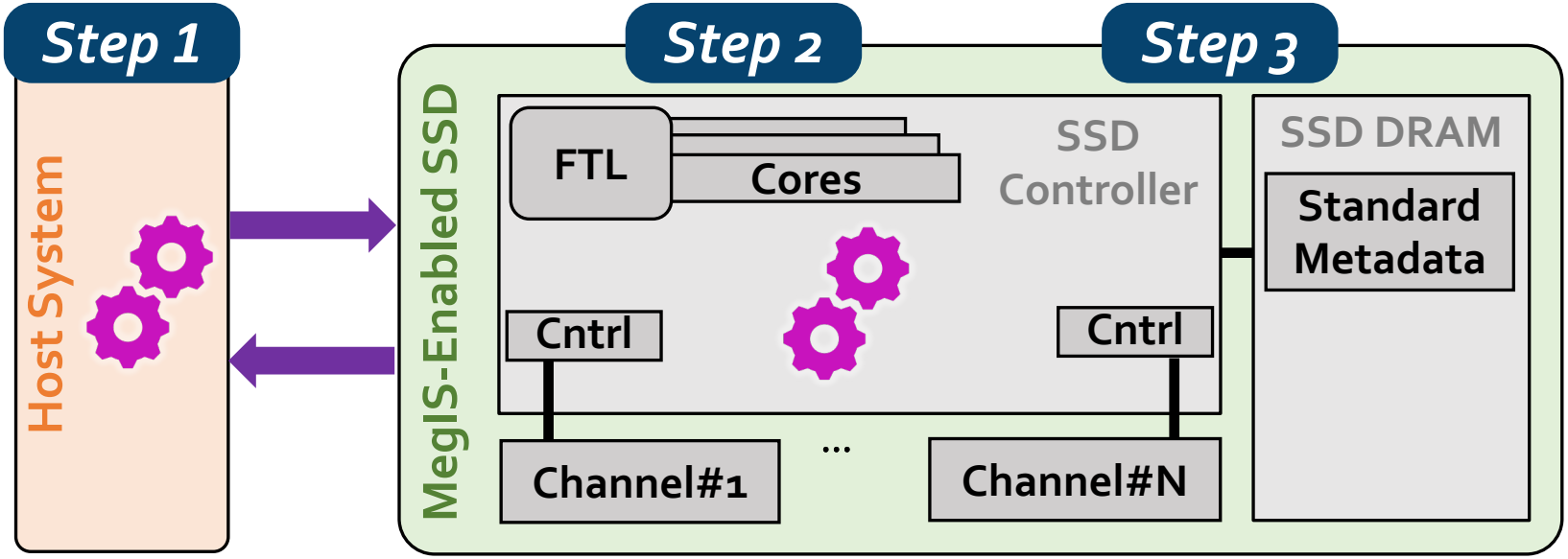

Storage-aware algorithms
- *Enable efficient access patterns to the SSD*

MegIS Hardware-Software Co-Design

Task partitioning and mapping
- *Each step executes in its most suitable system*

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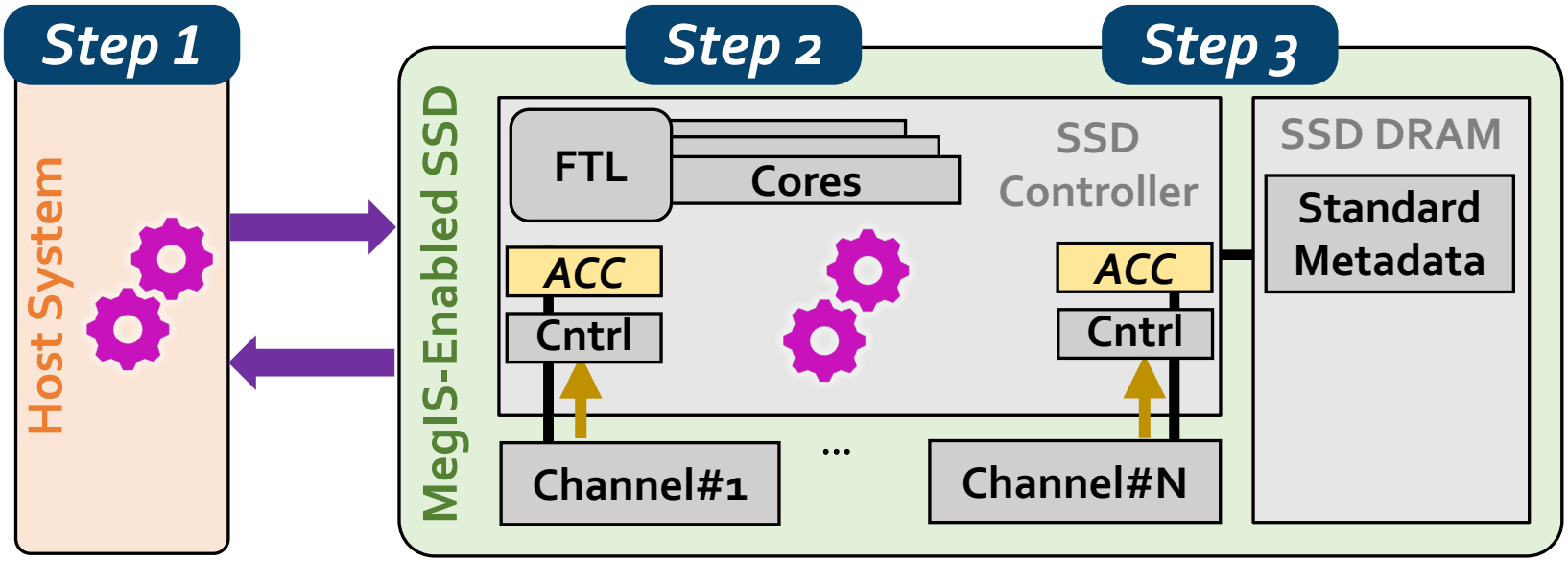


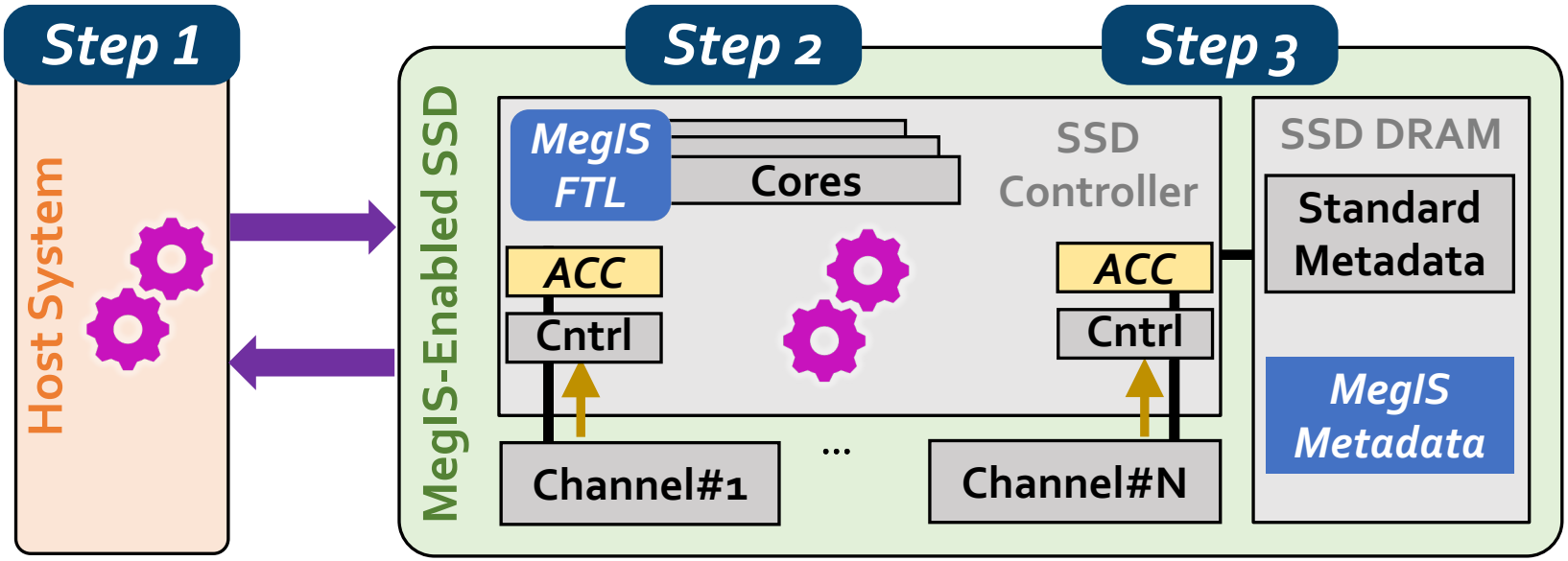
Storage-aware algorithms
- *Enable efficient access patterns to the SSD*

Lightweight in-storage accelerators
- *Minimize SRAM/DRAM buffer spaces needed inside the SSD*

MegIS Hardware-Software Co-Design

Task partitioning and mapping
- *Each step executes in its most suitable system*

Data/computation flow coordination
- *Reduce communication overhead*
- *Reduce #writes to flash chips*



Storage-aware algorithms
- *Enable efficient access patterns to the SSD*

Lightweight in-storage accelerators
- *Minimize SRAM/DRAM buffer spaces needed inside the SSD*

Data mapping scheme and Flash Translation Layer (FTL)
- *Specialize to the characteristics of metagenomic analysis*
- *Leverage the SSD's full internal bandwidth*

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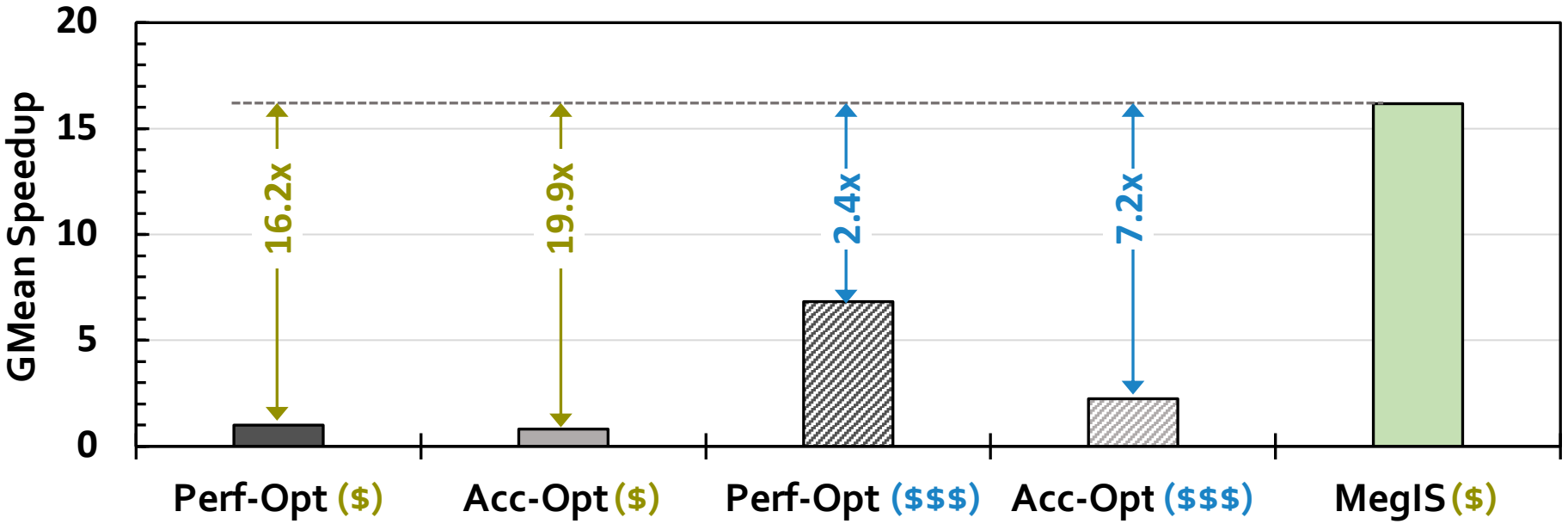
System Cost-Efficiency

- **Cost-optimized system ($):** With SSD-C and 64-GB DRAM
- **Performance-optimized system ($$$):** With SSD-P and 1-TB DRAM



MegIS outperforms the baselines

***even* when running on a much less costly system**

MegIS

High-Performance, Energy-Efficient, and Low-Cost Metagenomic Analysis with In-Storage Processing

https://arxiv.org/abs/2406.19113

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Specializing the Storage System for Genomics & Metagenomics Can Provide Large Benefits

Specializing the Storage System for Genomics & Metagenomics

Storage-centric designs

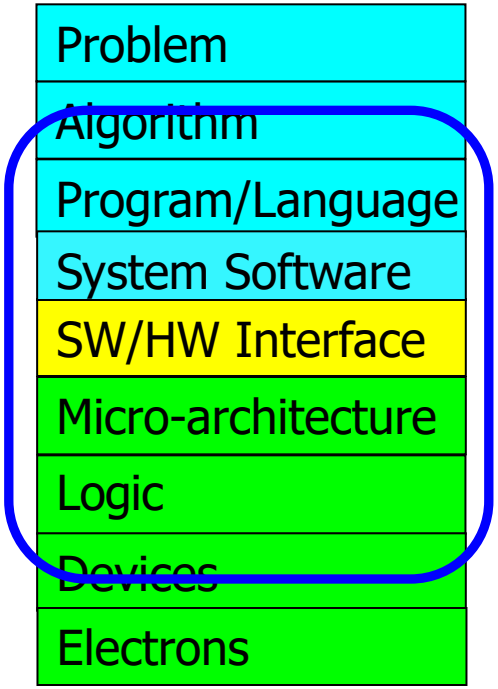
improve system cost-efficiency

and makes accurate (meta)genomics

more accessible for wider adoption

(Co-)Optimizing Algorithm-Architecture-Device is Critical

Computer Architecture (Expanded View)



More About My Research

My Website:

https://bit.ly/nikamgh

Works Described in This Talk		**GenStore** ASPLOS'22		**MegIS** ISCA'24	
Near-Data Processing *(Other Works)*	**ALP** IEEE TETC'22		**CODIC** ISCA'21		**SIMDRAM** ASPLOS'21
Optimizing Memory and Storage Systems	**Venice** ISCA'23	**FIGARO** MICRO'20	**CROW** ISCA'19	**CAL** MICRO'18	**FLIN** ISCA'18
Algorithms	**MLA** ISMB'24	**RawHash** ISMB'23	**BLEND** Bioinformatics'23		**TargetCall** APBC'23
Algorithm-Architecture Co-Design	**Scrooge** Bioinformatics'23		**SeGraM** ISCA'22		**SMASH** MICRO'19
Device-Architecture Co-Design		**Understanding and Modeling Ultra-Dense 3D Memory Systems** PACT SRC'24			

Storage-Centric Computing for Genomics and Metagenomics

Nika Mansouri Ghiasi

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Backup Slides

End-to-End Workflow of Genome Sequence Analysis

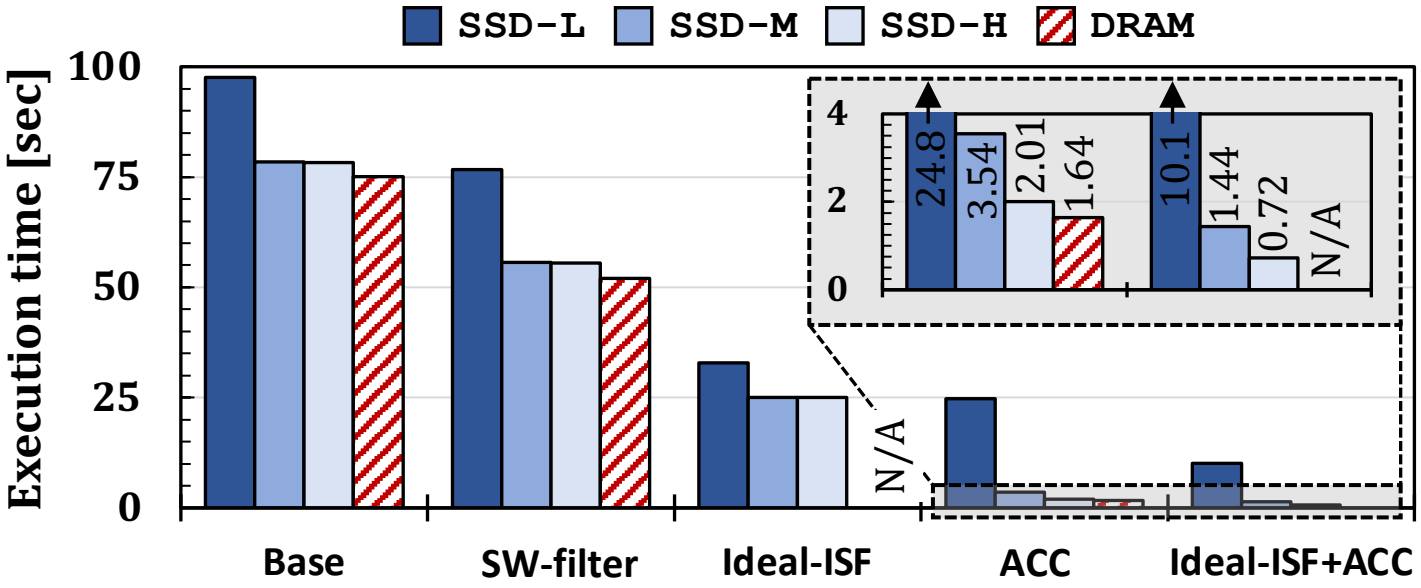
- There are three key initial steps in a standard genome sequencing and analysis workflow
  - Collection, preparation, and sequencing of a DNA sample in the laboratory
  - Basecalling
  - Read mapping

- Genomic read sets can be obtained by
  - Sequencing a DNA sample and storing the generated read set into the SSD of a sequencing machine
  - Downloading read sets from publicly available repositories and storing them into an SSD

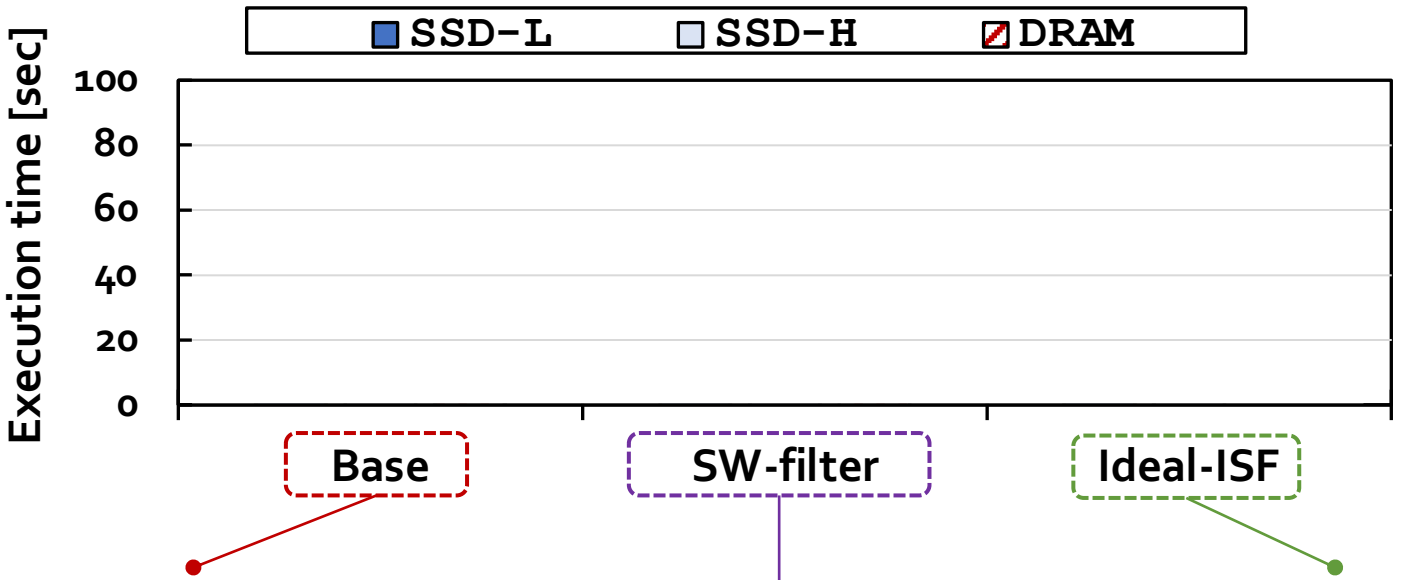
- We focus on optimizing the performance of read mapping because sequencing and basecalling are performed only once per read set, whereas read mapping can be performed many times
  - Analyzing the differences between a reads from an individual and many reference genomes of other individuals
  - Repeating the read mapping step many times to improve the outcome of read mapping

- Improving read mapping performance is critical in almost all genomic analyses that use sequencing
  - 45% of the execution time when discovering sequence variants in cancer genomics studies
  - 60% of the execution time when profiling the species composition of a multi-species (i.e., metagenomic) read

Motivation


SSD-L
SSD-M
SSD-H
DRAM
Execution time [sec]
100
75
50
25
0
4
2
0
24.8
3.54
2.01
1.64
10.1
1.44
0.72
N/A
N/A
Base
SW-filter
Ideal-ISF
ACC
Ideal-ISF+ACC

Motivation



State-of-the-art software read mapper, Minimap2

Base integrated with a software filter that prunes **80%** of exactly-matching reads

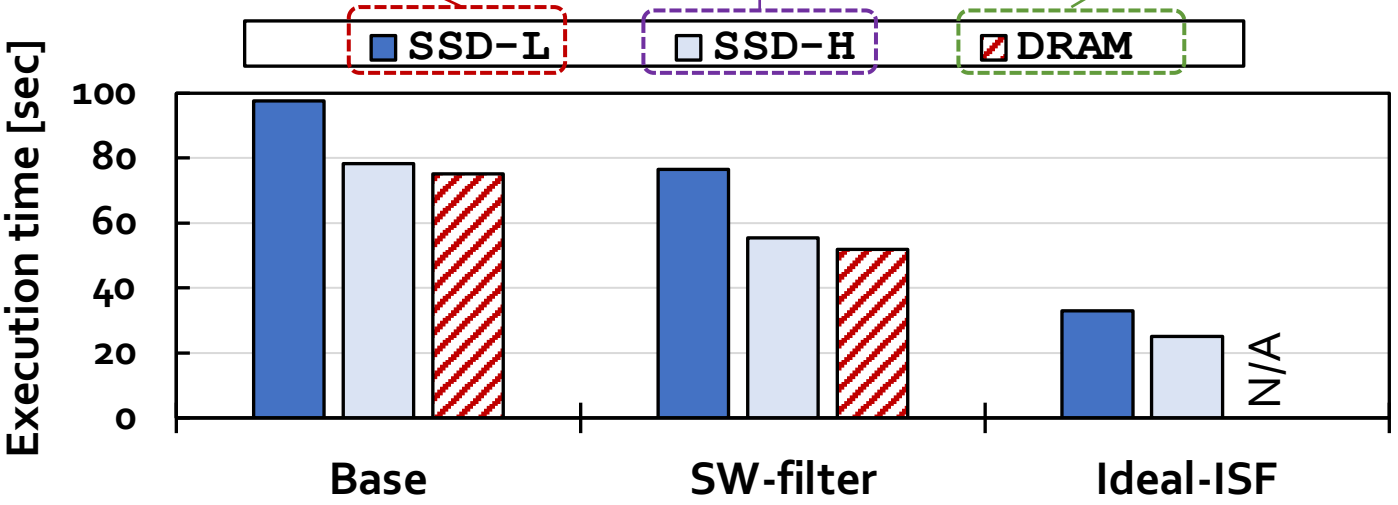
Base integrated with an ideal in-storage filter

Motivation

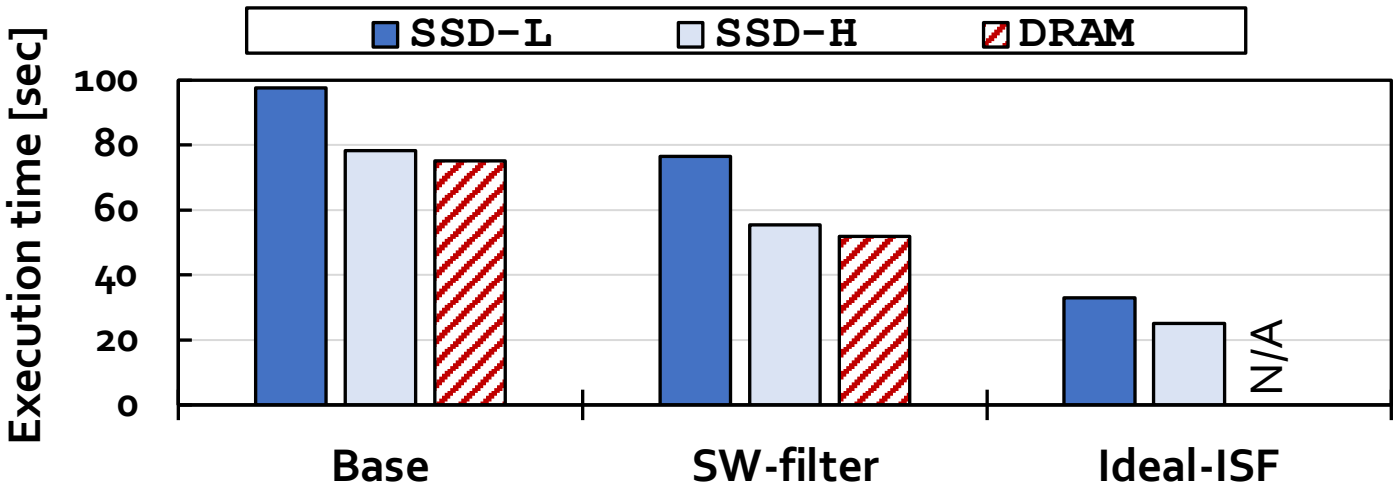
Low-end SSD with SATA3 interface (0.5 GB/s)

High-end SSD with PCIe Gen4 interface (7 GB/s)

Data preloaded in DRAM, with no I/O overhead



Benefits of Ideal In-Storage Filter

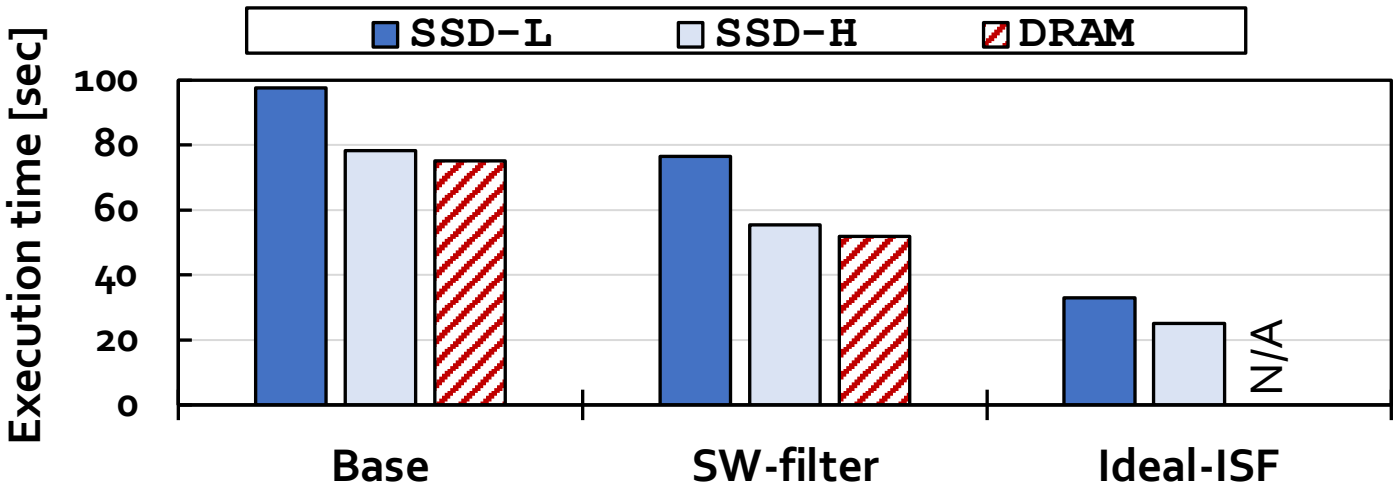


The ideal in-storage filter significantly improves performance by

1) Reducing computation overhead

2) Reducing data movement overhead

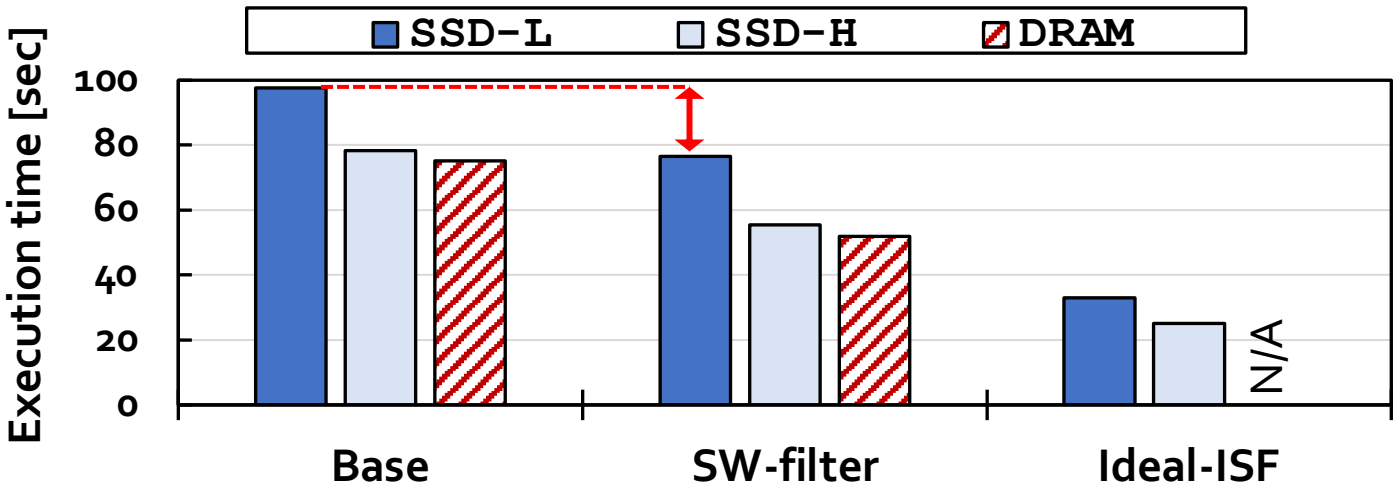
Overheads of Software Mappers



I/O has a significant impact on application performance

which can be alleviated at the cost of expensive storage devices and interfaces

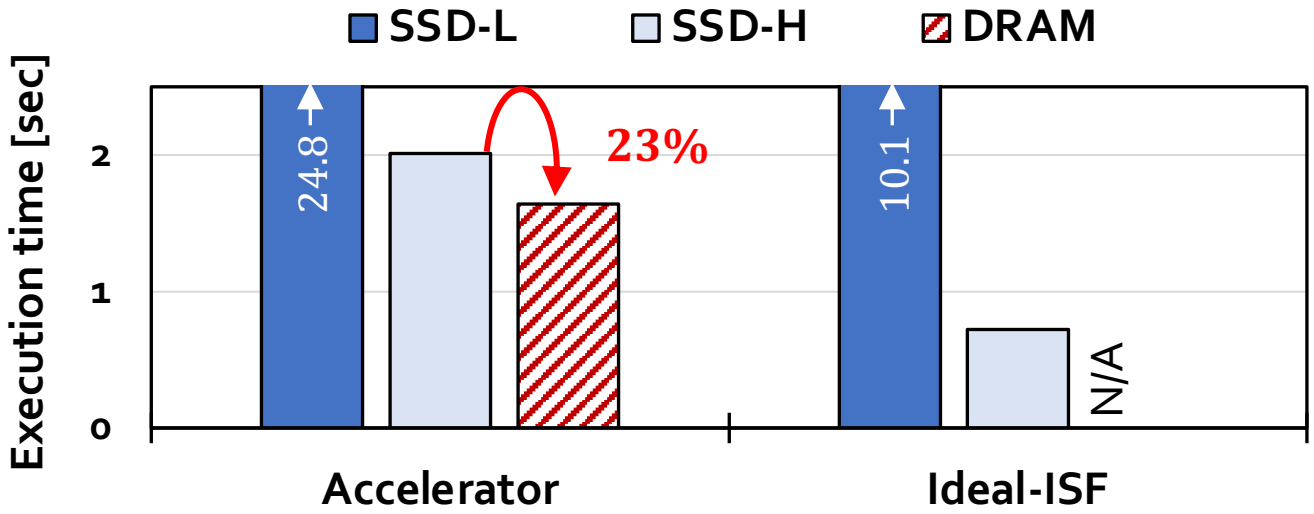
Overheads of Software Mappers



SW-filter provides limited benefits compared to Base

The filtering process outside the SSD must compete with the read mapping process for the resources in the system

Overheads of Hardware Mappers



Even the high-end SSD does not fully alleviate the storage bottleneck

The ideal in-storage filter significantly improves performance

Ideal-OSF

- Execution time of an ideal in-storage filter:

$$T_{\text{Ideal-ISF}} = T_{\text{I/O-Ref}} + \max\left\{T_{\text{I/O-Unfiltered}}, T_{\text{RM-Unfiltered}}\right\}$$

- Execution time of an ideal outside-storage filter:
  - 60% slower than Ideal-ISF in our analysis

$$T_{\text{Ideal-OSF}} = T_{\text{I/O-Ref}} + \max\left\{T_{\text{I/O-All-Reads}}, T_{\text{RM-Unfiltered}}\right\}$$

Comparison to PIM

- Even though read mapping applications could also benefit from other near-data, in-storage processing can fundamentally address the data movement problem by filtering large, low-reuse data where the data initially resides.

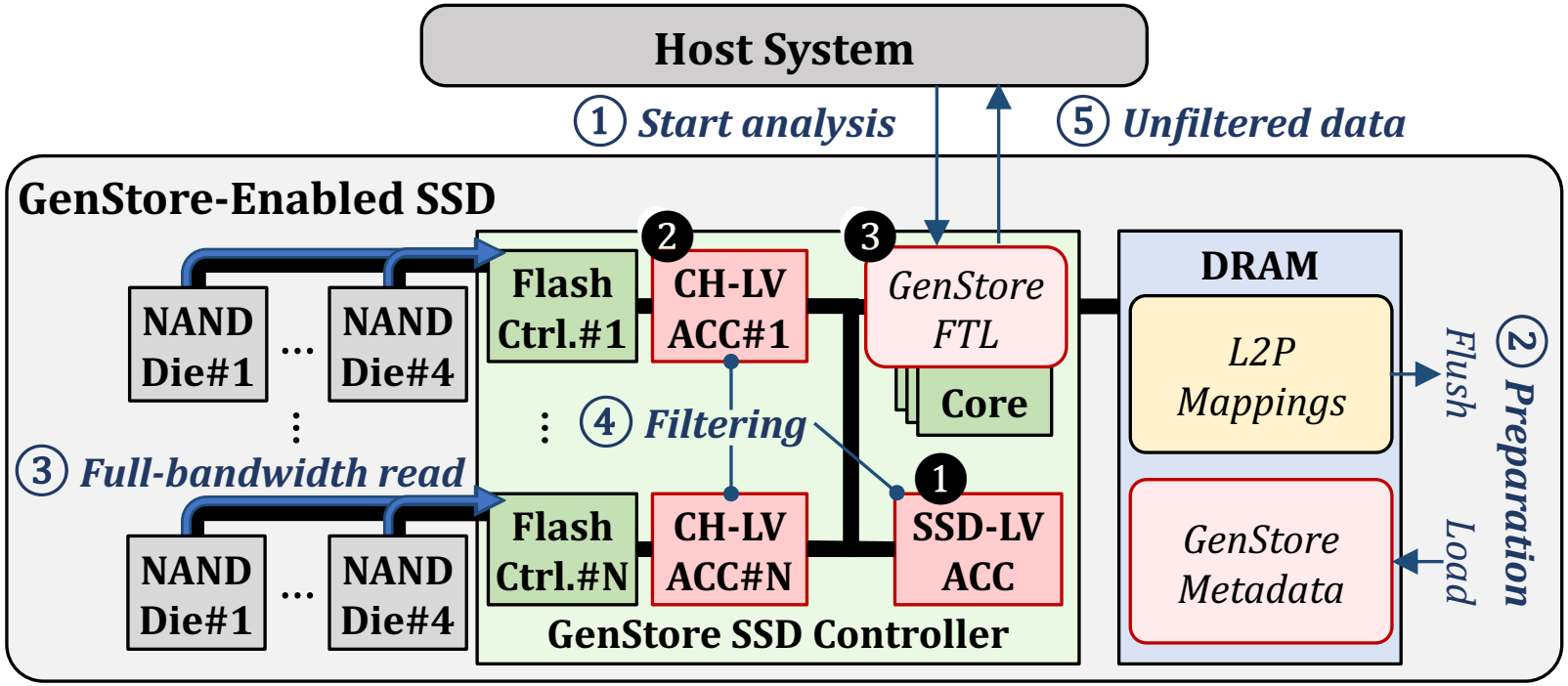
- Even if an ideal accelerator achieved a zero execution time, there would still exist the need to bring the data from storage to the accelerator.
  - 2.15x slower than the execution time that Ideal-ISF+ACC provides in our motivational analysis

In-storage filter can be integrated with any read mapping accelerator, including PIM accelerators, to alleviate their data movement overhead.

Long Read Use Cases

Use case	Input read set (Short/Long)	Size [GB]	Reference	Align [%]
Sequencing errors	ERR3988483 (L) [157] HG002_ONT_20200204 (L) [158]	54 371	hg38 [144]	**47.4** **69.3**
Rapidly evolving samples	SRR5413248 (L) [157] SRR12423642 (S) [157]	1.69 0.466	NZ_NJEX02 [159] NC_045512.2 [160]	**60.0** **23.1**
No reference	SRR6767727 (L) [157] SRR9953689 (L) [157]	12.4 15.9	NZ_NJEX02 [159]	**0.35** **37.0**
Contamination	SRR9953689 (L) [157]	15.9	hg38 [144]	**1.0**

FTL


Host System
1 Start analysis
5 Unfiltered data
GenStore-Enabled SSD
NAND Die#1
NAND Die#4
3 Full-bandwidth read
Flash Ctrl.#1
Flash Ctrl.#N
CH-LV ACC#1
CH-LV ACC#N
4 Filtering
GenStore FTL
Core
SSD-LV ACC
GenStore SSD Controller
DRAM
L2P Mappings
GenStore Metadata
2 Preparation
Flush
Load

FTL: Metadata

- GenStore metadata includes the mapping information of the data structures necessary for read mapping acceleration
- In accelerator mode, GenStore also keeps in internal DRAM other metadata structures of the regular FTL
  - Examples include the page status table and block read counts which need to be updated during the filtering process
- We carefully design GenStore to only sequentially access the underlying NAND flash chips while operating as an accelerator
  - Requires only a small amount of metadata to access the stored data

FTL: Data Placement

- GenStore needs to properly place its data structures to enable the full utilization of the internal SSD bandwidth
- When each data structure is initially written to the SSD, GenStore sequentially and evenly distributes it across NAND flash chips
- GenStore can specify the physical location of a 30-GB data structure by maintaining only the list of 1,250 (30 GB/24 MB) physical block addresses
- It significantly reduces the size of the necessary mapping information from 300 MB (with conventional 4-KiB page mapping) to only 5 KB (1,250 4 bytes)

FTL: SSD Management Tasks

- In accelerator mode, GenStore only reads data structures to perform filtering, and does not write any new data
  - GenStore does not require any write-related SSD-management tasks such as garbage collection and wear-leveling
- The other tasks necessary for ensuring data reliability can be done before or after the filtering process
  - GenStore significantly limits the amount of data whose retention age would exceed the manufacturer-specified threshold since GenStore's filtering process takes a short time.
  - GenStore-FTL can easily avoid read disturbance errors for data with high read counts since GenStore sequentially reads NAND flash blocks only once during filtering

Data Sizes

- Conventional k-mer index in Minimap2 + reference genome: 7 GB (k = 15)
- Read-sized k-mer index before optimization: 126 GB (k= 150)
- Read-sized k-mer index after optimization: 32 GB (k = 150)

SSD Specs

- **SSD-L:** SATA3 interface (0.5 GB/s sequential read)
  - 1.2 GB/s per channel bandwidth
  - 8 channels

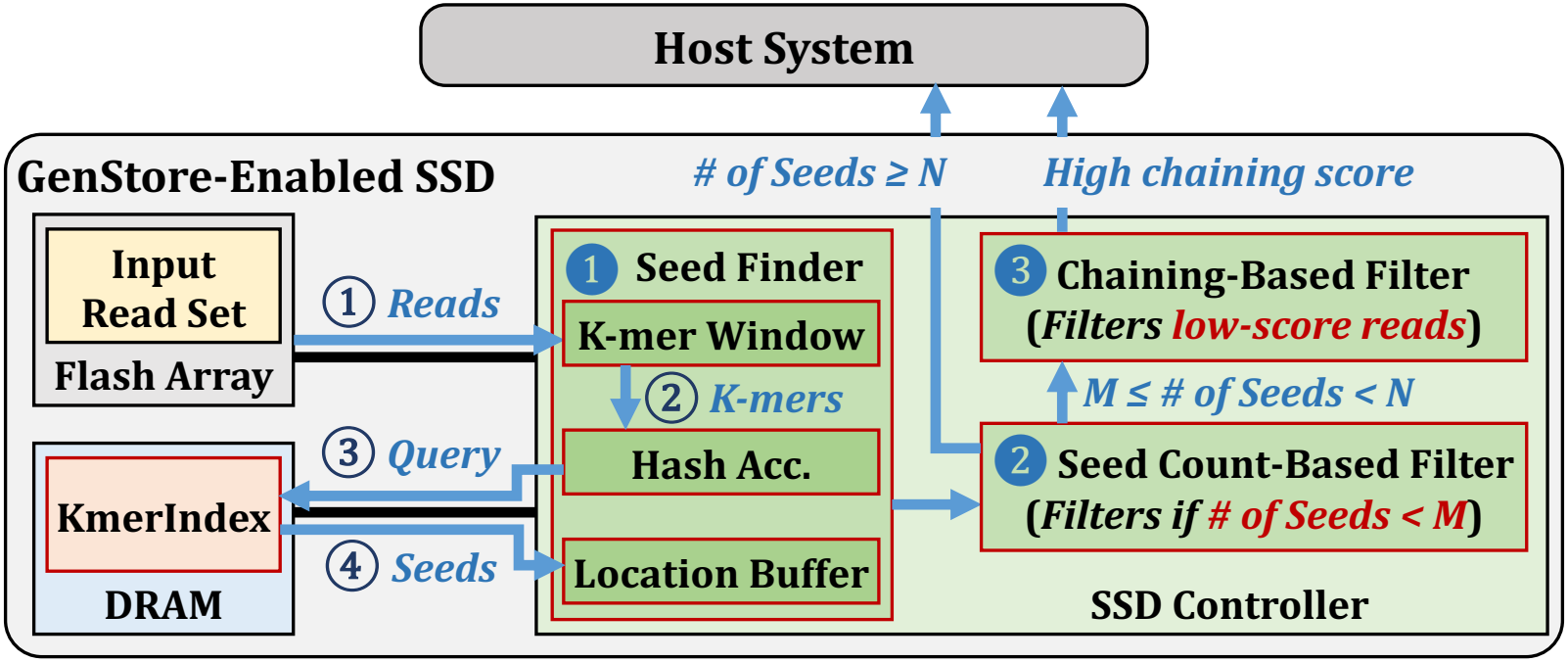
- **SSD-L:** PCIe Gen3 M.2 interface (3.5 GB/s sequential read)
  - 1.2 GB/s per channel bandwidth
  - 16 channels

- **SSD-L:** PCIe Gen4 interface (7 GB/s sequential read)
  - 1.2 GB/s per channel bandwidth
  - 16 channels

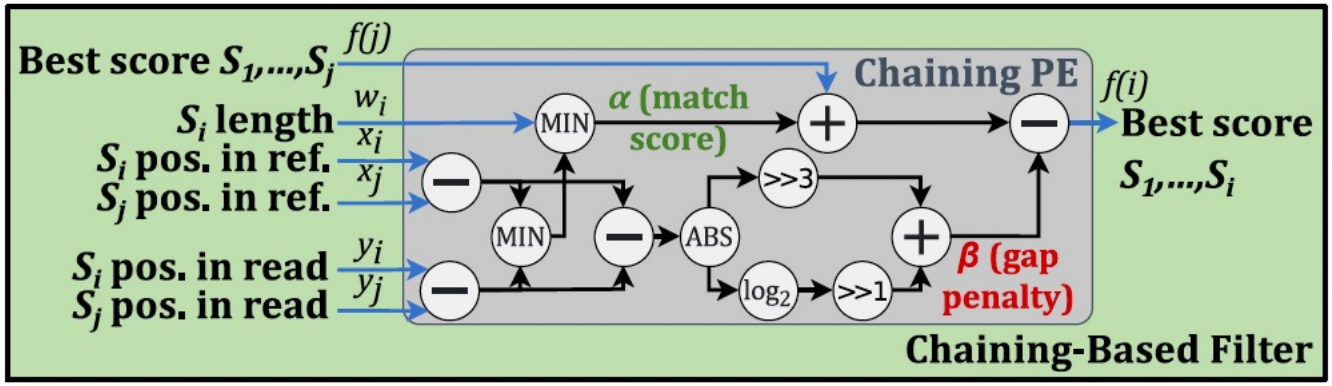
Evaluation Methodology

- **Performance modeling**
  - Ramulator for DRAM timing
  - MQSim for SSD timing
  - We model the end-to-end throughput of GenStore based on the throughput of each GenStore pipeline stage
    - Accessing NAND flash chips
    - Accessing internal DRAM
    - Accelerator computation
    - Transferring unfiltered data to the host
- **Real system results**
  - AMD EPYC 7742 CPU
  - 1TB DDR4 DRAM
  - AMD µProf

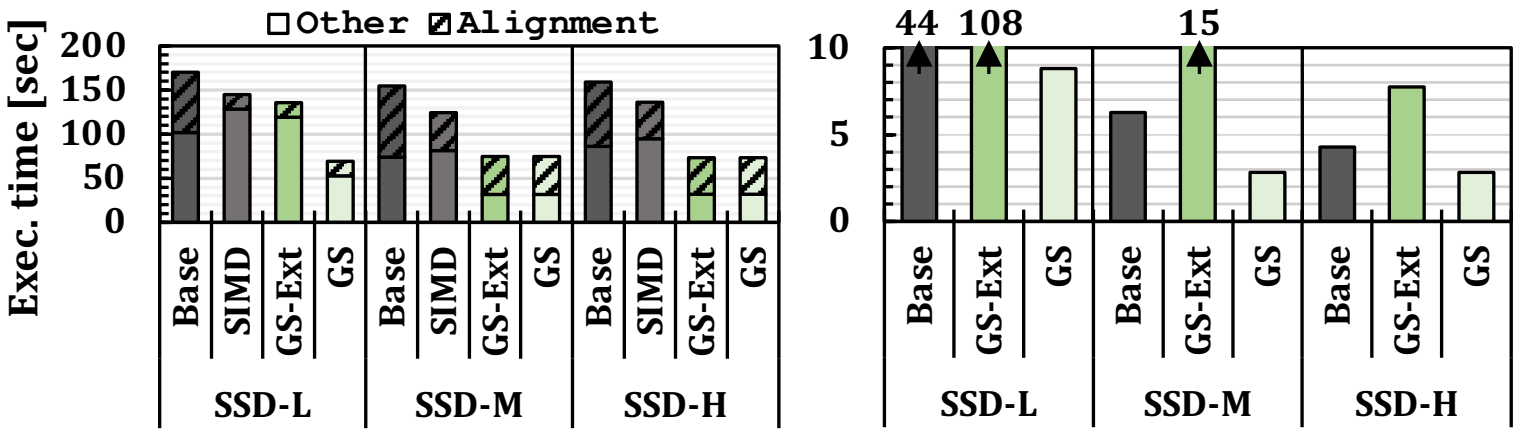
GenStore-NM


Host System
GenStore-Enabled SSD
# of Seeds ≥ N
High chaining score
Input Read Set
Flash Array
1 Reads
KmerIndex
DRAM
3 Query
4 Seeds
1 Seed Finder
K-mer Window
2 K-mers
Hash Acc.
Location Buffer
3 Chaining-Based Filter
(Filters low-score reads)
M ≤ # of Seeds < N
2 Seed Count-Based Filter
(Filters if # of Seeds < M)
SSD Controller

Chaining Processing Element



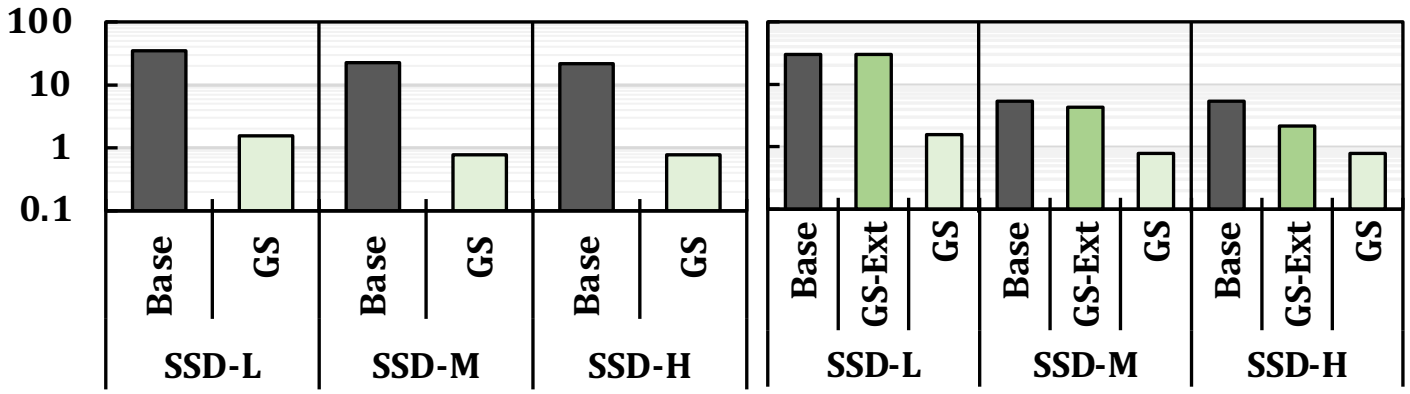
GenStore-EM



GS-Ext provides significant performance improvements over both Base and SIMD in SSD-M and SSD-H.

GS-Ext provides limited benefits over SIMD in SSD-L due to low external I/O bandwidth.

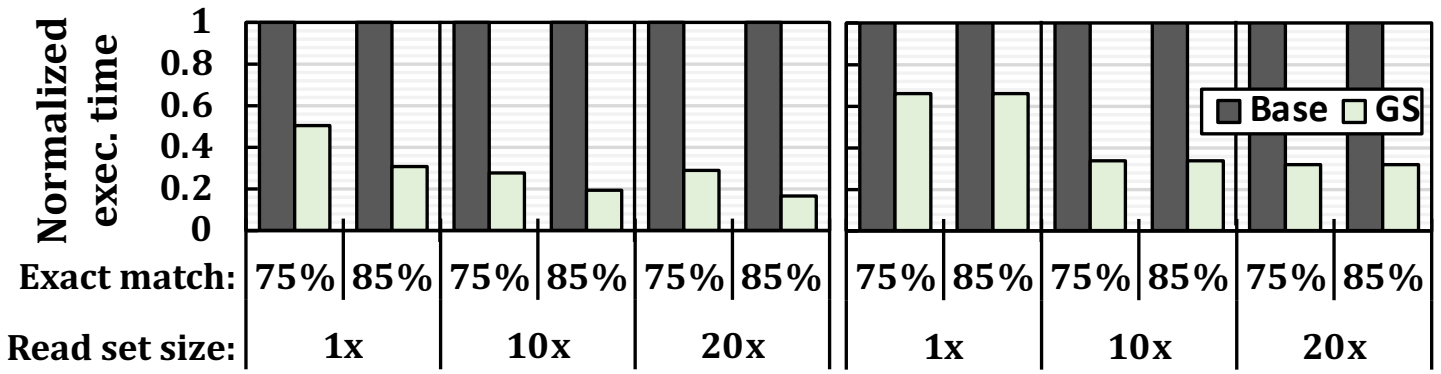
GenStore-NM



GS-Ext performs significantly slower than Base (2.28x - 1.91x) on all systems.

Effect of Inputs on GenStore-EM

$$DM\_Saving = \frac{Size_{Ref} + Size_{ReadSet}}{Size_{Ref} + Size_{ReadSet} \times (1 - Ratio_{Filter})}$$



Effect of Inputs on GenStore-NM

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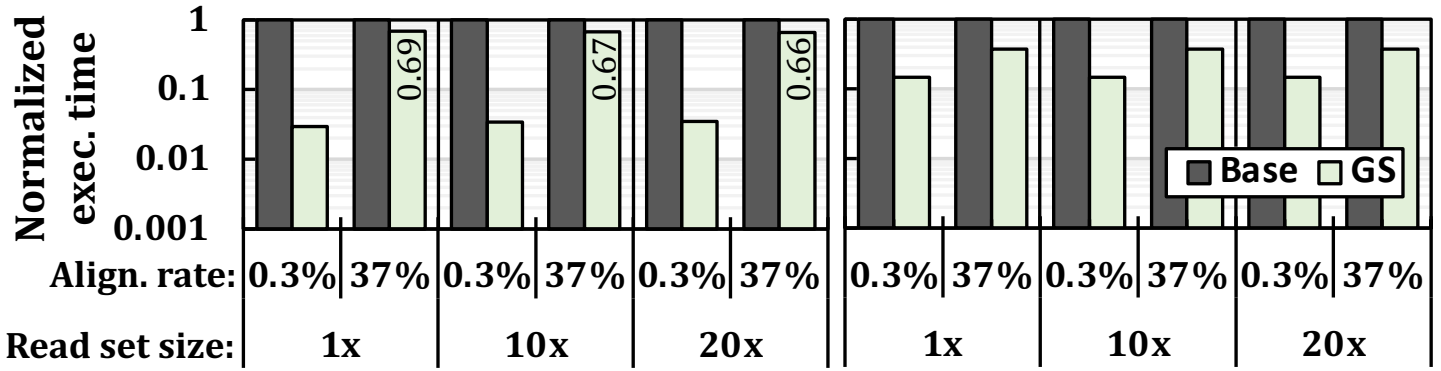


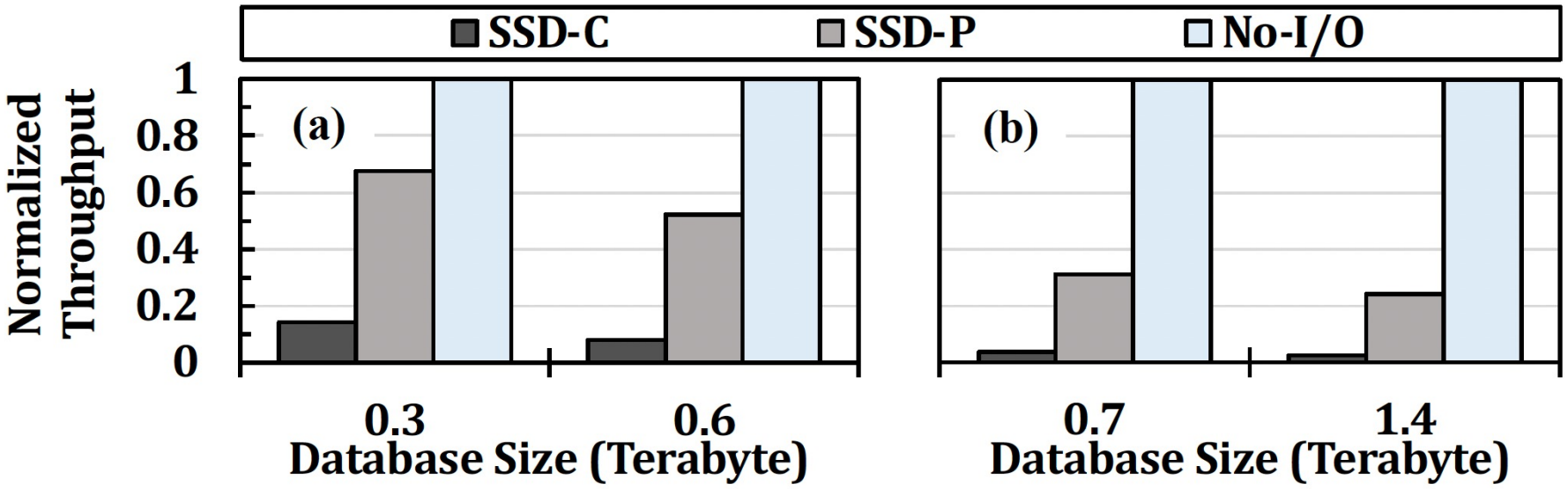
MegIS Backup Slides

Motivational Analysis

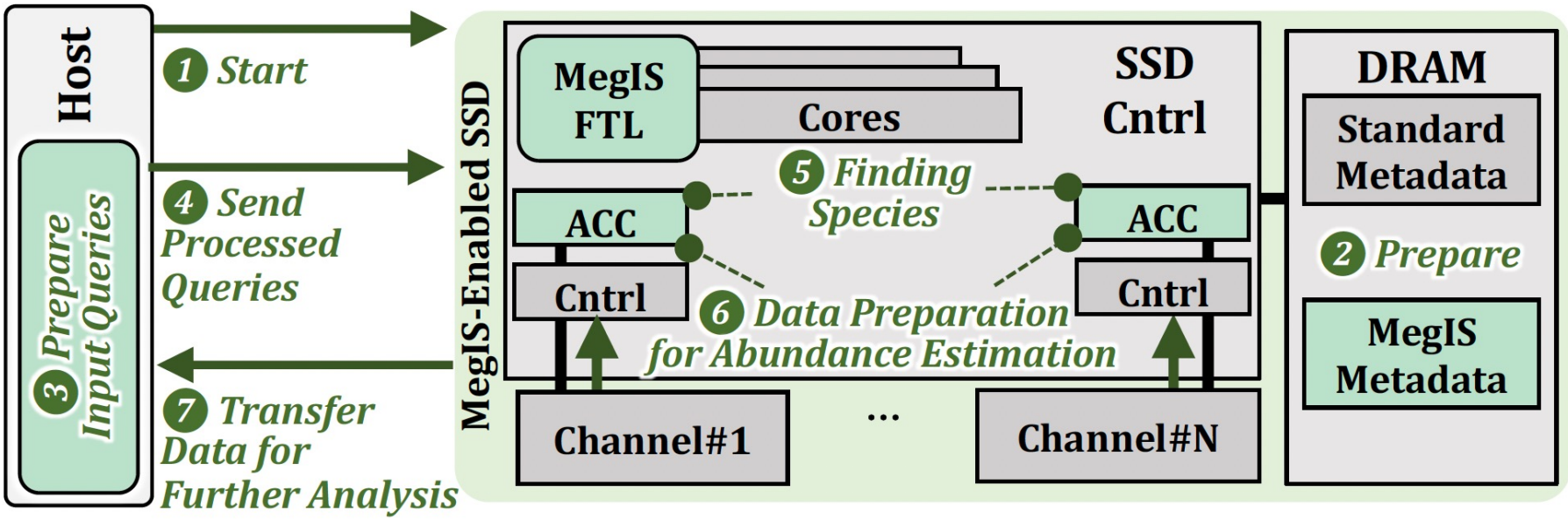
Database access patterns

(a)Random Query

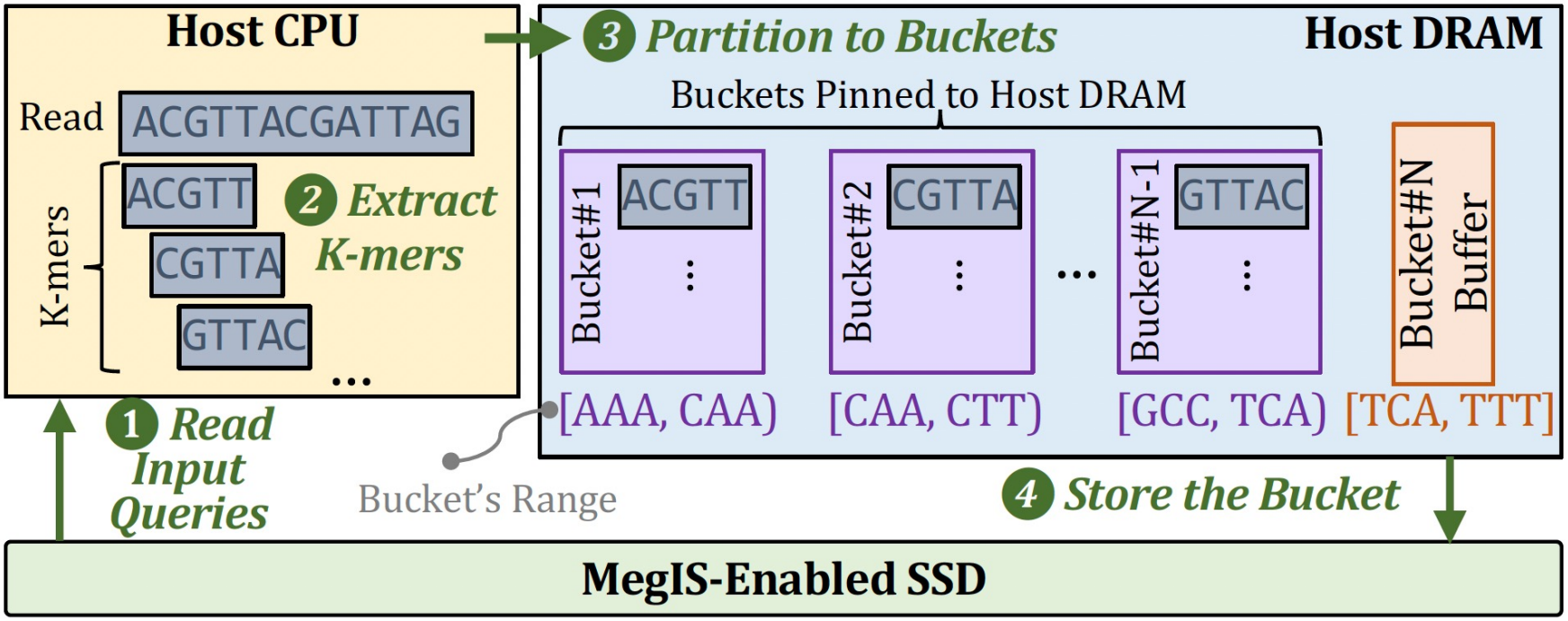
(b)Streaming Query



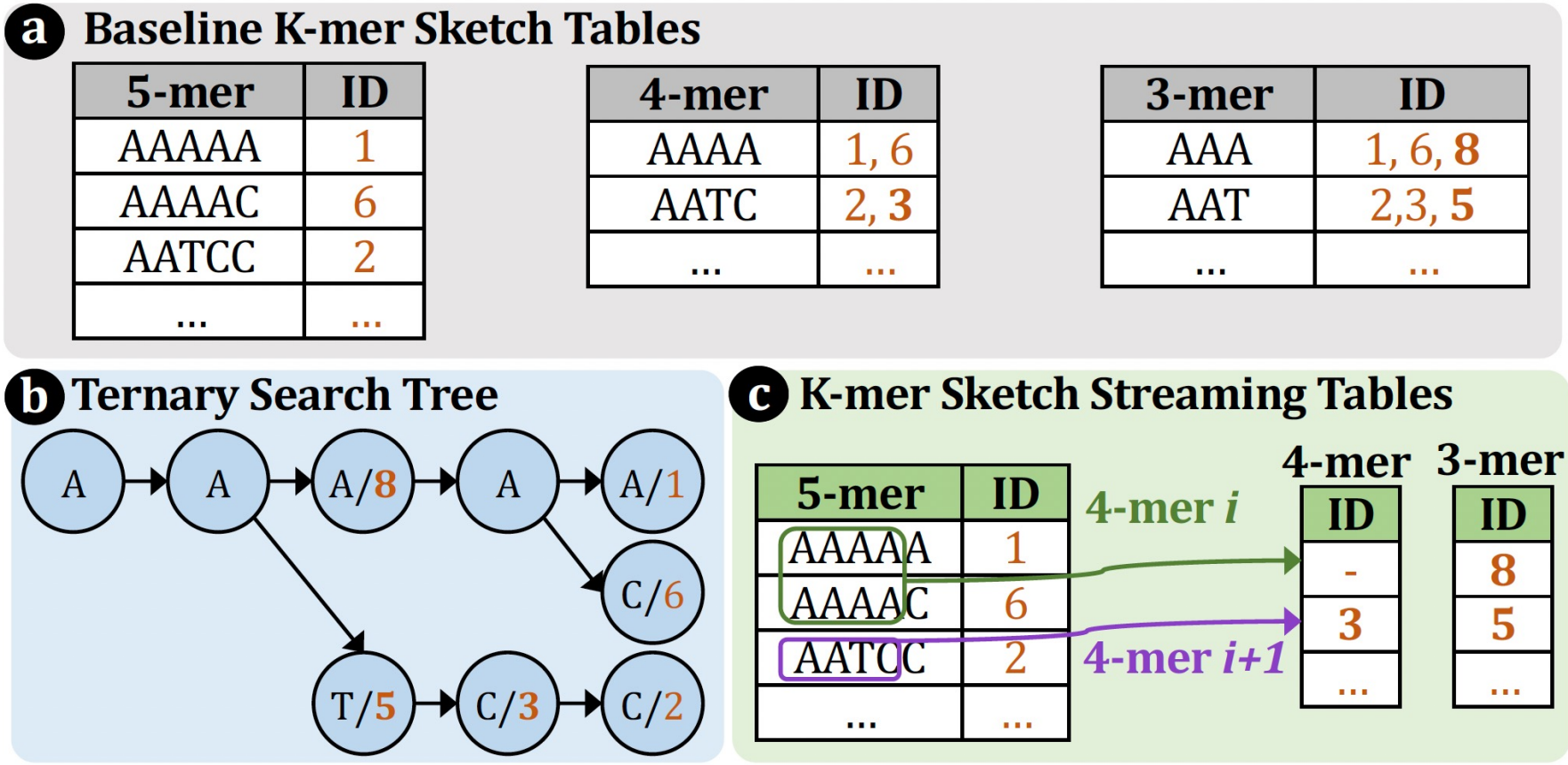
Overview of MegIS's Steps



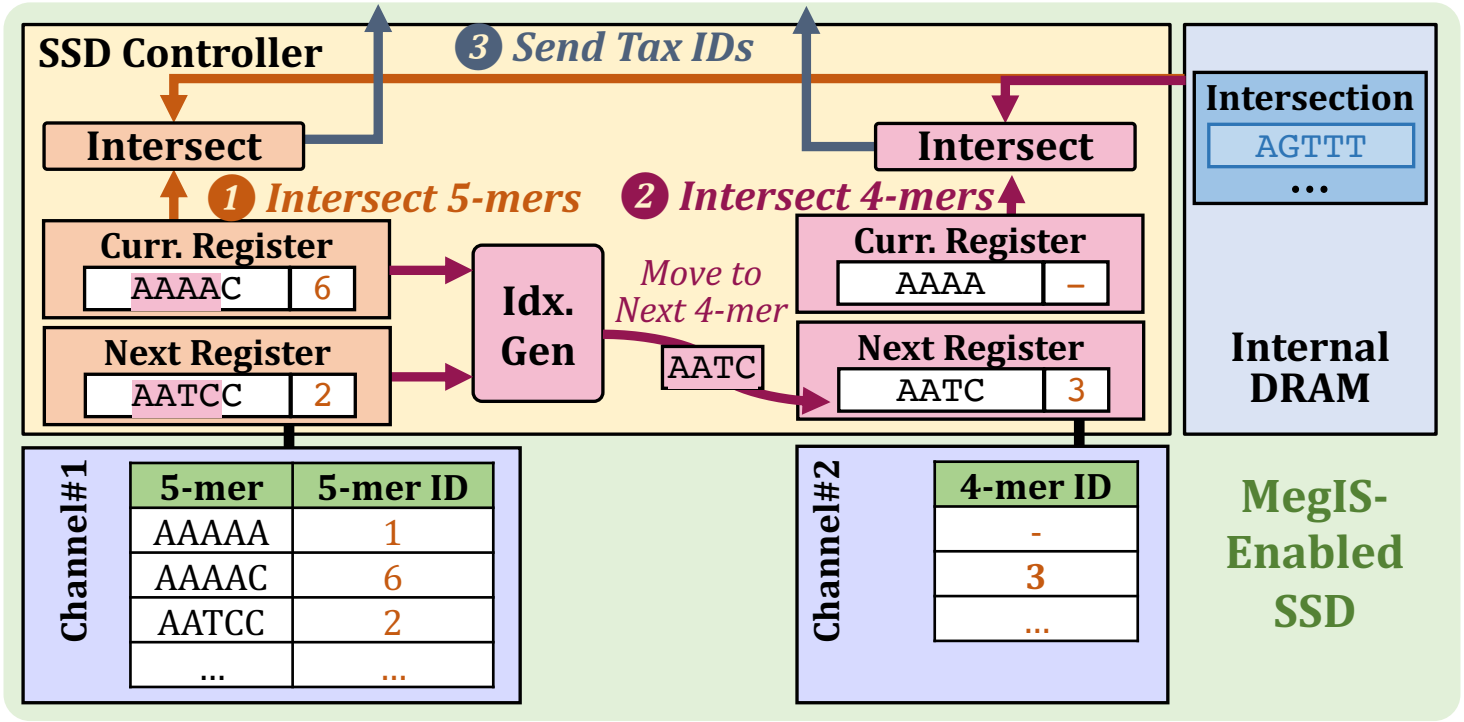
More Details on Step 1



K-mer Sketch Data Structures



K-mer Sketch Streaming Hardware Design



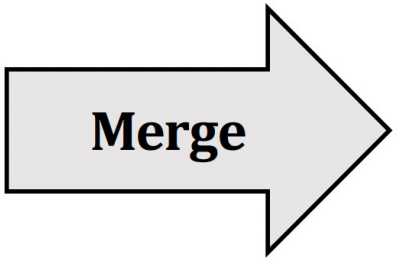
Index Generation in Step 3

K-mer	Loc.
ATT	14
CCA	9
GCT	5
…	…

Reference Index Organism A

K-mer	Loc.
AAG	2
CCA	21
TGC	4
…	…

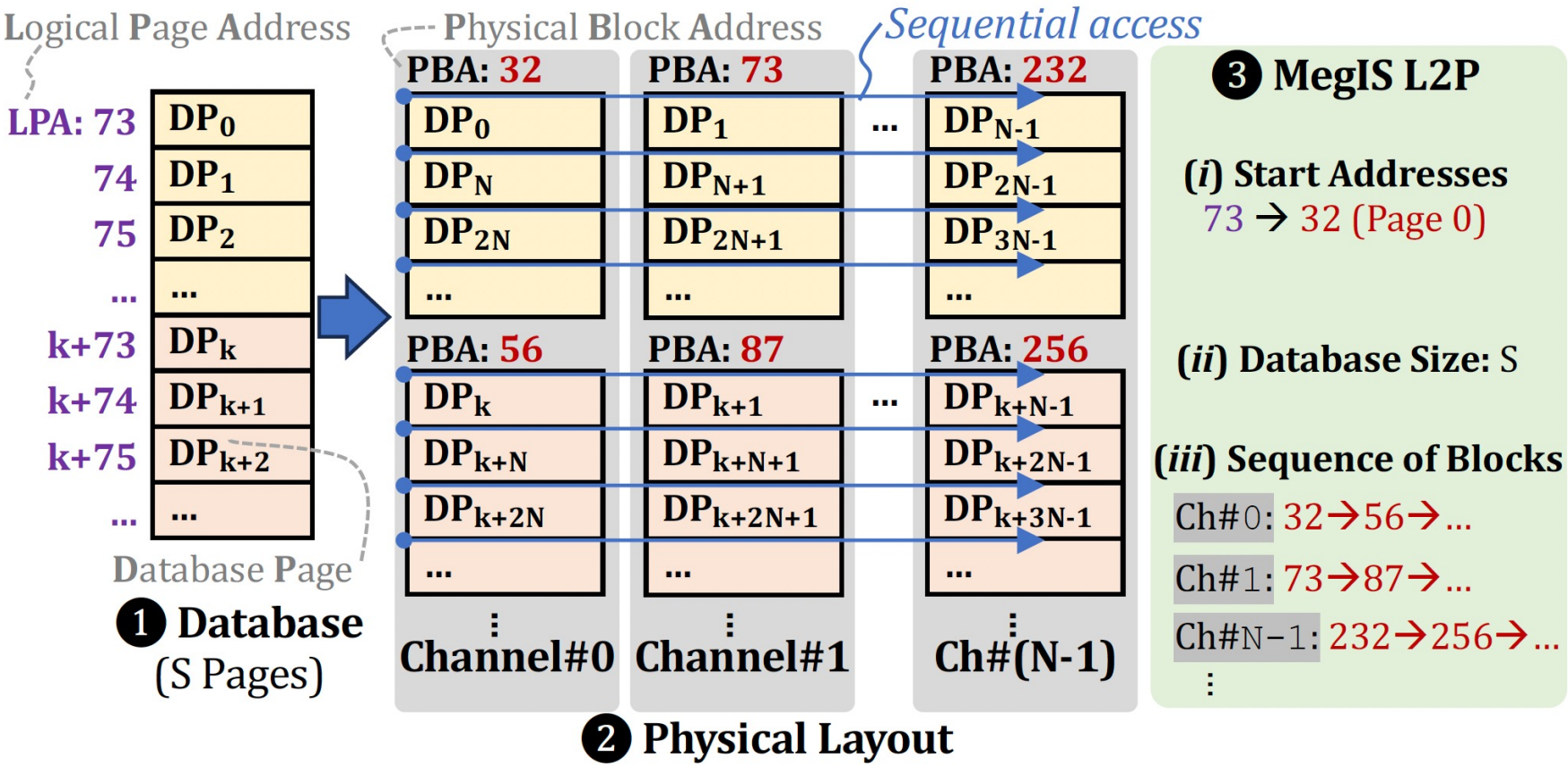
Reference Index Organism B



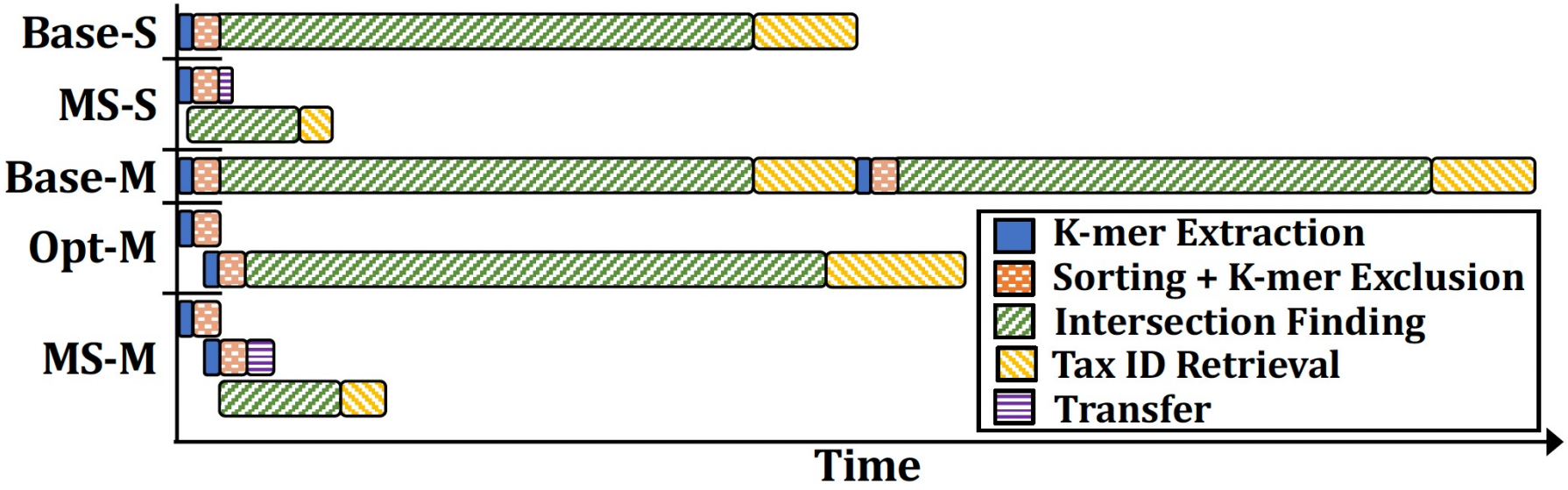
K-mer	Loc.
AAG	1002
ATT	14
CCA	9, 1021
GCT	5
TGC	1004
…	…

Unified Reference Index

MegIS FTL


Logical Page Address
Physical Block Address
Sequential access
LPA: 73
74
75
...
k+73
k+74
k+75
...
DP0
DP1
DP2
...
DPk
DPk+1
DPk+2
...
Database Page
1 Database
(S Pages)
PBA: 32
PBA: 73
PBA: 232
DP0
DP1
...
DPN-1
DPN
DPN+1
DP2N-1
DP2N
DP2N+1
DP3N-1
PBA: 56
PBA: 87
PBA: 256
DPk
DPk+1
DPk+N-1
DPk+N
DPk+N+1
DPk+2N-1
DPk+2N
DPk+2N+1
DPk+3N-1
Channel#0
Channel#1
Ch#(N-1)
2 Physical Layout
3 MegIS L2P
(i) Start Addresses
73 → 32 (Page 0)
(ii) Database Size: S
(iii) Sequence of Blocks
Ch#0: 32→56→...
Ch#1: 73→87→...
Ch#N-1: 232→256→...

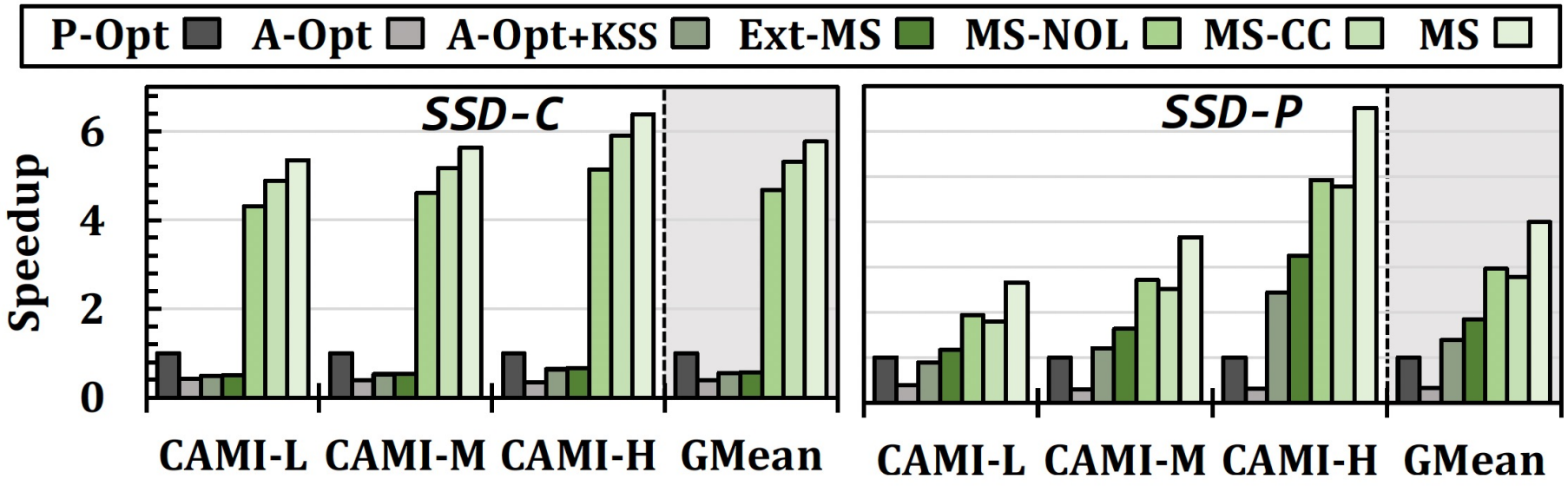
Multi-Sample Analysis



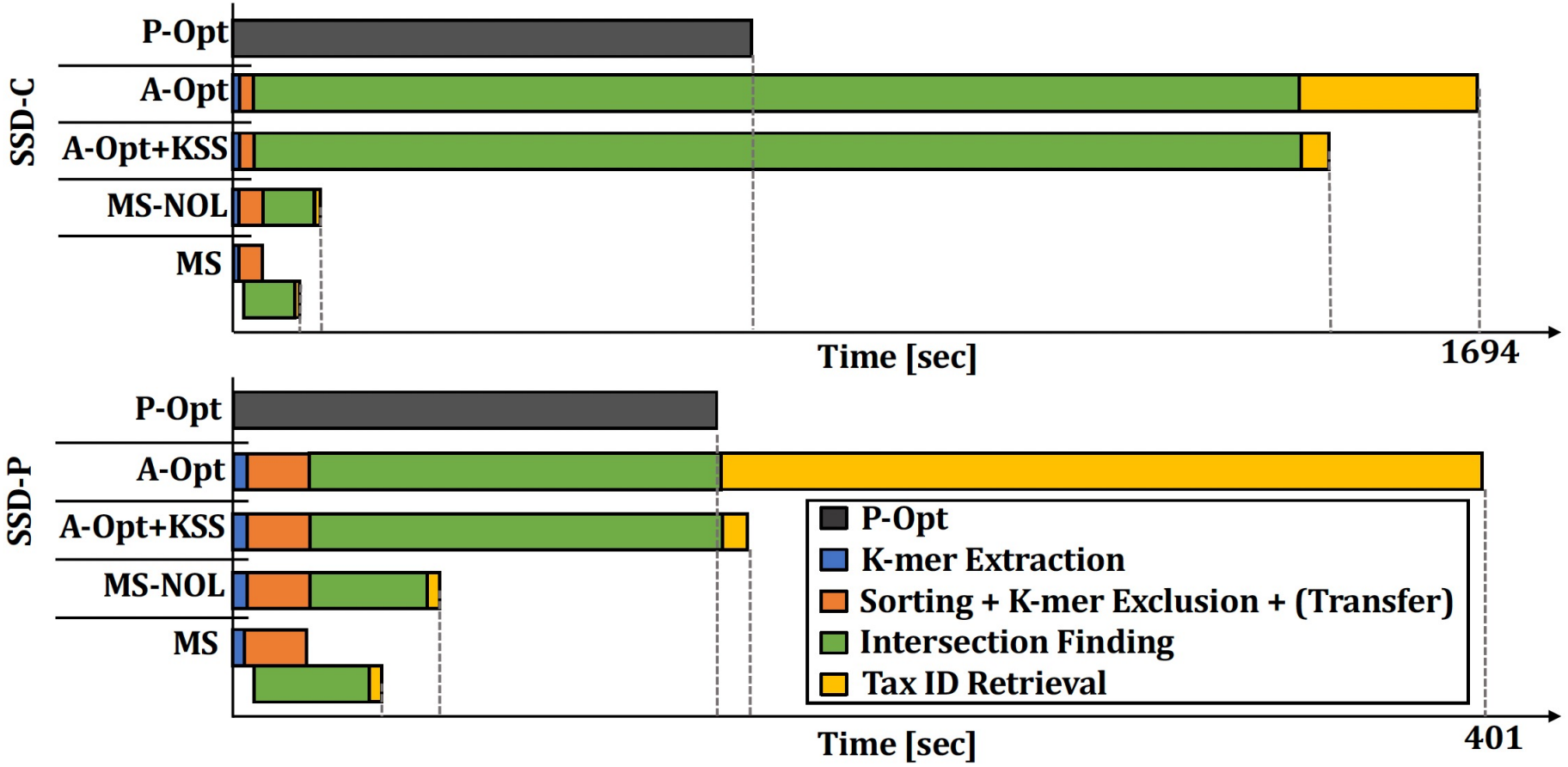
SSD Configurations

Specification	SSD-C	SSD-P
General	48-WL-layer 3D TLC NAND flash-based SSD 4 TB capacity, 4 GB internal LPDDR4 DRAM [226]	
Bandwidth (BW)	600 MB/s interface BW (SATA3); 560 MB/s sequential-read BW 1.2-GB/s channel I/O rate	8 GB/s interface BW (4-lane PCIe Gen4); 7 GB/s sequential-read BW 1.2-GB/s channel I/O rate
NAND Config	8 channels, 8 dies/channel, 4 planes/dies, 2,048 blocks/plane, 196 WLs/block, 16 KiB/page *(4/8/16 channels in Fig. 17)*	16 channels, 8 dies/channel, 2 planes/dies, 2,048 blocks/plane, 196 WLs/block, 16 KiB/page *(8/16/32 channels in Fig. 17)*
Latencies	Read (tR): 52.5 μs, Program (tPROG): 700 μs	
Embedded Cores	3 ARM Cortex-R4 cores [86]	4 ARM Cortex-R4 cores [86]

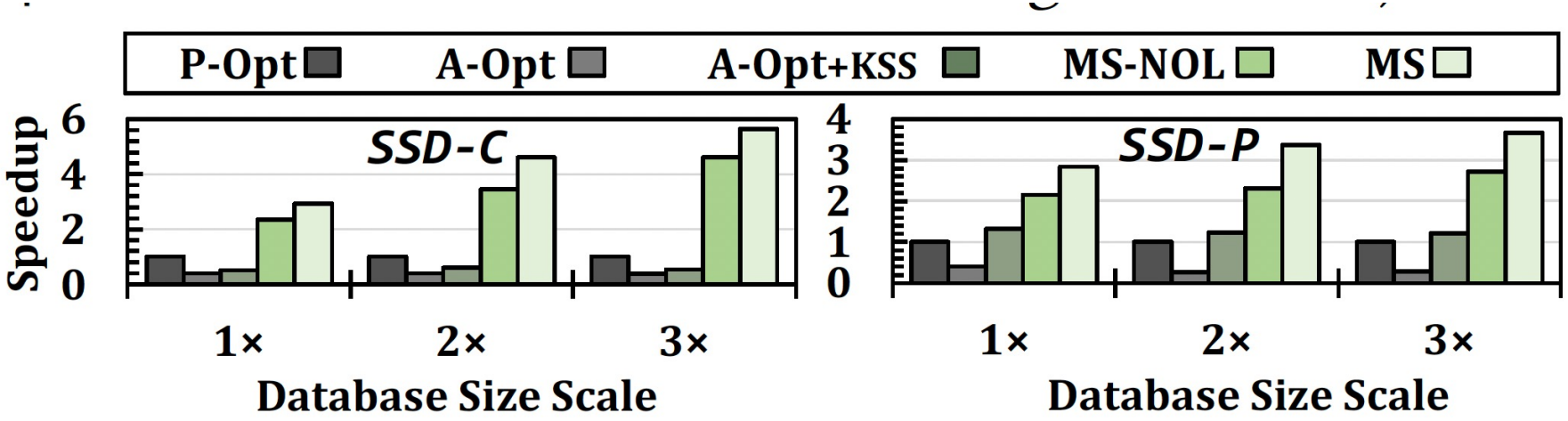
Impact of Different Optimizations



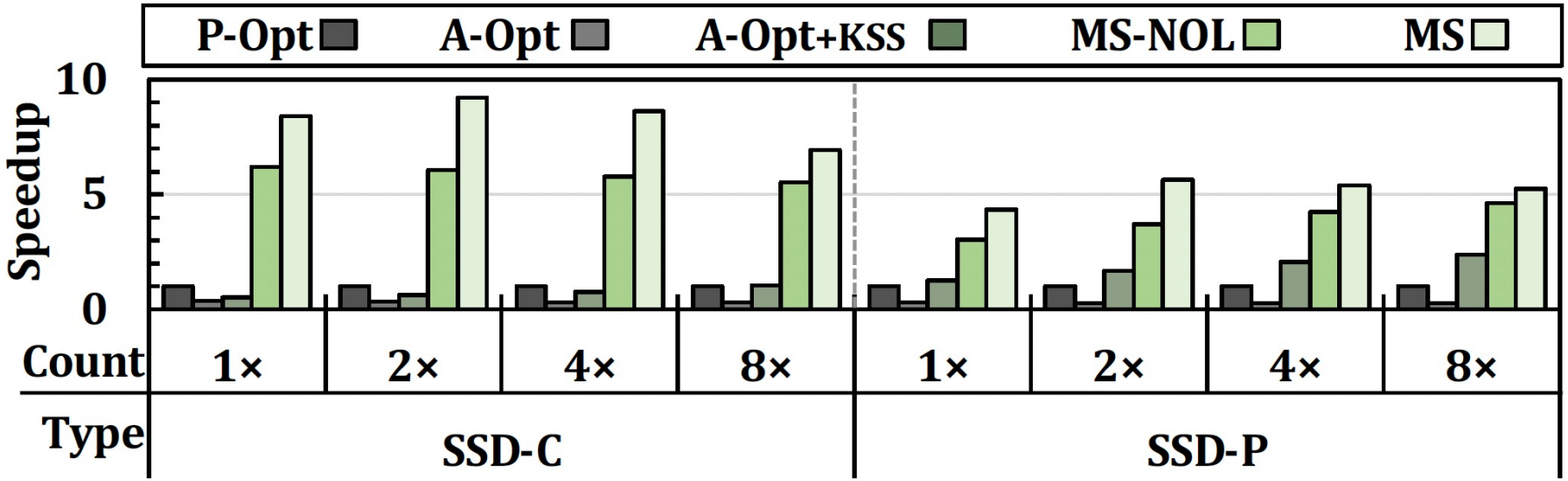
Impact of Different Optimizations



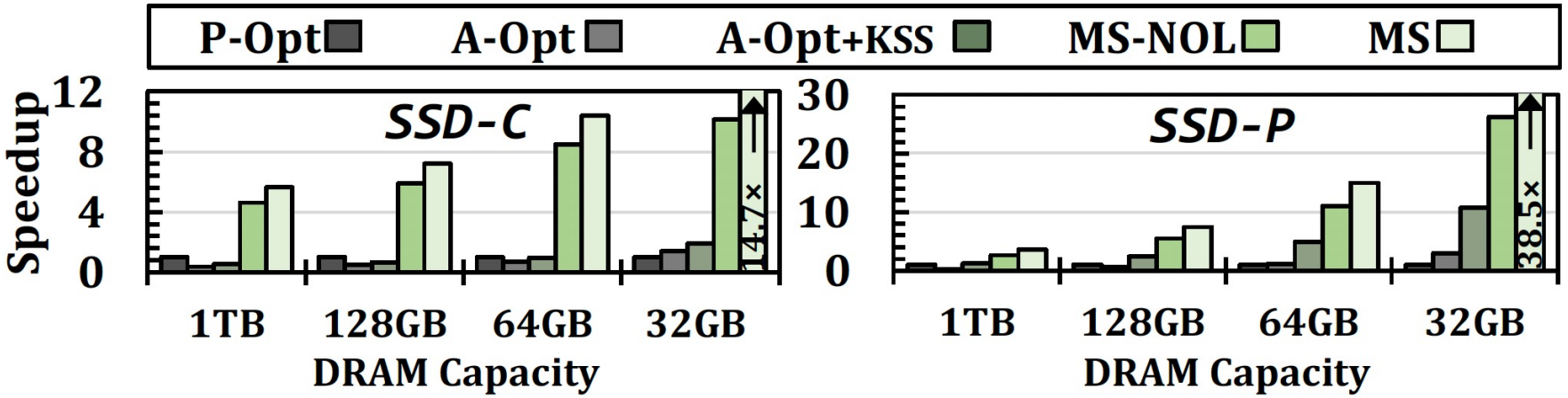
Speedup with Different Database Sizes



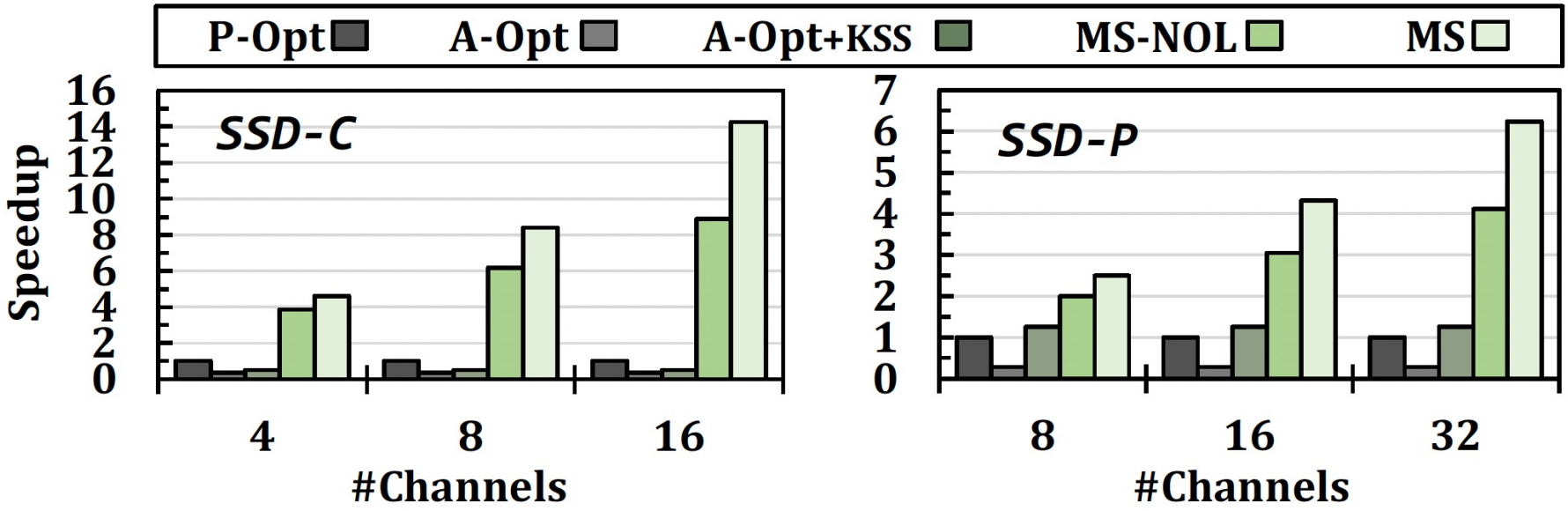
Speedup with Different #SSDs



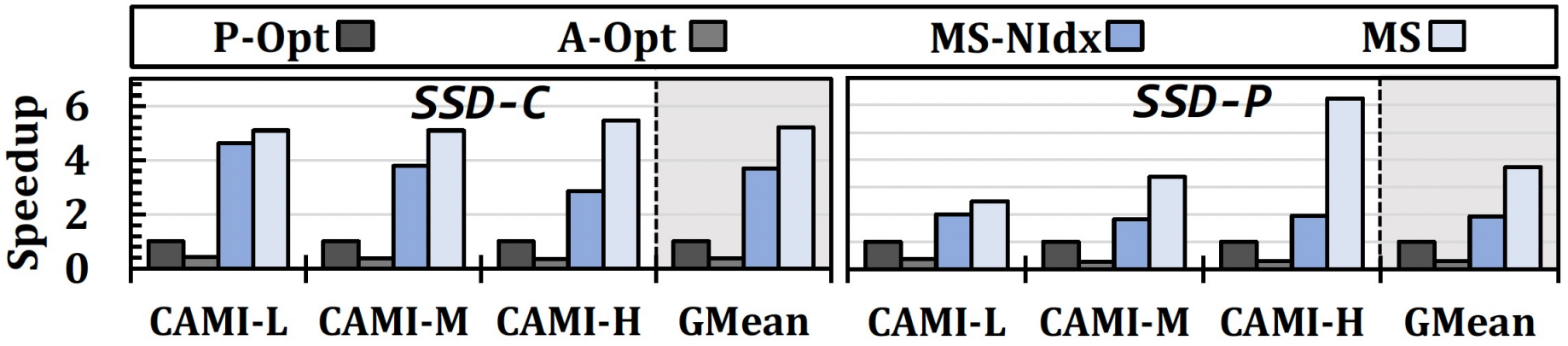
Speedup with Different Main Memory Capacities



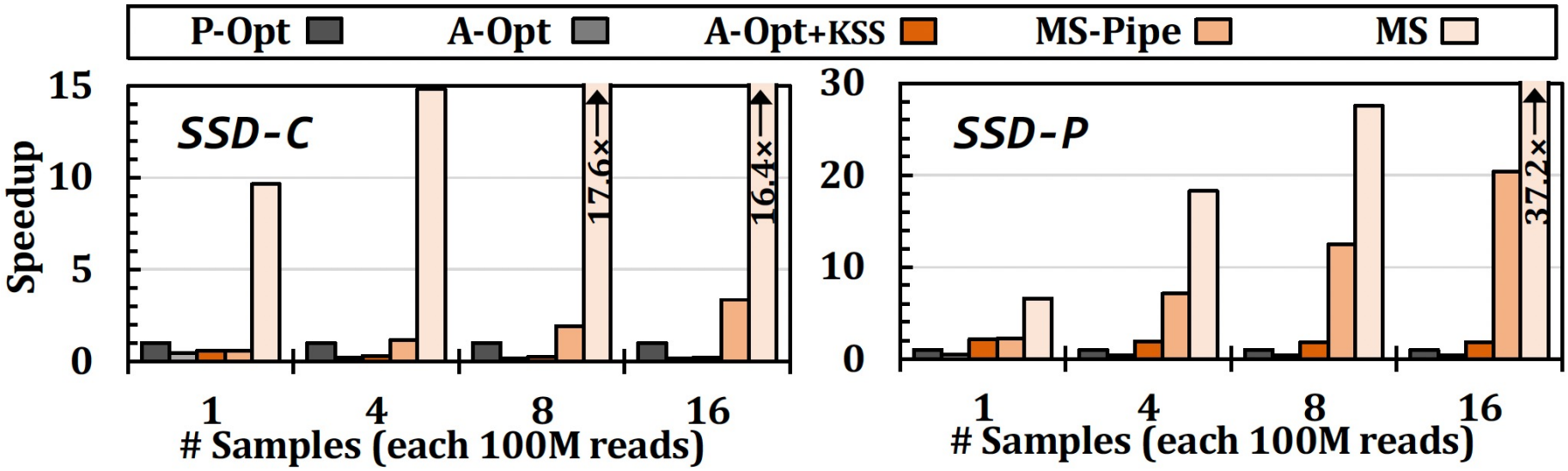
Speedup with Varying SSD Internal Bandwidth



Speedup of Abundance Estimation



Multi-Sample Use Case



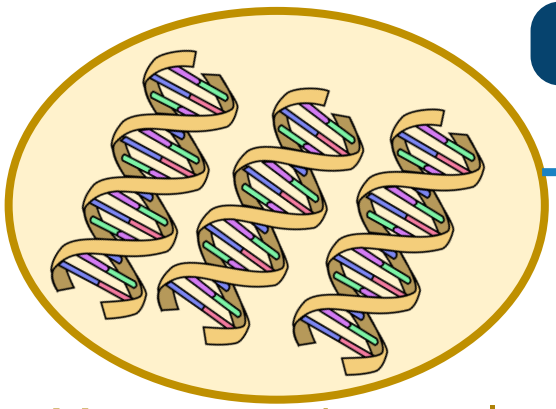
Area and Power

- Based on **synthesis** of **MegIS** accelerators using the Synopsys Design Compiler @ 65nm technology node

Logic Unit	# of instances	Area [mm²]	Power [mW]
Intersect (120-bit)	1 per channel	0.001361	0.284
k-mer Registers (2 x 120-bit)	1 per channel	0.002821	0.645
Index Generator (64-bit)	1 per channel	0.000272	0.025
Control Unit	1 per SSD	0.000188	0.026
Total for an 8-channel SSD	-	*0.04*	*7.658*

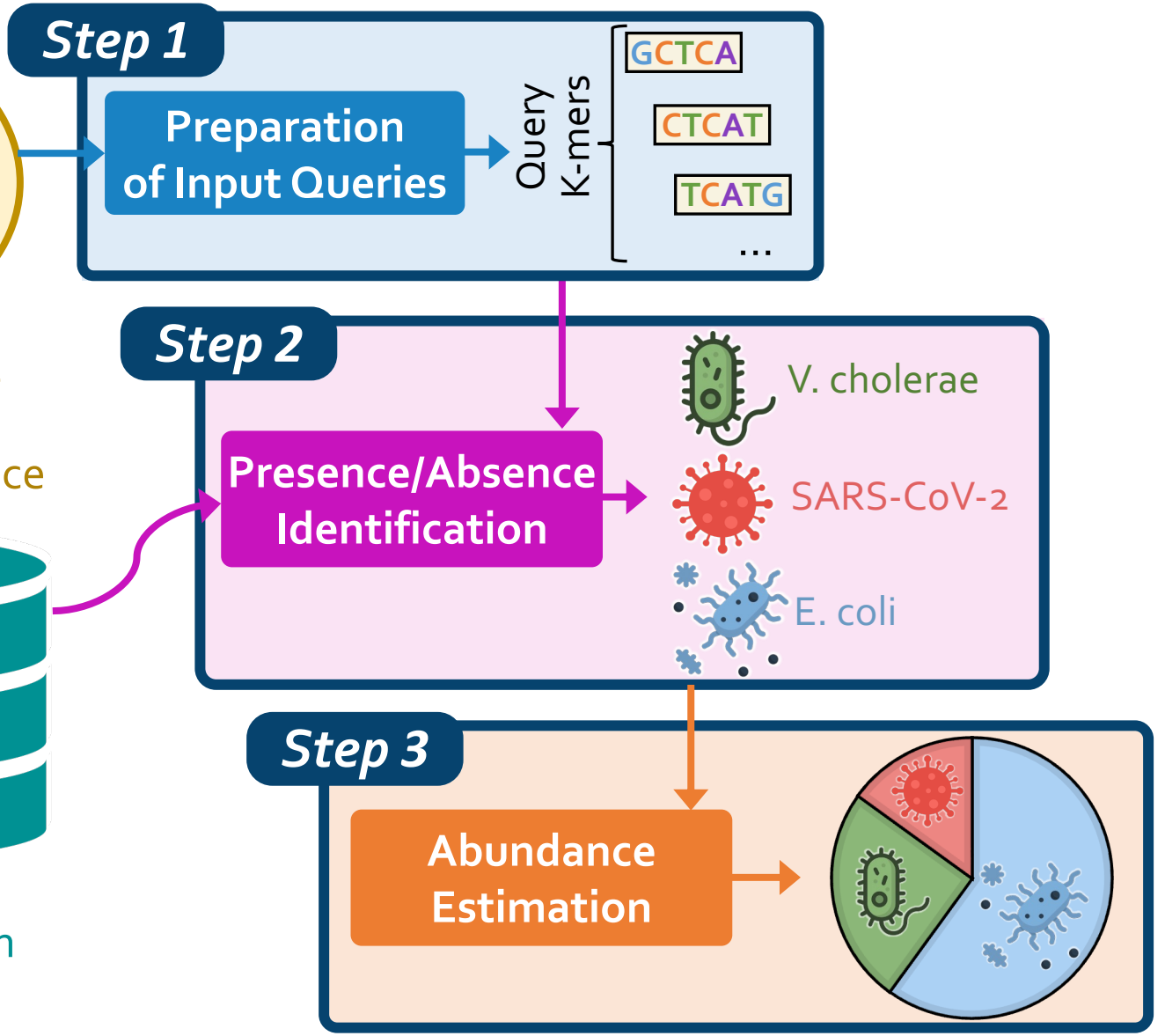
Only 1.7% of the area of three 28-nm ARM Cortex R4 cores in a SATA SSD controller

Step 1 Overview

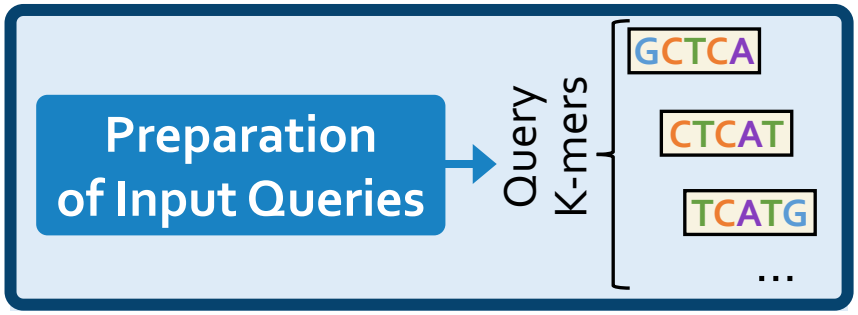


Metagenomic sample with species that are **not known** in advance

A large database containing information on **many species**



Step 1 Overview



*MegIS employs **sorted data structures** to avoid expensive random accesses to the SSD*

- **Extract k-mers** from the sample
- **Sort** the k-mers (database is sorted offline)

MegIS executes Step 1 in the host system

- Benefits from **larger DRAM** and **more powerful computation**
- Incurs **fewer writes** to NAND flash chips (than processing this step in the SSD)
- Enables **overlapping** Step 1 with Step 2

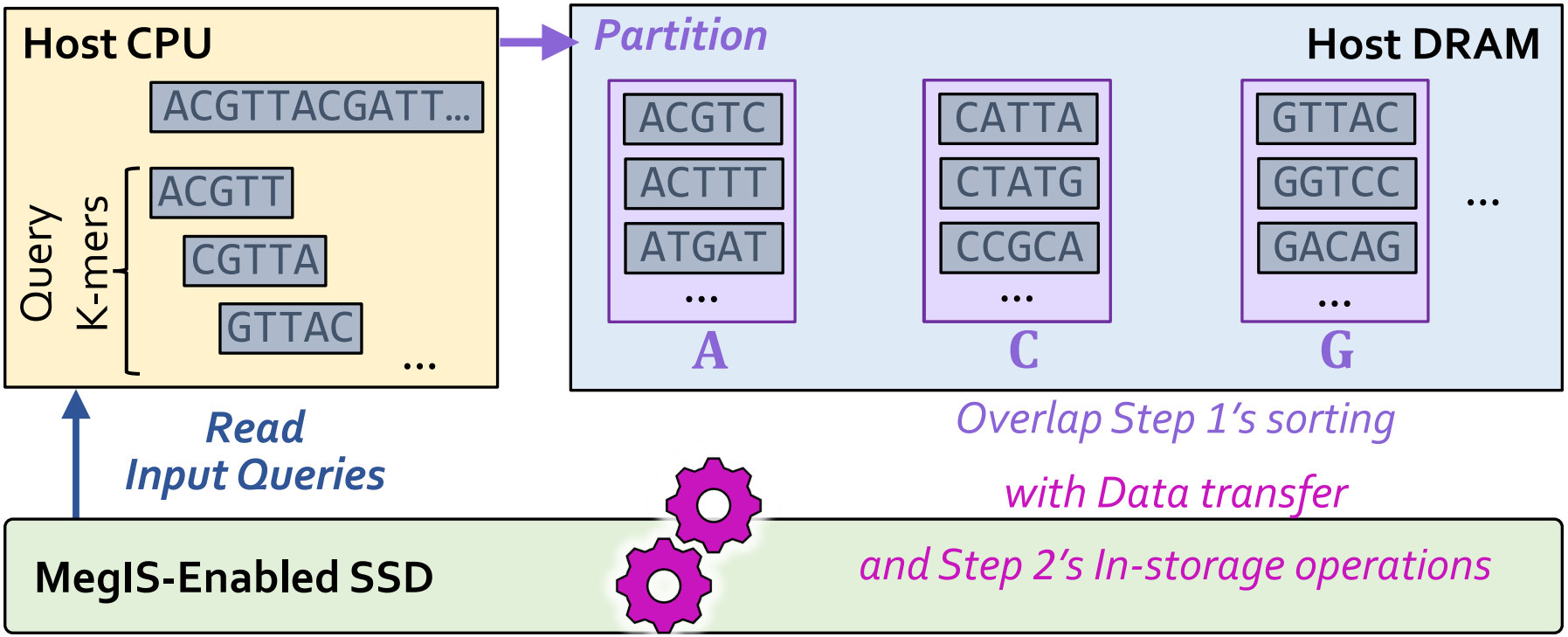
To execute Step 1 efficiently in the host system, MegIS needs to:

- Avoid significant overhead due to **data transfer time** between the steps
- Minimize **performance** and **lifetime** overheads *even* when host DRAM cannot hold all query k-mers

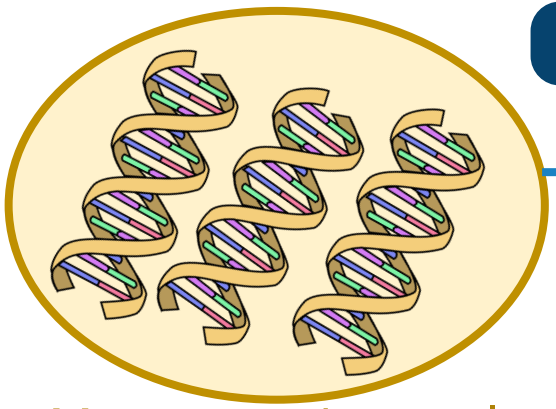
Step 1 Design

Divide k-mers into **independent partitions** by their alphabetical range

✓ **Can overlap operations on different partitions**



Step 2 Overview



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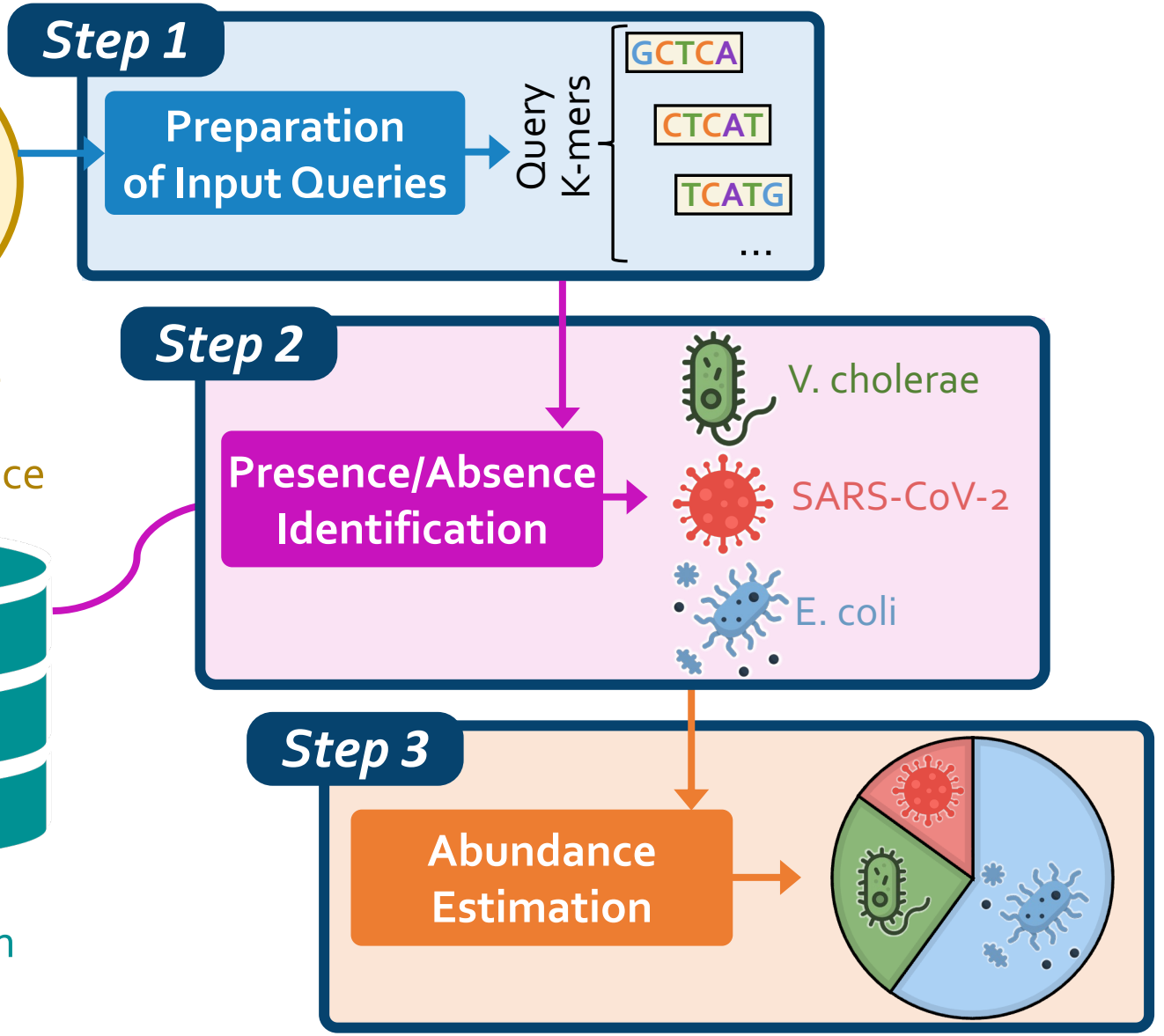
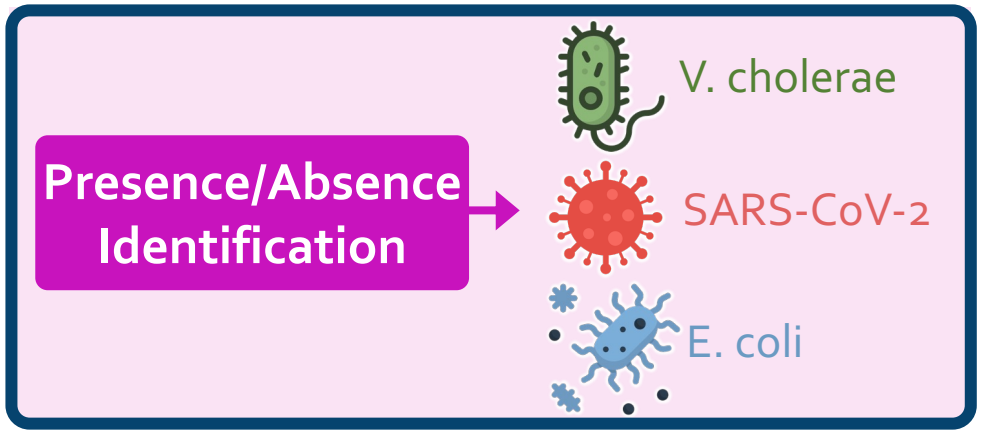


Step 2 Overview



- **Identify the common k-mers** between the query k-mers and the database k-mers
- **Retrieve the species IDs** of the common k-mers

MegIS executes Step 2 in the SSD

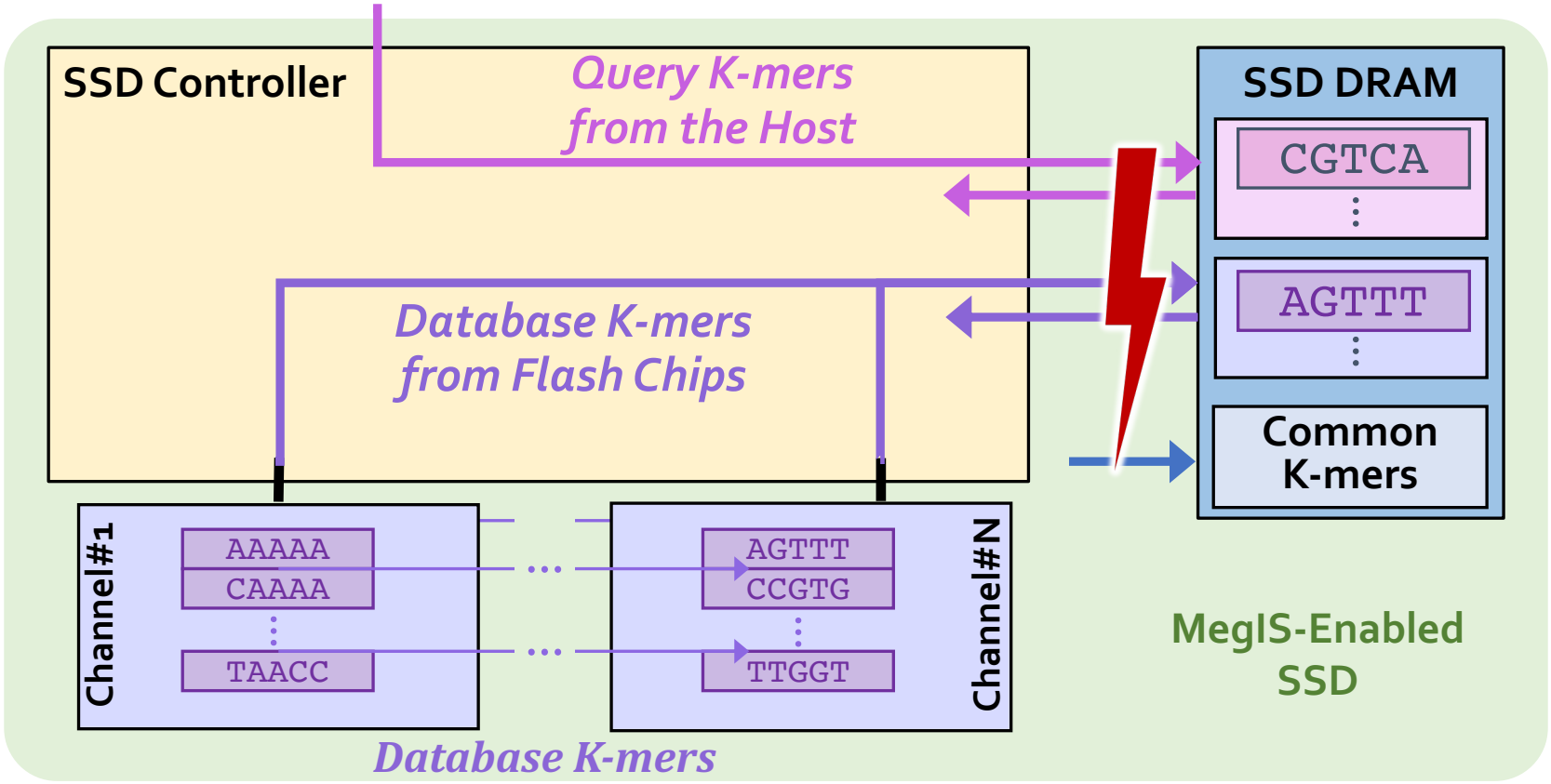
- Accesses **large data** with **low reuse**
- Involves **lightweight computation**

To execute Step 2 efficiently in the SSD, MegIS needs to:

- Leverage **internal bandwidth** efficiently
- Not require **expensive hardware inside the SSD** (e.g., large DRAM bandwidth/capacity and costly logic units)

Step 2 Design: Identifying the Common K-mers

- **Challenge:** Limited internal DRAM bandwidth

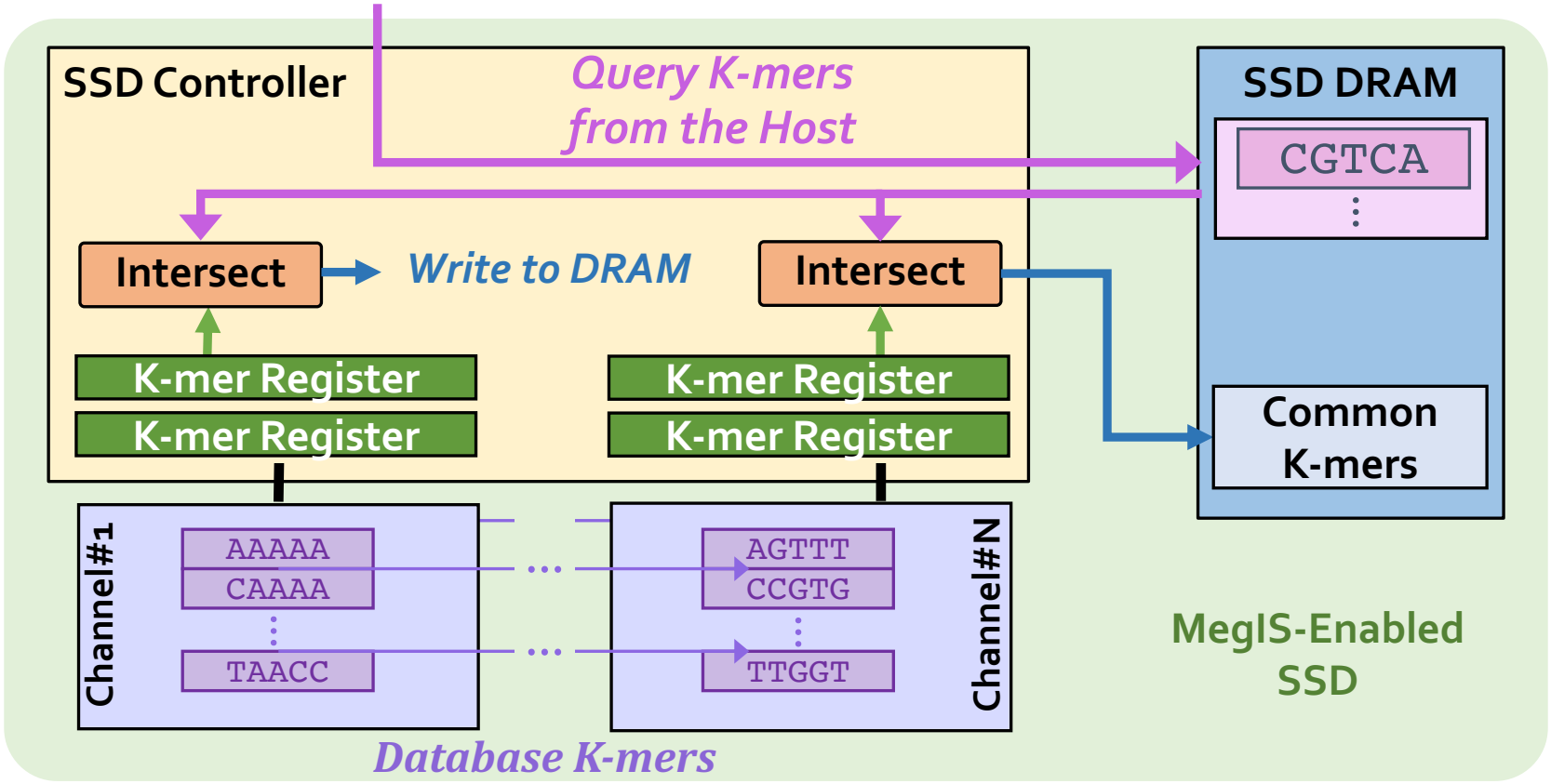


Step 2 Design: Identifying the Common K-mers

- **Challenge:** Limited internal DRAM bandwidth

✓ *Compute directly on the flash data streams* [Zou+, MICRO'22]

✓ *Reduce buffer size based on application features*

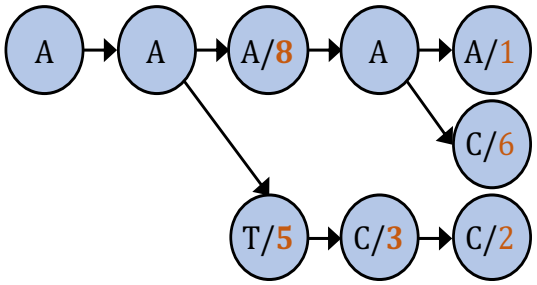


Step 2 Design: Retrieving the Species ID

- MegIS retrieves the species IDs of the **common k-mers** by looking up a **sketch database**

K-mer	
AAAAA	
AAAAC	
AATCC	
...	

Space-Inefficient



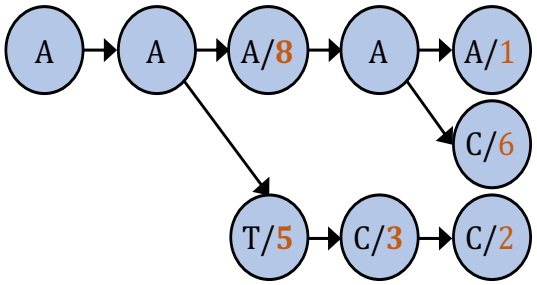
Space-Efficient

✗ *Slow inside the SSD due to long NAND flash latency*

Step 2 Design: Retrieving the Species ID

- MegIS retrieves the species IDs of the **common k-mers** by looking up a **sketch database**

K-mer	ID
AAAAA	1,5
AAAAC	6
AATCC	2, 9
...	...



K-mer Sketch Streaming is much more suitable for in-storage processing due to its streaming accesses

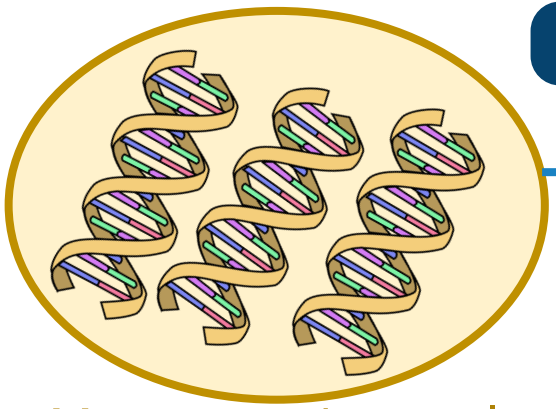
Step 2 Design: Retrieving the Species ID

- MegIS retrieves the species IDs of the **common k-mers** by looking up a **sketch database**

Design details are in the paper

K-mer Sketch Streaming is much more suitable for in-storage processing due to its streaming accesses

Step 3



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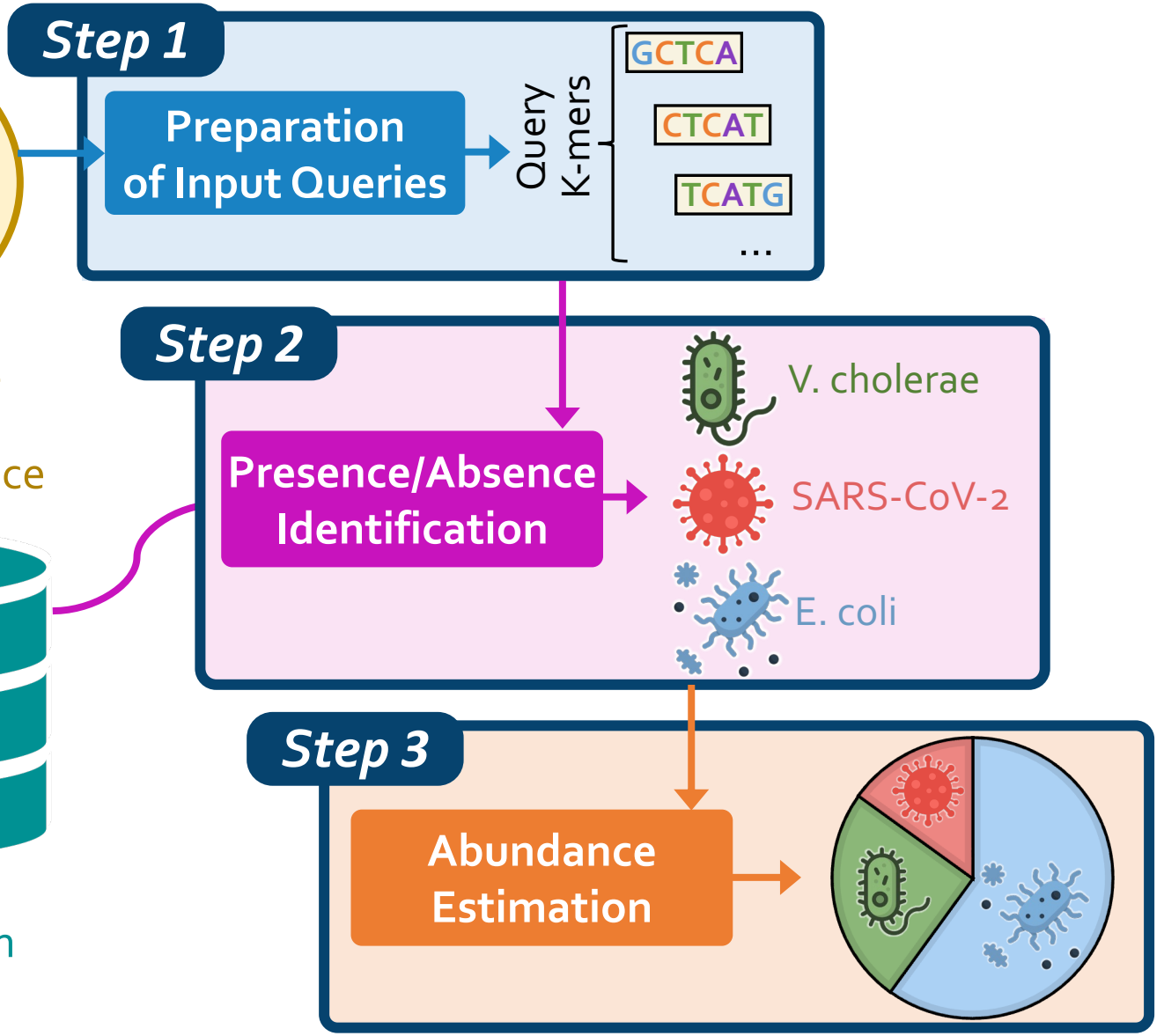
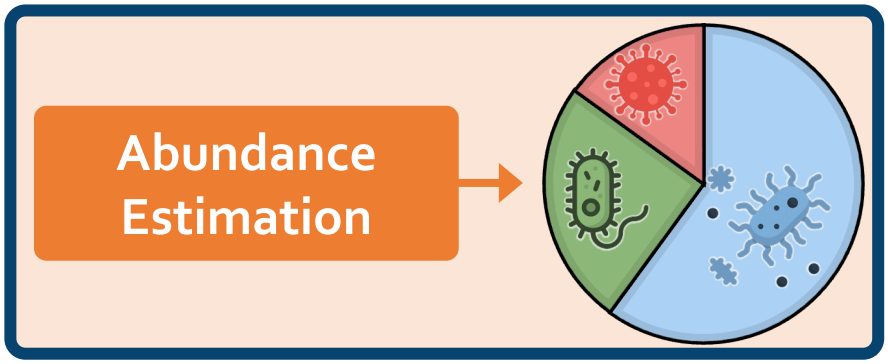


Step 3



MegIS performs additional analysis on species identified in the sample to estimate their abundance

MegIS can flexibly integrate with different approaches

1. **Lightweight statistical approaches**: Directly uses the output of Step 2
2. **More accurate and costly read mapping:** MegIS facilitates integration by preparing mapping indexes in the SSD

K-mer	Loc.
ATT	14
CCA	9
GCT	5
...	...

Reference Index Organism A

K-mer	Loc.
AAG	2
CCA	21
TGC	4
...	...

Reference Index Organism B

Merge

K-mer	Loc.
AAG	1002
ATT	14
CCA	9, 1021
GCT	5
TGC	1004
...	...

Unified Reference Index

Step 3 and MegIS FTL are in the paper