Accelerating Genome Analysis
via Algorithm-Architecture Co-Design

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DAC 2023 Special Session Talk

SAFARI

ETH zürich

60 DESIGN AUTOMATION CONFERENCE

FROM CHIPS TO SYSTEMS — LEARN TODAY, CREATE TOMORROW

Overview

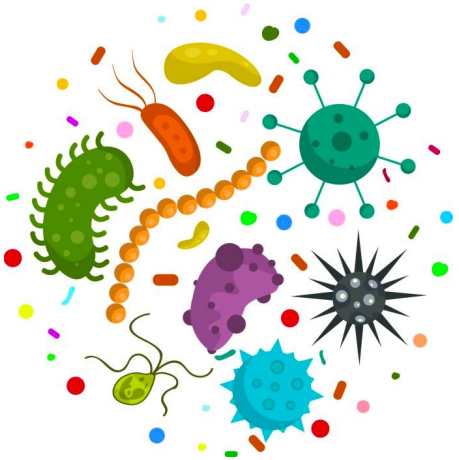
- System design for bioinformatics is a critical problem
  - It has large scientific, medical, societal, personal implications
- This talk is about accelerating a key step in bioinformatics: genome sequence analysis
  - Especially techniques for read mapping
- Many bottlenecks exist in accessing and manipulating huge amounts of genomic data during analysis
- Many recent ideas to accelerate read mapping
  - My personal journey since September 2006

Our Dream (circa 2007)

- An embedded device that can perform comprehensive genome analysis in real time (within a minute)
  - Which of these DNAs does this DNA segment match with?
  - What is the likely genetic disposition of this patient to this drug?
  - What disease/condition might this particular DNA/RNA piece associated with?
  - . . .

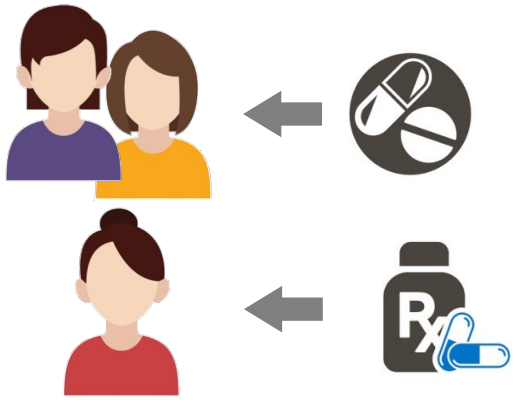
We Need Faster & Scalable Genome Analysis

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



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

Rapid surveillance of **disease outbreaks**



Developing **personalized medicine**

And, many, many other applications …

A Bright Future for Intelligent Genome Analysis

Mohammed Alser, Zülal Bingöl, Damla Senol Cali, Jeremie Kim, Saugata Ghose, Can Alkan, Onur Mutlu
"Accelerating Genome Analysis: A Primer on an Ongoing Journey" IEEE Micro, August 2020.

MinION from ONT

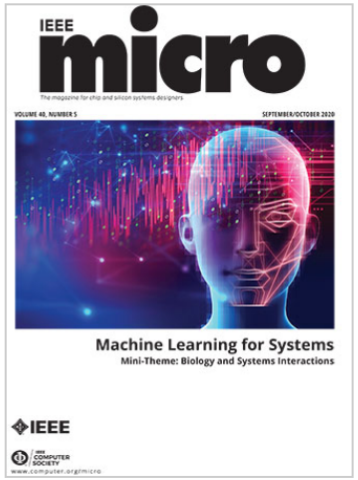
Accelerating Genome Analysis: A Primer on an Ongoing Journey
Sept.-Oct. 2020, pp. 65-75, vol. 40
DOI Bookmark: 10.1109/MM.2020.3013728

FPGA-Based Near-Memory Acceleration of Modern Data-Intensive Applications
July-Aug. 2021, pp. 39-48, vol. 41
DOI Bookmark: 10.1109/MM.2021.3088396

SmidgION from ONT

A Few Overview Readings (I)

Mohammed Alser, Zülal Bingöl, Damla Senol Cali, Jeremie Kim, Saugata Ghose, Can Alkan, Onur Mutlu
"Accelerating Genome Analysis: A Primer on an Ongoing Journey"
IEEE Micro, August 2020.



IEEE Micro

Accelerating Genome Analysis: A Primer on an Ongoing Journey

Sept.-Oct. 2020, pp. 65-75, vol. 40
DOI Bookmark: 10.1109/MM.2020.3013728

Authors

Mohammed Alser, ETH Zürich
Zulal Bingol, Bilkent University
Damla Senol Cali, Carnegie Mellon University
Jeremie Kim, ETH Zurich and Carnegie Mellon University
Saugata Ghose, University of Illinois at Urbana–Champaign and Carnegie Mellon University
Can Alkan, Bilkent University
Onur Mutlu, ETH Zurich, Carnegie Mellon University, and Bilkent University

https://arxiv.org/pdf/2008.00961.pdf

A Few Overview Readings (II)

Gagandeep Singh, Mohammed Alser, Damla Senol Cali, Dionysios Diamantopoulos, Juan Gomez-Luna, Henk Corporaal, Onur Mutlu,
"**FPGA-Based Near-Memory Acceleration of Modern Data-Intensive Applications**"
IEEE Micro, 2021.
[Source Code]

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FPGA-Based Near-Memory Acceleration of Modern Data-Intensive Applications

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Authors

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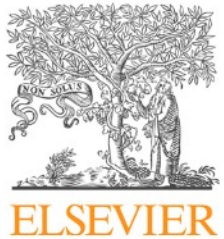
Mohammed Alser, ETH Zürich, Zürich, Switzerland
Damla Senol Cali, Carnegie Mellon University, Pittsburgh, PA, USA
Dionysios Diamantopoulos, Zürich Lab, IBM Research Europe, Rüschlikon, Switzerland
Juan Gomez-Luna, ETH Zürich, Zürich, Switzerland
Henk Corporaal, Eindhoven University of Technology, Eindhoven, The Netherlands
Onur Mutlu, ETH Zürich, Zürich, Switzerland

https://arxiv.org/pdf/2106.06433.pdf

A Few Overview Readings (III)

Mohammed Alser, Joel Lindegger, Can Firtina, Nour Almadhoun, Haiyu Mao, Gagandeep Singh, Juan Gomez-Luna, Onur Mutlu
"**From Molecules to Genomic Variations: Intelligent Algorithms and Architectures for Intelligent Genome Analysis**"
Computational and Structural Biotechnology Journal, 2022
[Source code]



journal homepage: www.elsevier.com/locate/csbj

Review

From molecules to genomic variations: Accelerating genome analysis via intelligent algorithms and architectures

Mohammed Alser *, Joel Lindegger, Can Firtina, Nour Almadhoun, Haiyu Mao, Gagandeep Singh, Juan Gomez-Luna, Onur Mutlu *

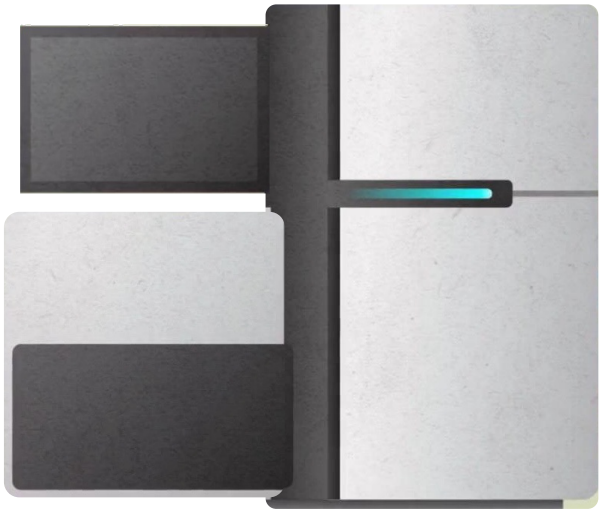
ETH Zurich, Gloriastrasse 35, 8092 Zürich, Switzerland

https://arxiv.org/pdf/2205.07957.pdf

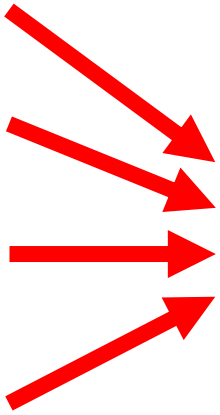
Accelerating Genome Analysis [DAC 2023]

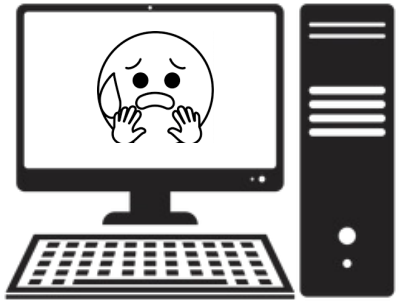
- Onur Mutlu and Can Firtina,
  "Accelerating Genome Analysis via Algorithm-Architecture Co-Design"
  *Invited Special Session Paper in Proceedings of the 60th Design Automation Conference (**DAC**)*, San Francisco, CA, USA, July 2023.
  [arXiv version]

Problems with (Genome) Analysis Today



Special-Purpose Machine
for **Data Generation**





General-Purpose Machine
for **Data Analysis**

FAST

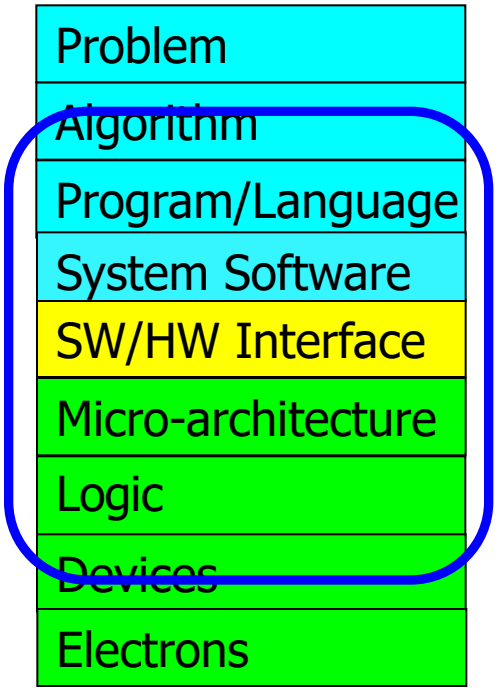
SLOW

Slow and inefficient processing capability
Large amounts of data movement

This picture is similar for many "data generators & analyzers" today

Algorithm-Arch-Device Co-Design is Critical

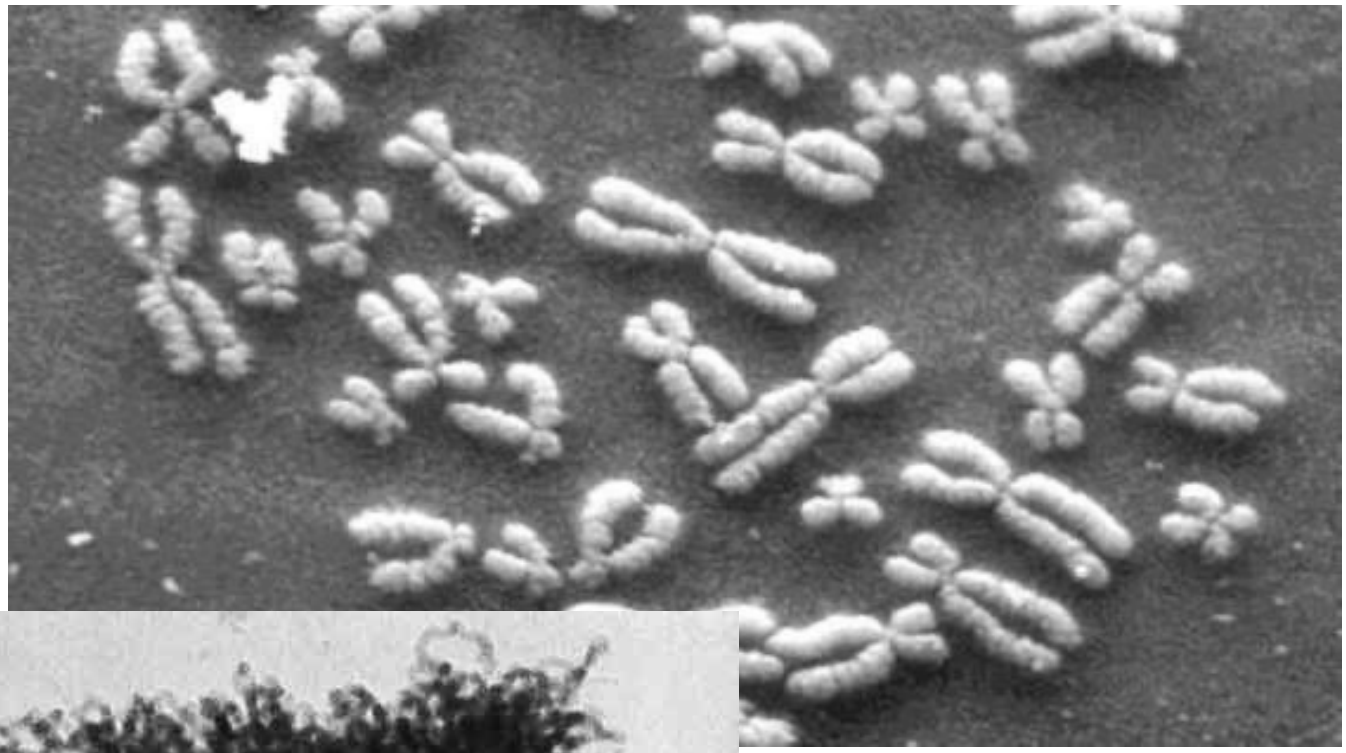
Computer Architecture (expanded view)

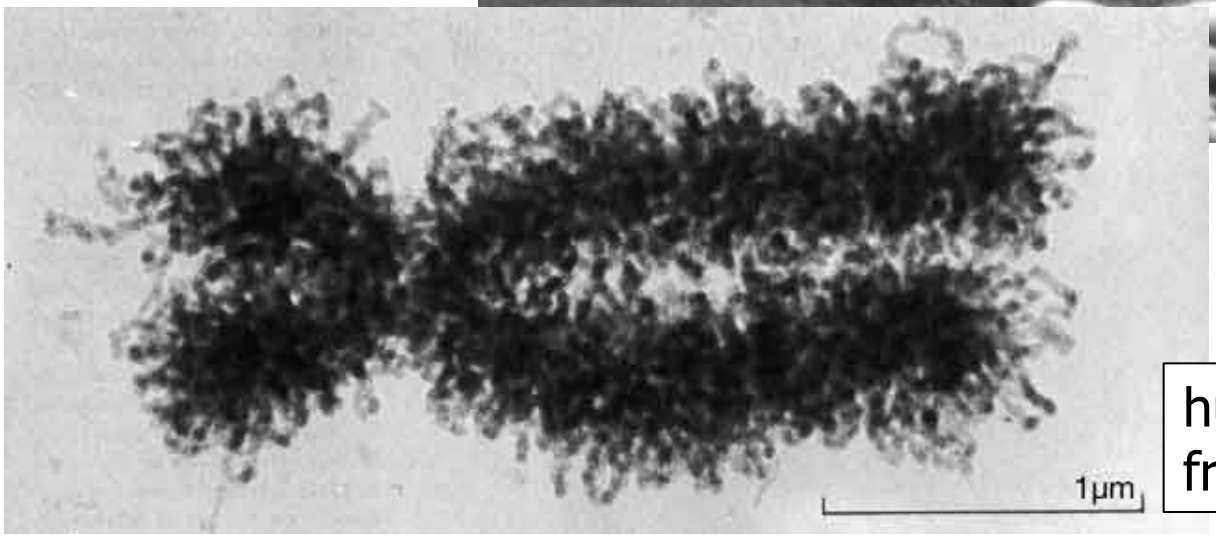


Agenda

- The Problem: DNA Read Mapping
  - State-of-the-art Read Mapper Design
- Algorithmic Acceleration
  - Exploiting Structure of the Genome
  - Exploiting SIMD Instructions
- Hardware Acceleration
  - Specialized Architectures
  - Processing in Memory & Storage
- Future Opportunities: New Technologies & Applications

DNA Under Electron Microscope





human chromosome #12
from HeLa's cell

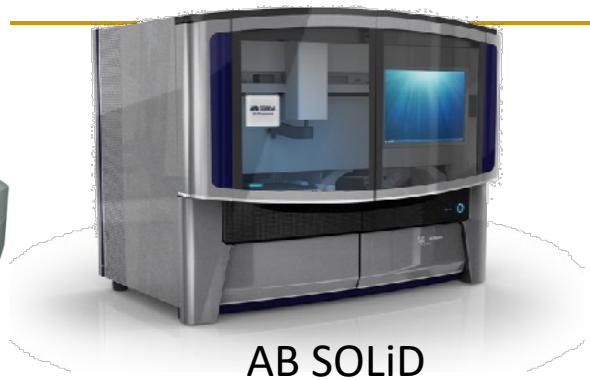
CCTCCTCAGTGCCACCCAGCCCACTGGCAGCTCCCAAACA
GGCTCTTATTAAAACACCCTGTTCCCTGCCCCTTGGAGTG
AGGTGTCAAGGACCTAAACTAAAAAAAAAAAAAGAAAA
AGAAAAGAAAAAGAATTTAAAATTTAAGTAATTCTTTGAA
AAAAACTAATTTCTAAGCTTCTTCATGTCAAGGACCTAATG
TGCTAAACAGCACTTTT**TTGACCATTAT**TTTGGATCTGAAA
GAAATCAAGAATAAATGAAGGACTTGATACATTGGAAGA
GGAGAGTCAAGGACCTACAGAAAAAAAAAAAAAAGAAA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

DNA Sequencing

- Goal:
  - Find the complete sequence of A, C, G, T's in an organism's DNA
- Challenge:
  - There is no machine that takes long DNA as an input, and gives the complete sequence as output
  - All sequencing machines chop DNA into pieces and identify relatively small pieces (but not how they fit together)

Genome Sequencers

Roche/454



AB SOLiD

Illumina MiSeq

Complete Genomics

Oxford Nanopore MinION

Illumina HiSeq2000

Pacific Biosciences RS

Oxford Nanopore GridION

Illumina NovaSeq 6000

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.

Newer Genome Sequencing Technologies

Nanopore sequencing technology and tools for genome assembly: computational analysis of the current state, bottlenecks and future directions

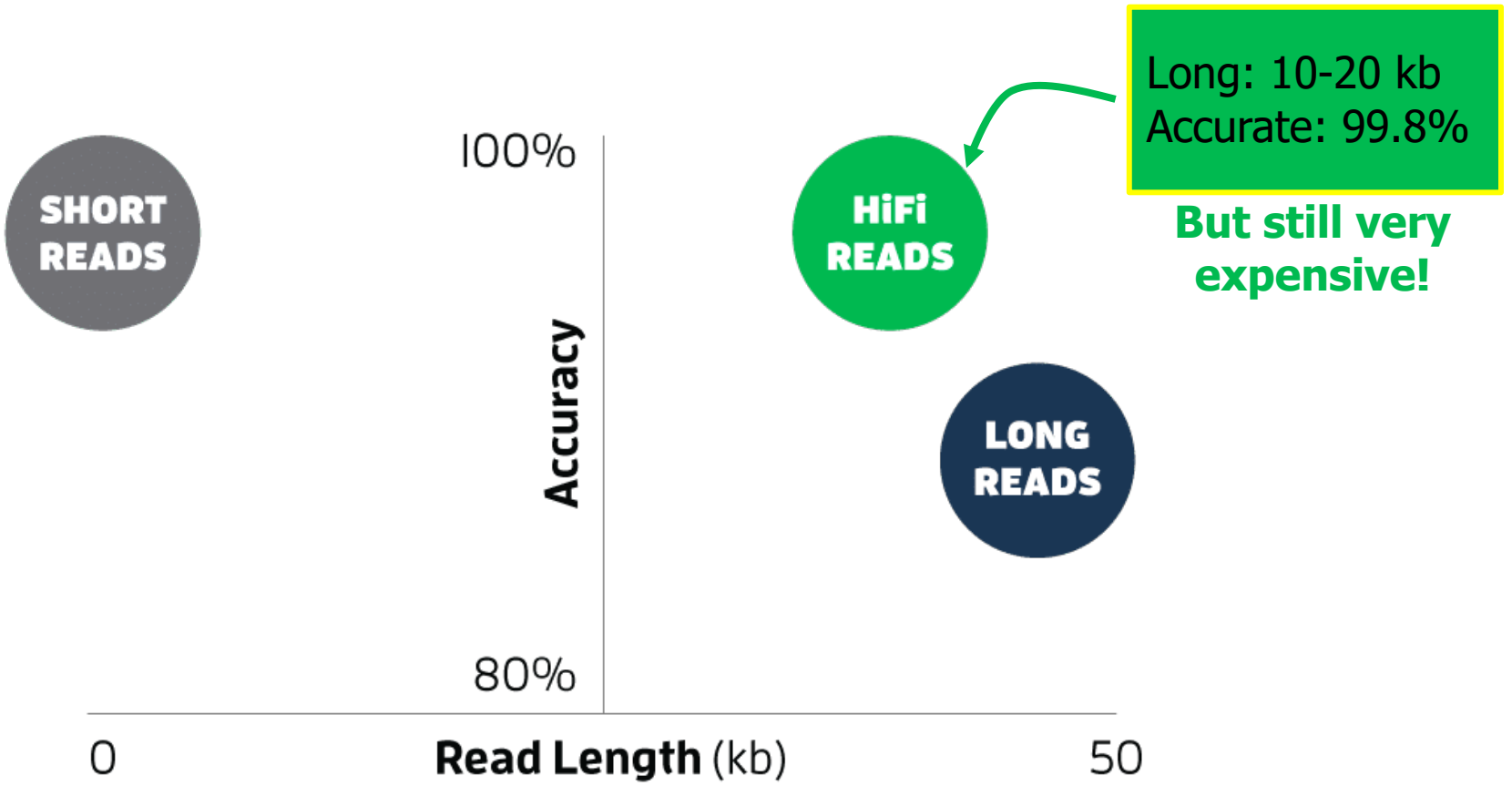
Damla Senol Cali ✉, Jeremie S Kim, Saugata Ghose, Can Alkan, Onur Mutlu

Briefings in Bioinformatics, bby017, https://doi.org/10.1093/bib/bby017
Published: 02 April 2018 **Article history** ▾

Oxford Nanopore MinION

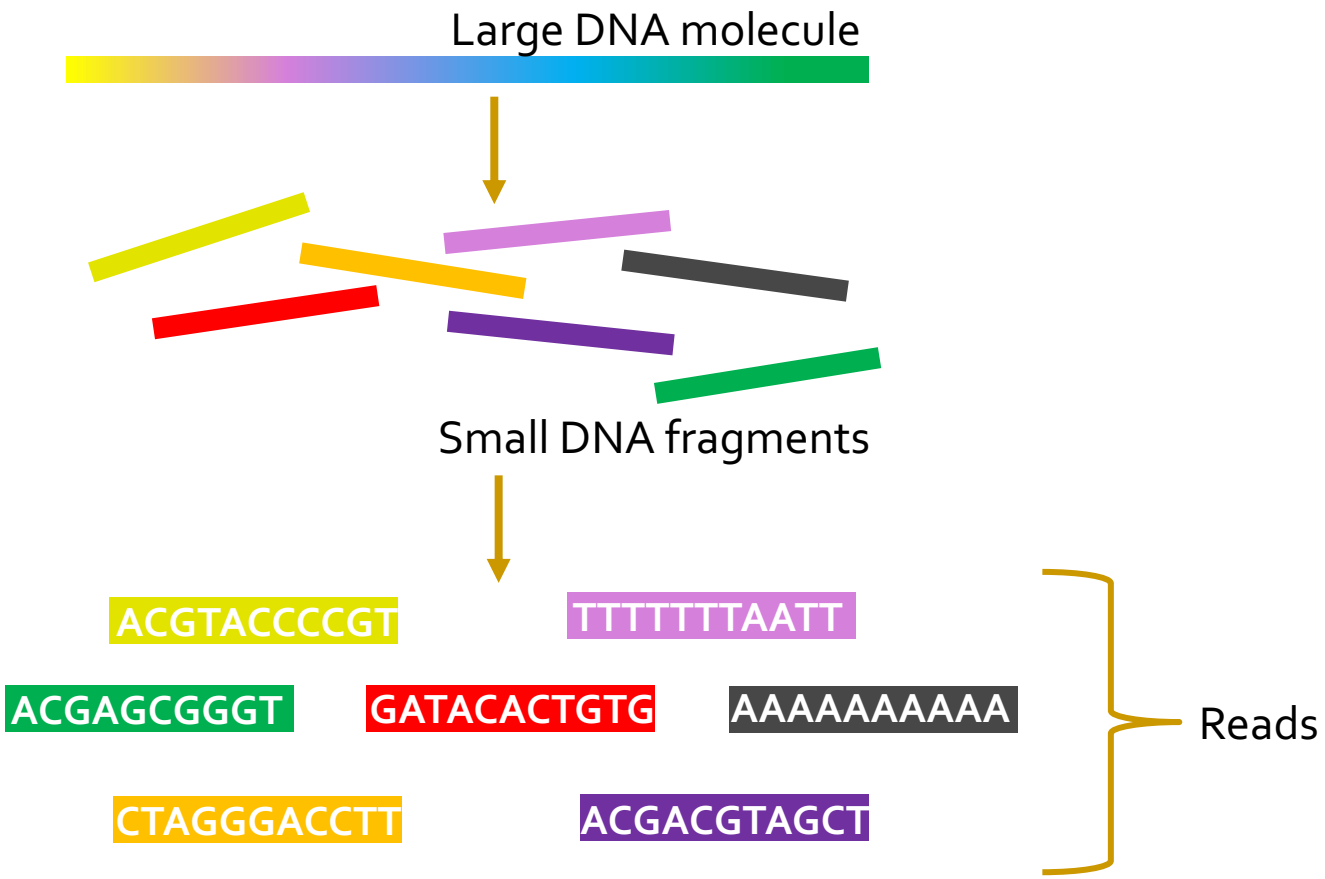
Senol Cali+, "**Nanopore Sequencing Technology and Tools for Genome Assembly: Computational Analysis of the Current State, Bottlenecks and Future Directions**," Briefings in Bioinformatics, 2018.
[Open arxiv.org version] [Slides (pptx) (pdf)] [Talk Video at AACBB 2019]

Types of Genomic Reads



Wenger+, "Accurate circular consensus long-read sequencing improves variant detection and assembly of a human genome", *Nature Biotechnology*, 2019

Genome Sequencing

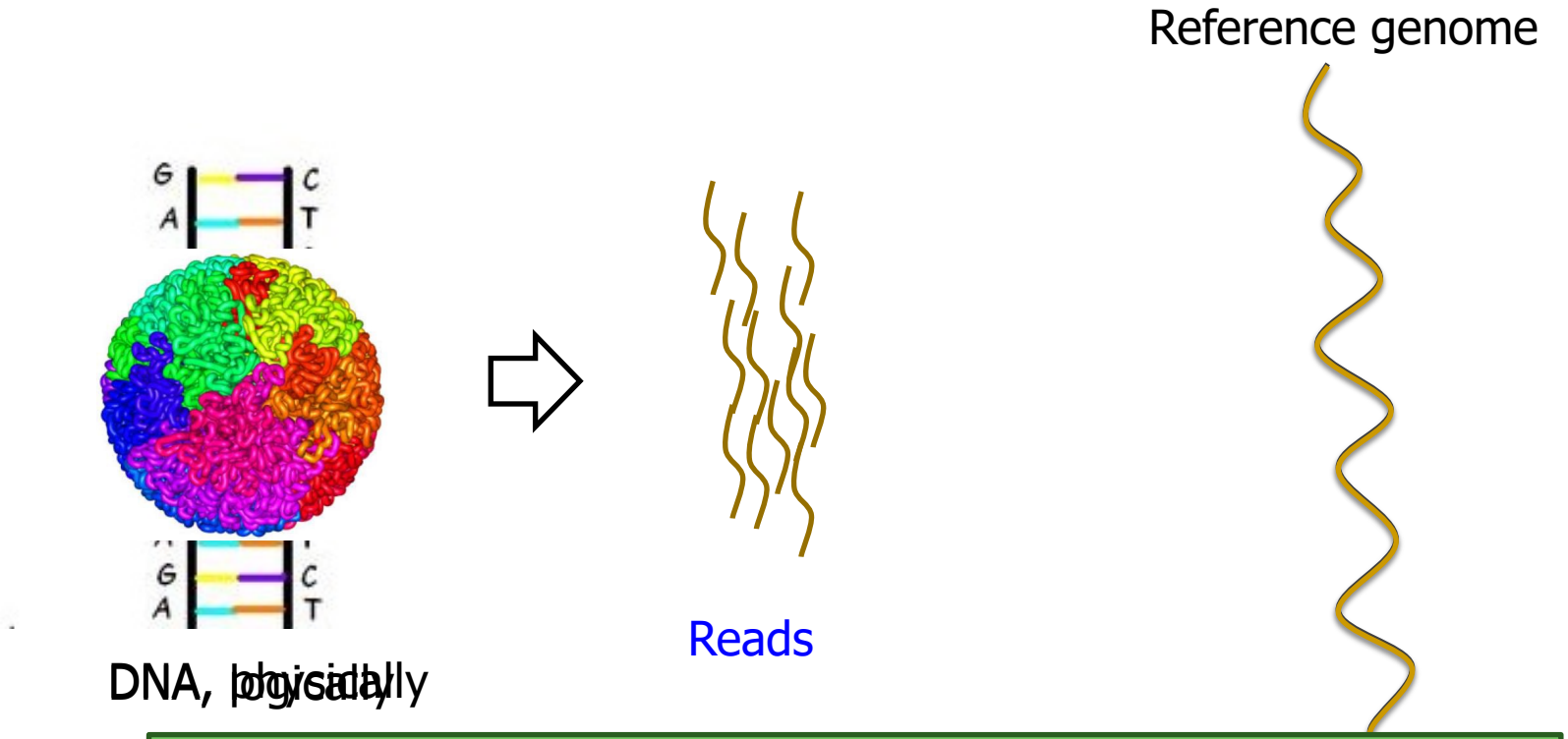


One Problem

Need to construct
the entire genome
from many sequenced reads

Read Mapping

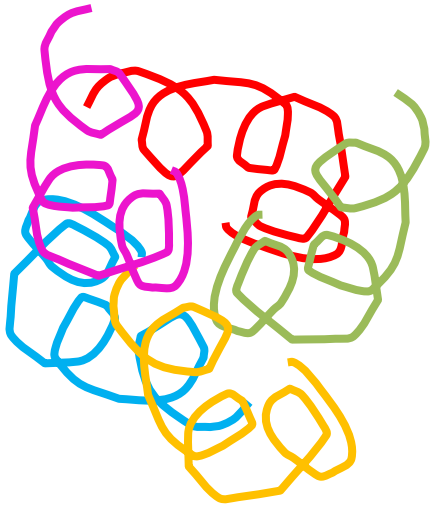
- Map many short DNA fragments (reads) to a known reference genome with some differences allowed



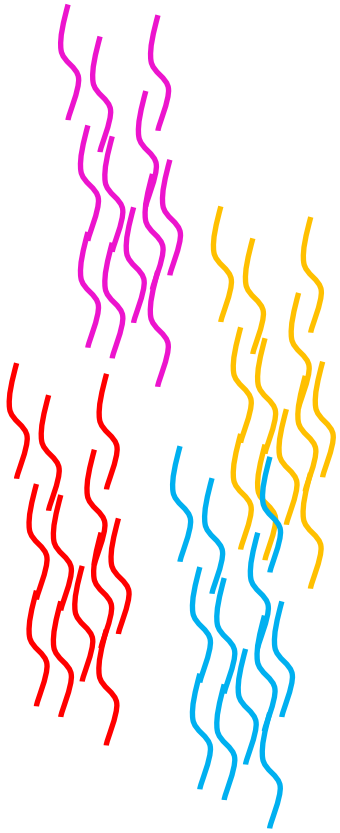
Mapping short reads to reference genome is challenging (billions of 50-300 base pair reads)

Read Mapping for Metagenomic Analysis

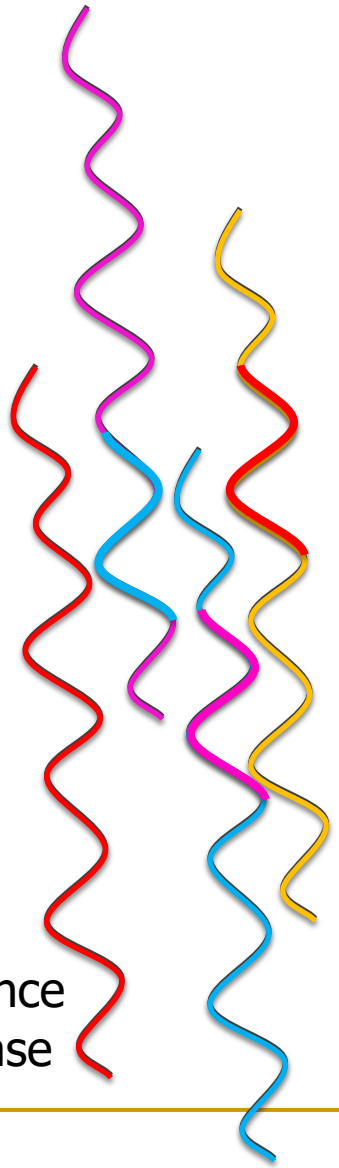
Reads from different unknown donors at sequencing time are mapped to many known reference genomes



Genetic material recovered directly from environmental samples



Reads in "text format"



Reference Database

Matching Each Read to Reference Genome

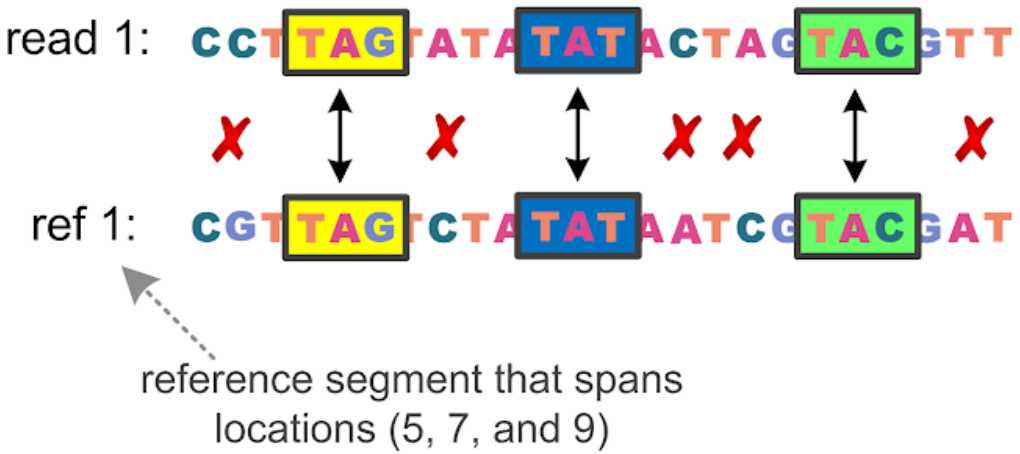
Reference Genome .FASTA file:

```
>NG_008679.1:5001-38170 Homo sapiens paired box 6 (PAX6)
ACCCT[redacted]TCATTGACATTTAAACTCTGGGGCAGGT[redacted]GAACGCGGCTGTCAGATCT
GCCACTTCCCCTGCCGAGCGGCGGTGAGAAGTGTGGGAACCGGCGCTGCCAGGCTCACCTGCCTCCCCGC
CCTCCGCTCCCAGGTAACCGCC[redacted]CCCCGGCCCGGCTCGGGGCCCGCGGGGCCTCTCCGCTG
CCAGCGACTGCTGTCCCCAAATCAAAGCCCGCCCCAAGTGGCCCCGGGGCTTGATTTTTGCTTTTAAAAG
GAGGCATACAAAGATGGAAGCGAGTTACTGAGGGAGGGATAGGAAGGGGGGTGGAGGAGGGACTTGTCTT
TG[redacted]CCGAGTGT[redacted]CAAAAGTAGCA[redacted]CTCCTAA[redacted]TCCAGTCCG[redacted]GCCCT
GAGCTGGGAGTAGGGGGCGGGAGTCTGCTGCTGCTGTCTGCTAAAGCCACTCGCGACCGCGAAAAATGCA
GGAGGTGGGGACGCACTTTGCATCCAGACCTCCTCTGCATCGCAGTTC[redacted]CGCTTGGGAAAG
TCCGTACCCGCGCCT[redacted]AAAGACACCCTGCCGCGGGTCGGGCGAGGTGCAGCAGAAGTTTCCC
GCGGTTGCAAAGTGCAGATGGCTGGACCGCAACAAAGTCTAGAGATGGGGTTCGTTTCTCAGAAAGACGC
```

Sequenced Reads .FASTQ file:

```
@HWI-EAS209_0006_FC706VJ:5:58:5894:21141#ATCACG/1
T[redacted]AATAAATCT[redacted]TTAGATN[redacted]NNNNNNNNTAG
+HWI-EAS209_0006_FC706VJ:5:58:5894:21141#ATCACG/1
efcfffffcfeefffcffffffddf`feed]`]_Ba_^__[YBBBBBBBBBBRTT
```

Base-by-Base Comparison



Read Alignment/Verification

- **Edit distance** is defined as the minimum number of edits (i.e., insertions, deletions, or substitutions) needed to make the read exactly match (i.e., align with) the reference segment

NETHERLANDS x SWITZERLAND

N	E	-	T	H	E	R	L	A	N	D	S
S	W	I	T	Z	E	R	L	A	N	D	-

match
deletion
insertion
mismatch

Challenges in Read Mapping

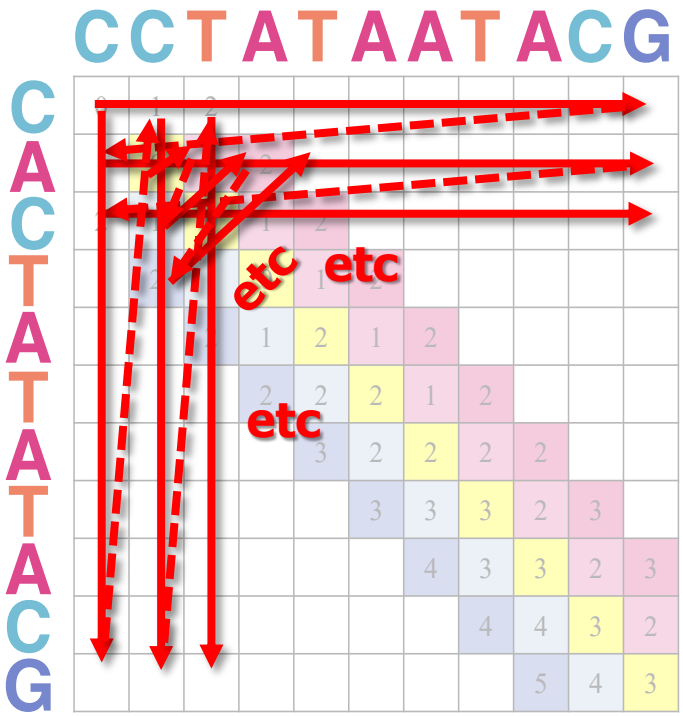
- Need to find many mappings of each read
  - A short read may map to many locations, especially with High-Throughput DNA Sequencing technologies
  - How can we find all mappings efficiently?

- Need to tolerate small variances/errors in each read
  - Each individual is different: Subject's DNA may slightly differ from the reference (Mismatches, insertions, deletions) + Sequencer errors
  - How can we efficiently map each read with up to *e* errors present?

- Need to map each read very fast (i.e., performance is important)
  - Human DNA is 3.2 billion base pairs long → Millions to billions of reads (State-of-the-art mappers take weeks to map a human's DNA)
  - How can we design a much higher performance read mapper?

Why Is Read Alignment Slow?

- Quadratic-time dynamic-programming algorithm(s)
- Data dependencies limit the computation parallelism
- Entire matrix computed even though strings may be dissimilar



Read Alignment

Computational Cost is Mathematically Proven

Computer Science > Computational Complexity

[Submitted on 1 Dec 2014 (v1), last revised 15 Aug 2017 (this version, v4)]

Edit Distance Cannot Be Computed in Strongly Subquadratic Time (unless SETH is false)

Arturs Backurs, Piotr Indyk

The edit distance (a.k.a. the Levenshtein distance) between two strings is defined as the minimum number of insertions, deletions or substitutions of symbols needed to transform one string into another. The problem of computing the edit distance between two strings is a classical computational task, with a well-known algorithm based on dynamic programming. Unfortunately, all known algorithms for this problem run in nearly quadratic time.

In this paper we provide evidence that the near-quadratic running time bounds known for the problem of computing edit distance might be tight. Specifically, we show that, if the edit distance can be computed in time $O(n^{2-\delta})$ for some constant $\delta > 0$, then the satisfiability of conjunctive normal form formulas with N variables and M clauses can be solved in time $M^{O(1)}2^{(1-\epsilon)N}$ for a constant $\epsilon > 0$. The latter result would violate the Strong Exponential Time Hypothesis, which postulates that such algorithms do not exist.

https://arxiv.org/abs/1412.0348

Read Mapping Techniques in 111 Pages

In-depth analysis of 107 read mappers (1988-2020)

Mohammed Alser, Jeremy Rotman, Dhrithi Deshpande, Kodi Taraszka, Huwenbo Shi, Pelin Icer Baykal, Harry Taegyun Yang, Victor Xue, Sergey Knyazev, Benjamin D. Singer, Brunilda Balliu, David Koslicki, Pavel Skums, Alex Zelikovsky, Can Alkan, Onur Mutlu, Serghei Mangul
"Technology dictates algorithms: Recent developments in read alignment"
Genome Biology, 2021
[Source code]

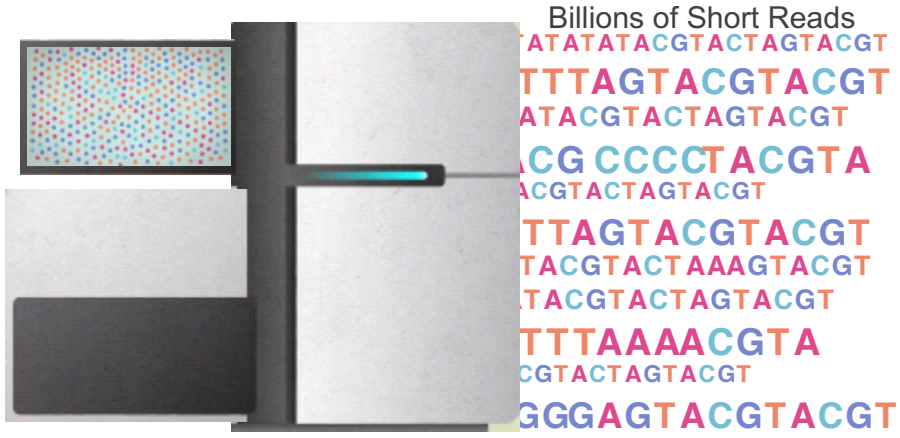
Alser *et al. Genome Biology* (2021) 22:249
https://doi.org/10.1186/s13059-021-02443-7

Genome Biology

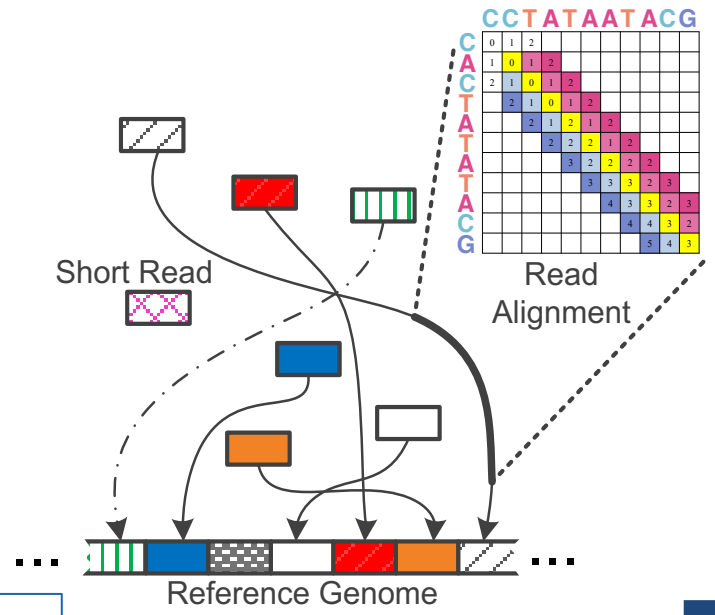
REVIEW Open Access

Technology dictates algorithms: recent developments in read alignment

Mohammed Alser[1,2,3†], Jeremy Rotman[4†], Dhrithi Deshpande[5], Kodi Taraszka[4], Huwenbo Shi[6,7], Pelin Icer Baykal[8], Harry Taegyun Yang[4,9], Victor Xue[4], Sergey Knyazev[8], Benjamin D. Singer[10,11,12], Brunilda Balliu[13], David Koslicki[14,15,16], Pavel Skums[8], Alex Zelikovsky[8,17], Can Alkan[2,18], Onur Mutlu[1,2,3†] and Serghei Mangul[5*†]



1 Sequencing



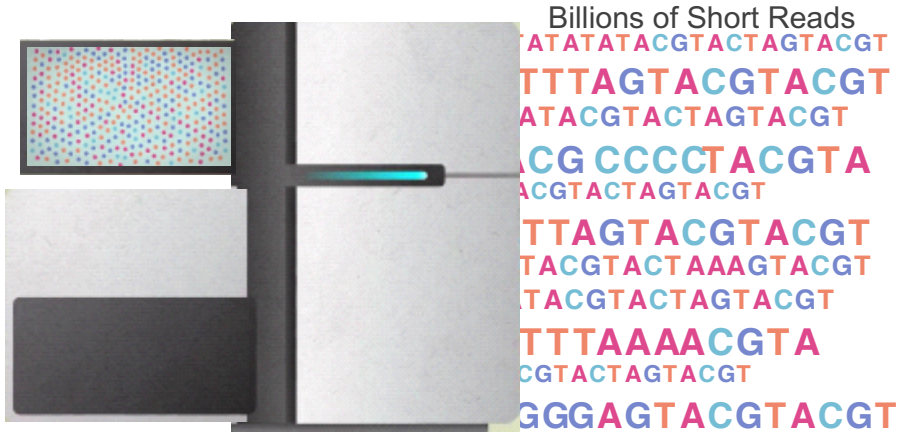
2 Read Mapping

Genome Analysis

```
reference: TTTATCGCTTCCATGACGCAG
read1:       ATCGCATCC
read2:      TATCGCATC
read3:           CATCCATGA
read4:         CGCTTCCAT
read5:               CCATGACGC
read6:             TTCCATGAC
```

3 Variant Calling

Scientific Discovery 4



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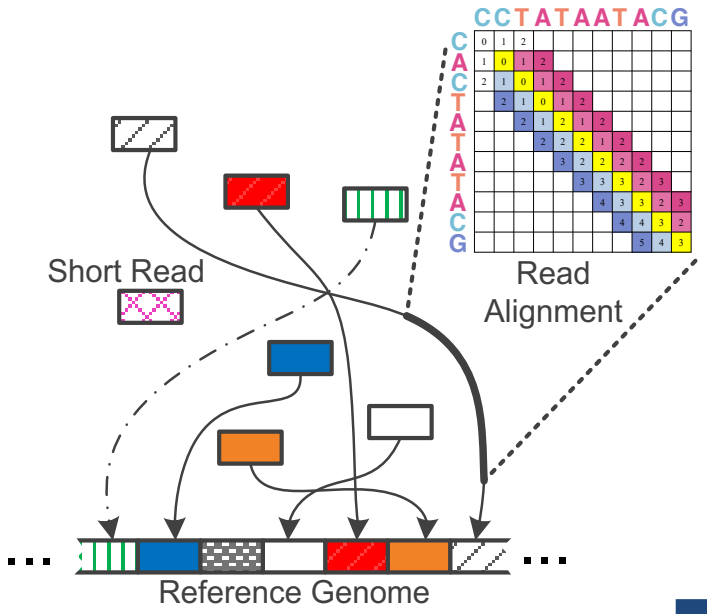
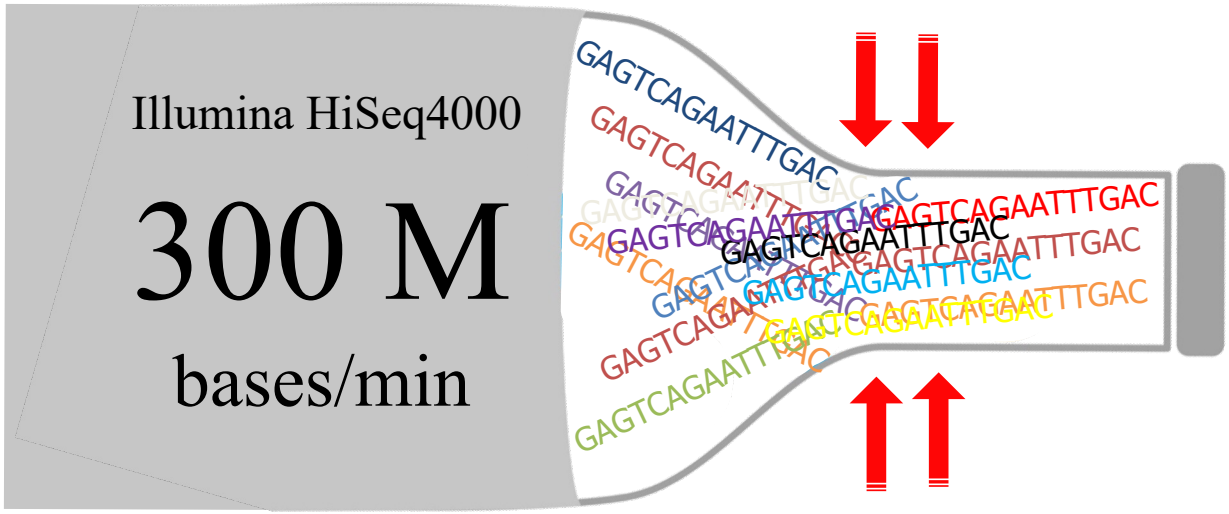


Read Mapping 2

We Are Bottlenecked in Read Mapping



on average

2 M

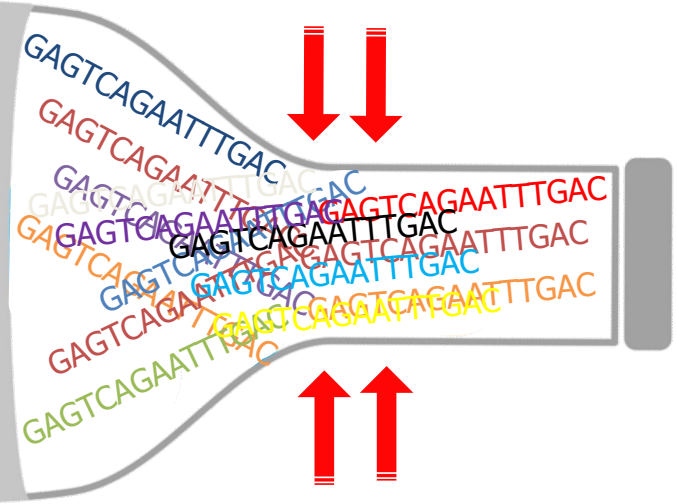
bases/min

(0.6%)

The Read Mapping Bottleneck

300 Million bases/minute

Read Sequencing **



2 Million bases/minute

Read Mapping *

150x slower

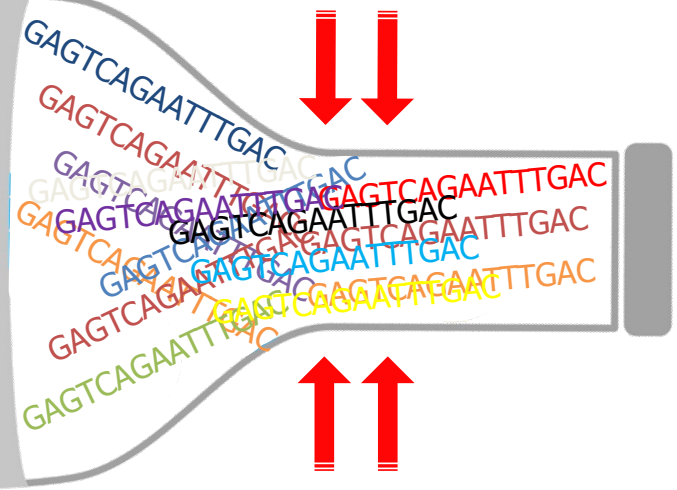
* BWA-MEM
** HiSeqX10, MinION

The Read Mapping Bottleneck

48 Human whole genomes

at 30× coverage

in about 2 days

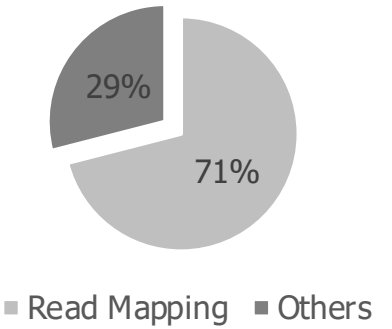


Illumina NovaSeq 6000

1 Human genome

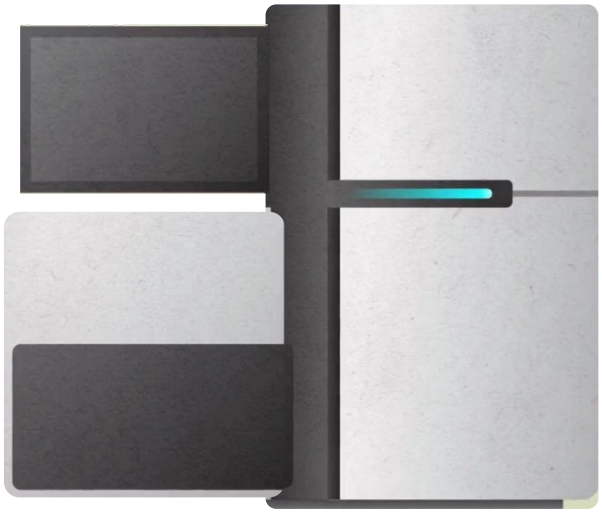
32 CPU hours

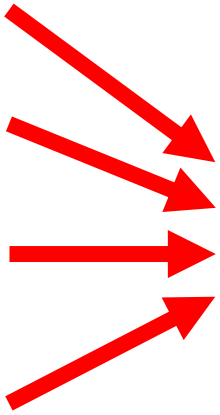
on a 48-core processor

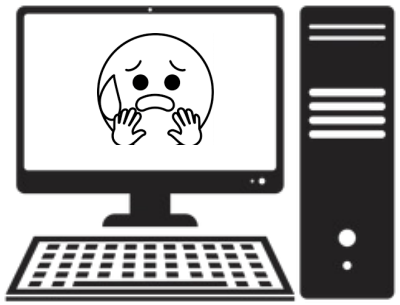


Goyal+, "Ultra-fast next generation human genome sequencing data processing using DRAGENTM bio-IT processor for precision medicine", *Open Journal of Genetics,* 2017.

Problems with (Genome) Analysis Today







Special-Purpose Machine
for **Data Generation**

General-Purpose Machine
for **Data Analysis**

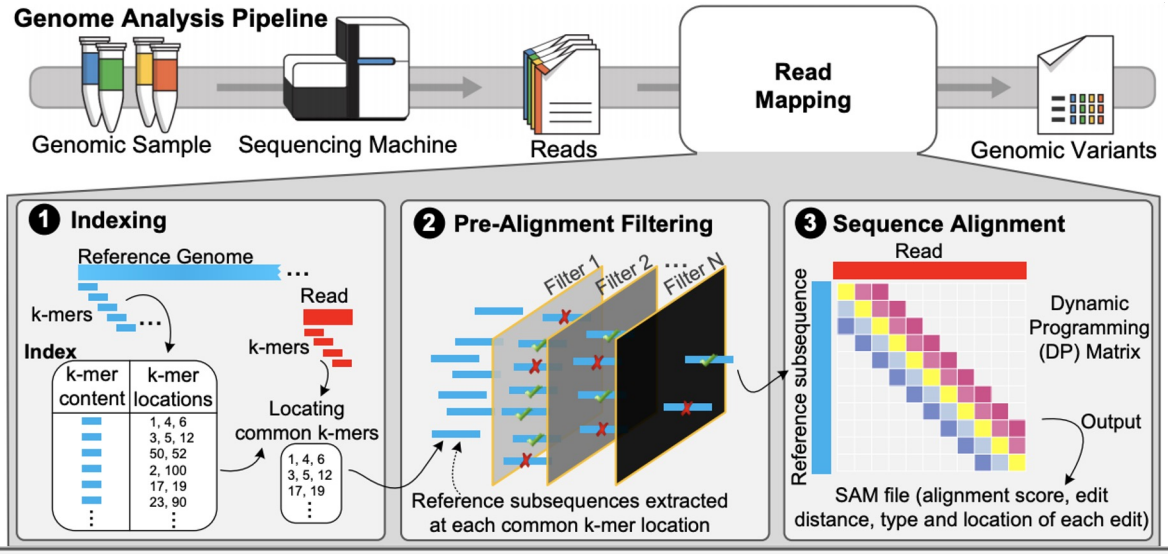
FAST

SLOW

Slow and inefficient processing capability
Large amounts of data movement

This picture is similar for many "data generators & analyzers" today

Accelerating Read Mapping



Accelerating Indexing	Accelerating Pre-Alignment Filtering	Accelerating Alignment
Reducing the number of seeds	q-gram filtering	Accurate alignment accelerators
Reducing data movement during indexing	Pigeonhole principle	Heuristic-based alignment accelerators
	Base counting	
	Sparse DP	

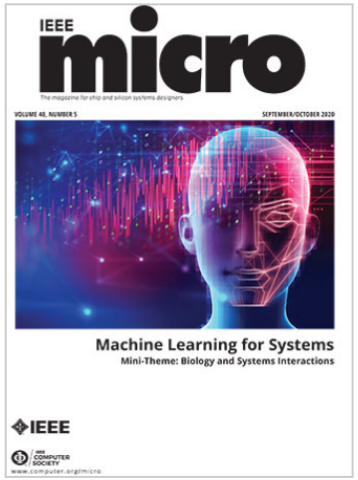
Alser+, "Accelerating Genome Analysis: A Primer on an Ongoing Journey", IEEE Micro, 2020.

Detailed Analysis of Tackling the Bottleneck

Mohammed Alser, Zülal Bingöl, Damla Senol Cali, Jeremie Kim, Saugata Ghose, Can Alkan, Onur Mutlu

"Accelerating Genome Analysis: A Primer on an Ongoing Journey"

IEEE Micro, August 2020.



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IEEE Micro

Accelerating Genome Analysis: A Primer on an Ongoing Journey

Sept.-Oct. 2020, pp. 65-75, vol. 40
DOI Bookmark: 10.1109/MM.2020.3013728

Authors

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Can Alkan, Bilkent University
Onur Mutlu, ETH Zurich, Carnegie Mellon University, and Bilkent University

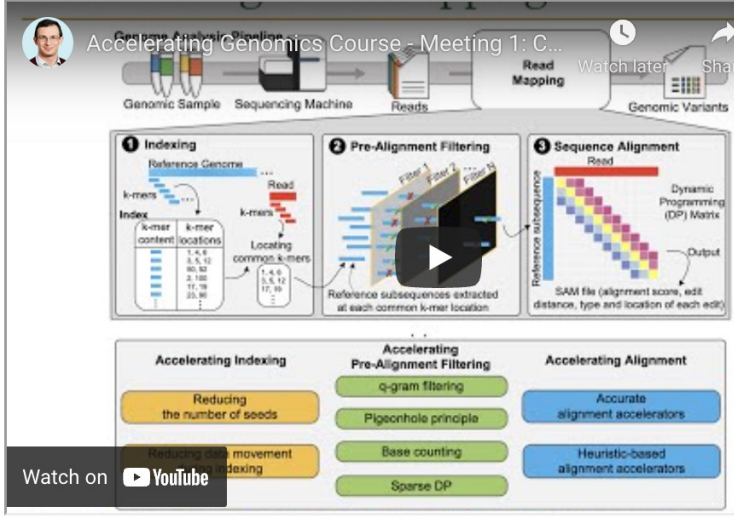
Genomics Course (Fall 2022)

- **Fall 2022 Edition:**
  - https://safari.ethz.ch/projects_and_seminars/fall2022/doku.php?id=bioinformatics
- **Spring 2022 Edition:**
  - https://safari.ethz.ch/projects_and_seminars/spring2022/doku.php?id=bioinformatics

- **Youtube Livestream (Fall 2022):**
  - https://www.youtube.com/watch?v=nA41964-9r8&list=PL5Q2soXY2Zi8tFlQvdxOdizD_EhVAMVQV
- **Youtube Livestream (Spring 2022):**
  - https://www.youtube.com/watch?v=DEL_5A_Y3TI&list=PL5Q2soXY2Zi8NrPDgOR1yRU_Cxxjw-u18

- Project course
  - Taken by Bachelor's/Master's students
  - Genomics lectures
  - Hands-on research exploration
  - Many research readings

https://www.youtube.com/onurmutlulectures



Spring 2022 Meetings/Schedule

Week	Date	Livestream	Meeting	Learning Materials
W1	11.3 Fri.	YouTube Live	M1: P&S Accelerating Genomics Course Introduction & Project Proposals (PDF) (PPT)	Required Materials Recommended Materials
W2	18.3 Fri.	YouTube Live	M2: Introduction to Sequencing (PDF) (PPT)	
W3	25.3 Fri.	YouTube Premiere	M3: Read Mapping (PDF) (PPT)	
W4	01.04 Fri.	YouTube Premiere	M4: GateKeeper (PDF) (PPT)	
W5	08.04 Fri.	YouTube Premiere	M5: MAGNET & Shouji (PDF) (PPT)	
W6	15.4 Fri.	YouTube Premiere	M6: SneakySnake (PDF) (PPT)	
W7	29.4 Fri.	YouTube Premiere	M7: GenStore (PDF) (PPT)	
W8	06.05 Fri.	YouTube Premiere	M8: GRIM-Filter (PDF) (PPT)	
W9	13.05 Fri.	YouTube Premiere	M9: Genome Assembly (PDF) (PPT)	
W10	20.05 Fri.	YouTube Live	M10: Genomic Data Sharing Under Differential Privacy (PDF) (PPT)	
W11	10.06 Fri.	YouTube Premiere	M11: Accelerating Genome Sequence Analysis (PDF) (PPT)	

BIO-Arch Workshop at RECOMB 2023

- April 14, 2023

BIO-Arch: Workshop on Hardware Acceleration of Bioinformatics Workloads

About

BIO-Arch is a new forum for presenting and discussing new ideas in accelerating bioinformatics workloads with the co-design of hardware & software and the use of new computer architectures. Our goal is to discuss new system designs tailored for bioinformatics. BIO-Arch aims to bring together researchers in the bioinformatics, computational biology, and computer architecture communities to strengthen the progress in accelerating bioinformatics analysis (e.g., genome analysis) with efficient system designs that include hardware acceleration and software systems tailored fo new hardware technologies.

Venue

BIO-Arch will be held in The Social Facilities of İstanbul Technical University on **April 14**. Detailed information about how to arrive at the venue location with various transportation options can be found on the RECOMB website.

Our panel discussion will be held in conjunction with the main RECOMB conference. The panel discussion will be held in Marriott Şişli on **April 17 at 17:00**. You can find

https://www.youtube.com/watch?v=2rCsb4-nLmg

https://safari.ethz.ch/recomb23-arch-workshop/

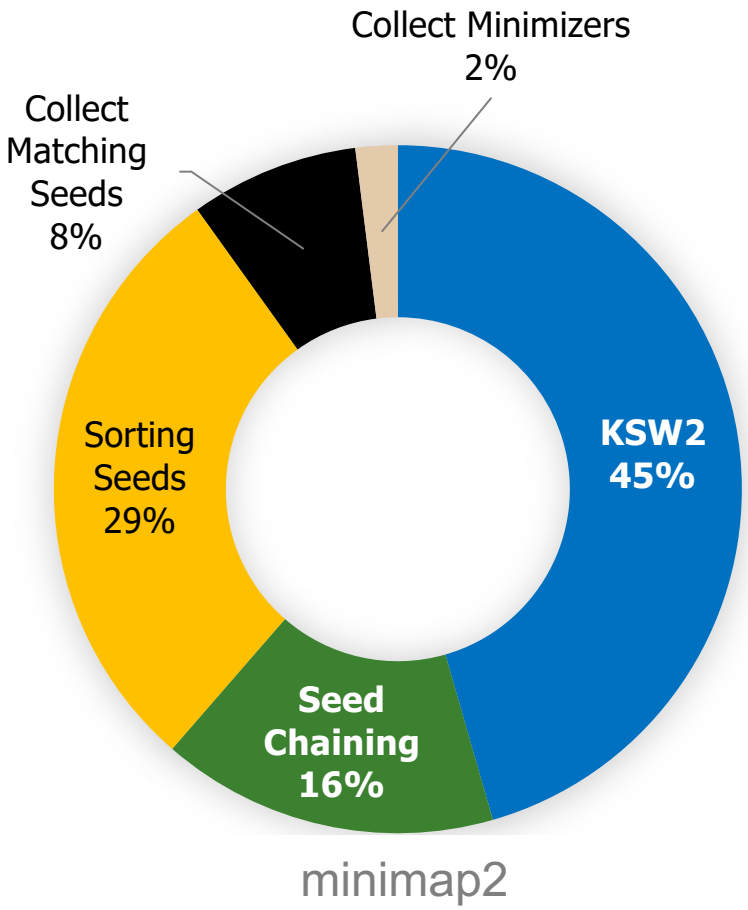
Agenda

- The Problem: DNA Read Mapping
  - State-of-the-art Read Mapper Design
- Algorithmic Acceleration
  - Exploiting Structure of the Genome
  - Exploiting SIMD Instructions
- Hardware Acceleration
  - Specialized Architectures
  - Processing in Memory & Storage
- Future Opportunities: New Technologies & Applications

Read Mapping Execution Time (Modern)

>60%

of the read mapper's execution time is spent in sequence alignment



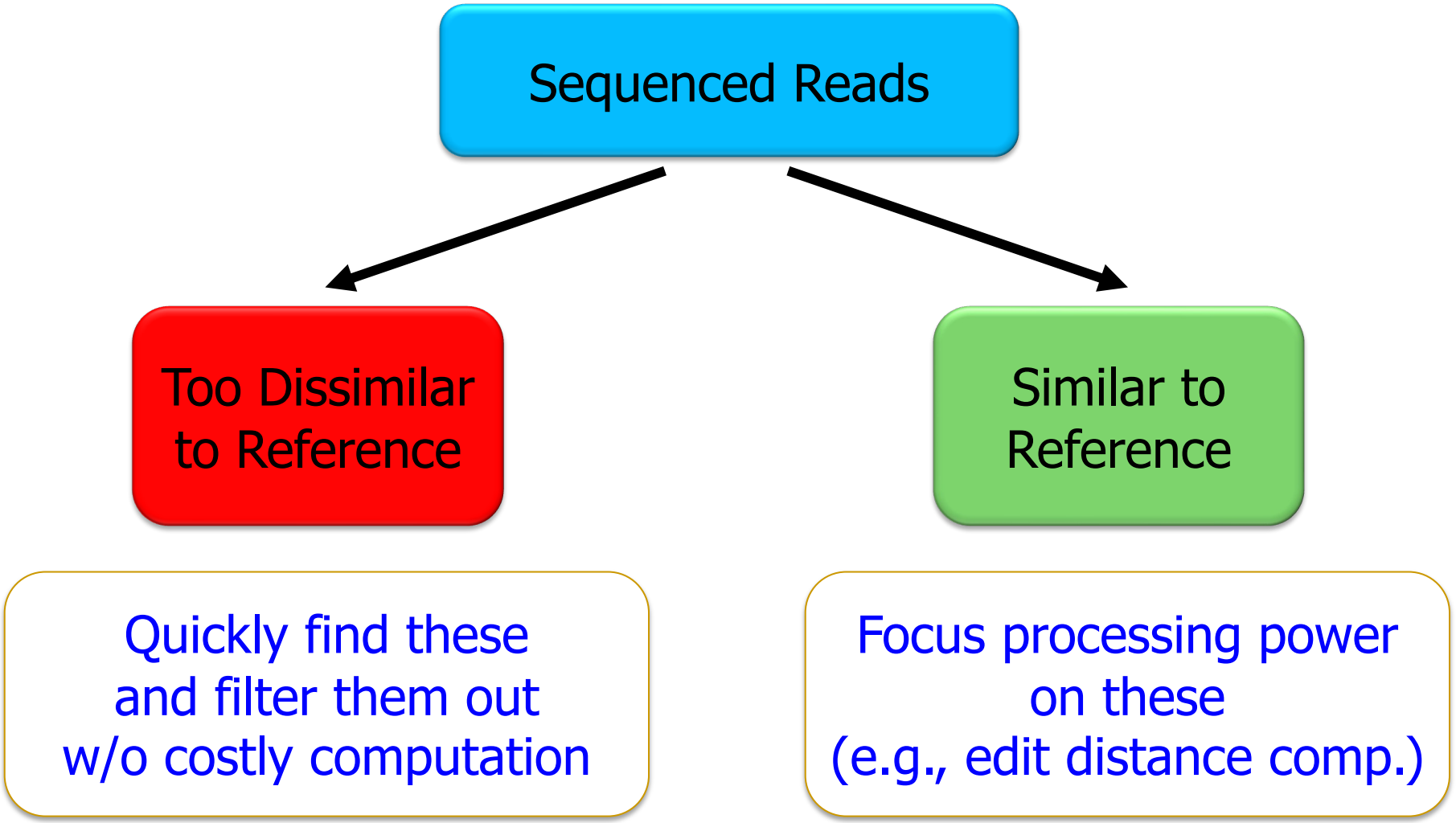
ONT FASTQ size: 103MB (151 reads), Mean length: 356,403 bp, std: 173,168 bp, longest length: 817,917 bp

Overarching Key Idea

Filter fast before you align

Minimize costly
edit distance computations
("approximate string comparisons")

Overarching Key Idea



Our First Filter: Pure Software Approach

- Download the source code and try for yourself
  - Download link to FastHASH

Xin *et al. BMC Genomics* 2013, **14**(Suppl 1):S13
http://www.biomedcentral.com/1471-2164/14/S1/S13

BMC Genomics

PROCEEDINGS Open Access

Accelerating read mapping with FastHASH

Hongyi Xin[1], Donghyuk Lee[1], Farhad Hormozdiari[2], Samihan Yedkar[1], Onur Mutlu[1*], Can Alkan[3*]

From The Eleventh Asia Pacific Bioinformatics Conference (APBC 2013)
Vancouver, Canada. 21-24 January 2013

Xin+, **"Accelerating Read Mapping with FastHASH"**, BMC Genomics 2013.

Shifted Hamming Distance: SIMD Acceleration

https://github.com/CMU-SAFARI/Shifted-Hamming-Distance

Bioinformatics, 31(10), 2015, 1553–1560
doi: 10.1093/bioinformatics/btu856
Advance Access Publication Date: 10 January 2015
Original Paper

Sequence analysis

Shifted Hamming distance: a fast and accurate SIMD-friendly filter to accelerate alignment verification in read mapping

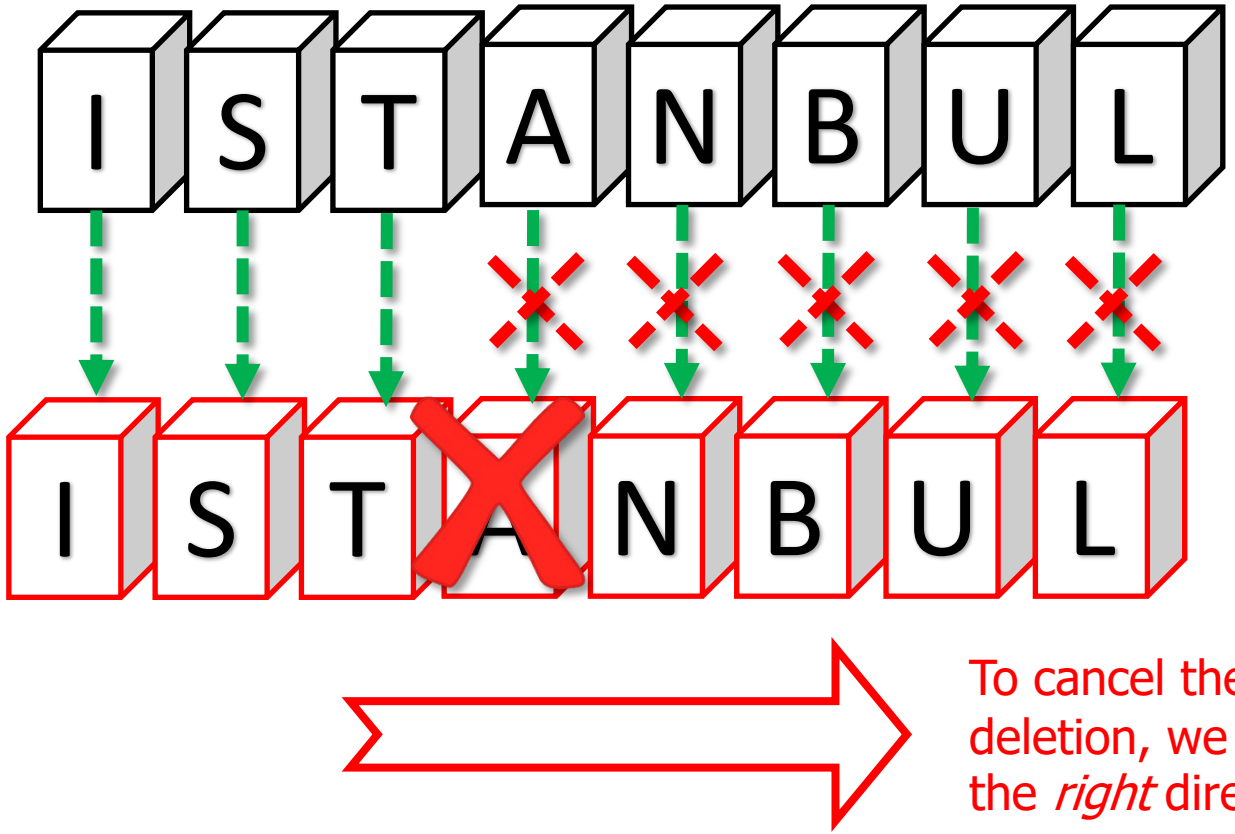
Hongyi Xin[1,*], John Greth[2], John Emmons[2], Gennady Pekhimenko[1], Carl Kingsford[3], Can Alkan[4,*] and Onur Mutlu[2,*]

Xin+, **"Shifted Hamming Distance: A Fast and Accurate SIMD-friendly Filter to Accelerate Alignment Verification in Read Mapping", Bioinformatics 2015.**

Hamming Distance (∑⊕)

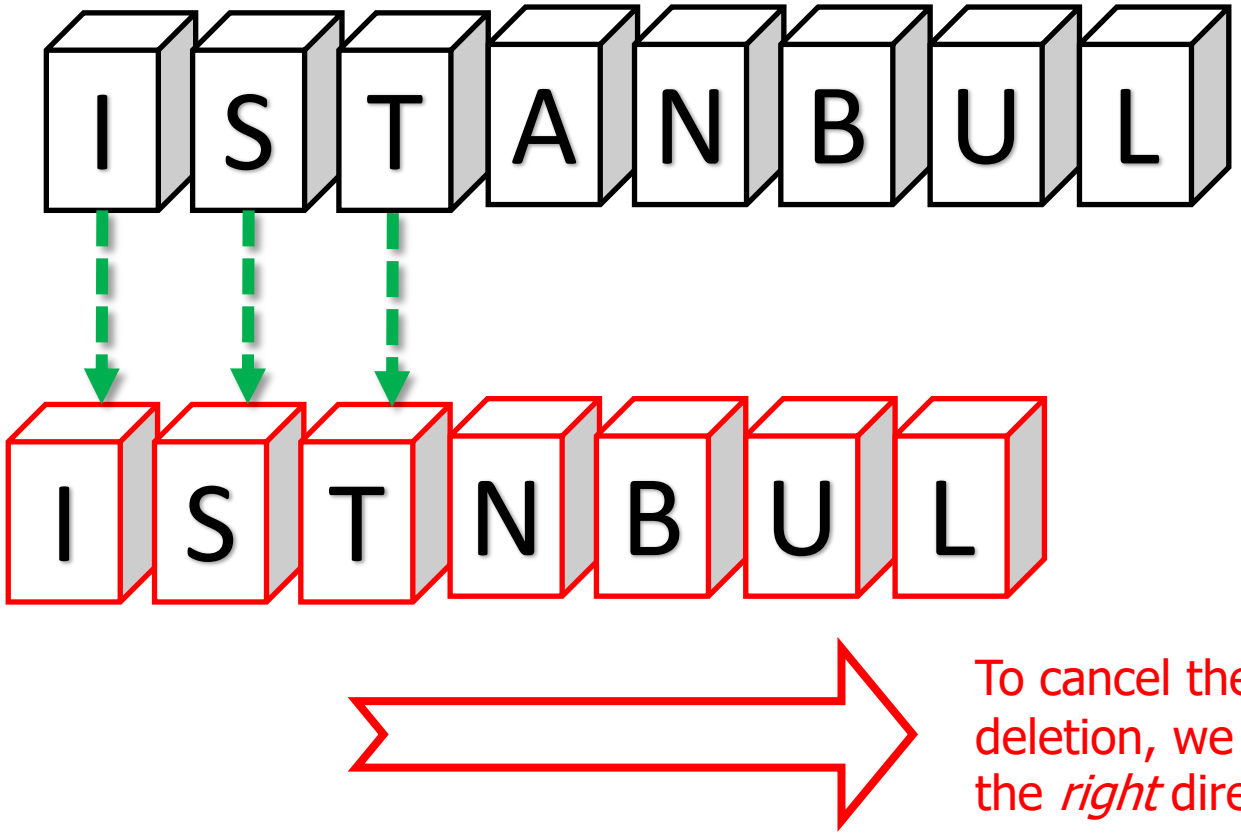
3 matches 5 mismatches

Edit = 1 Deletion

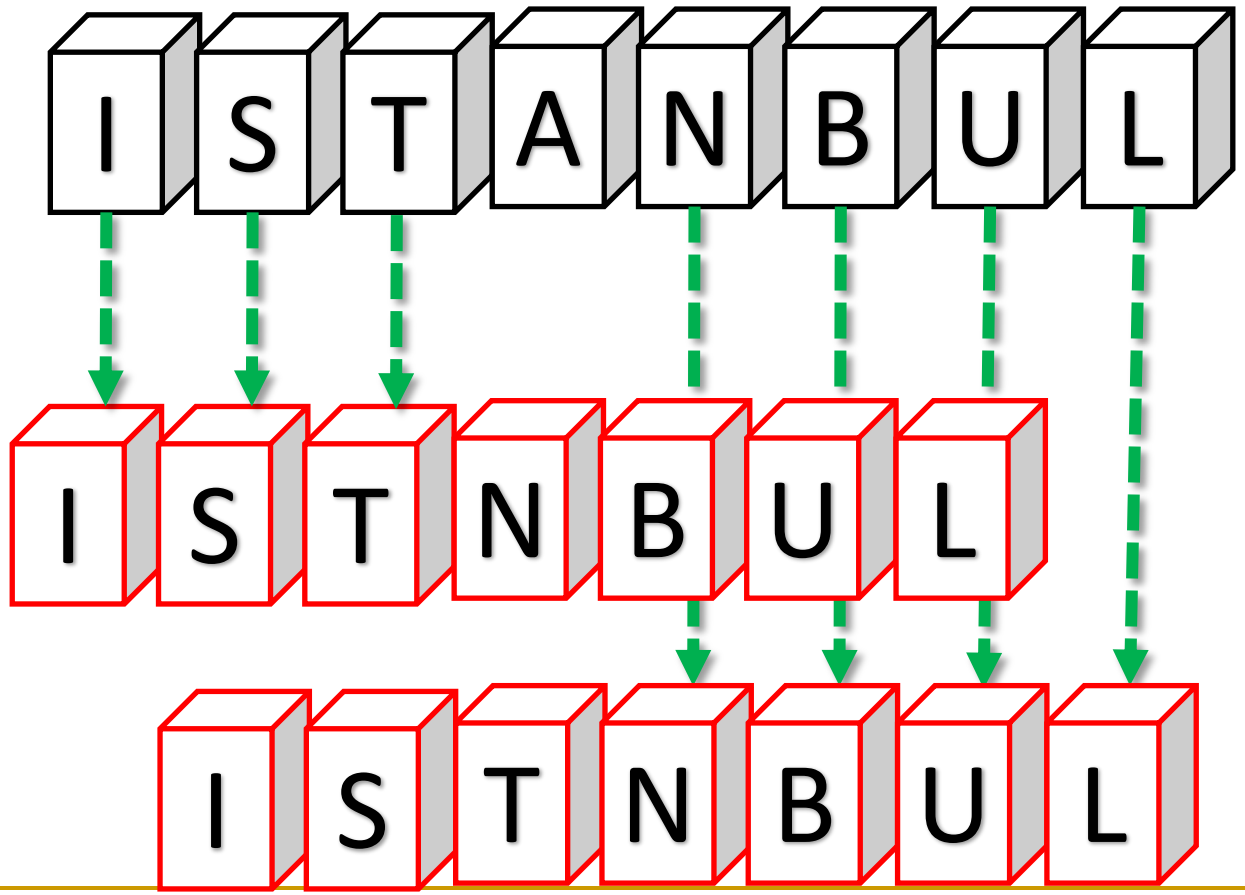


Insight: Shifting a String Helps Similarity Search

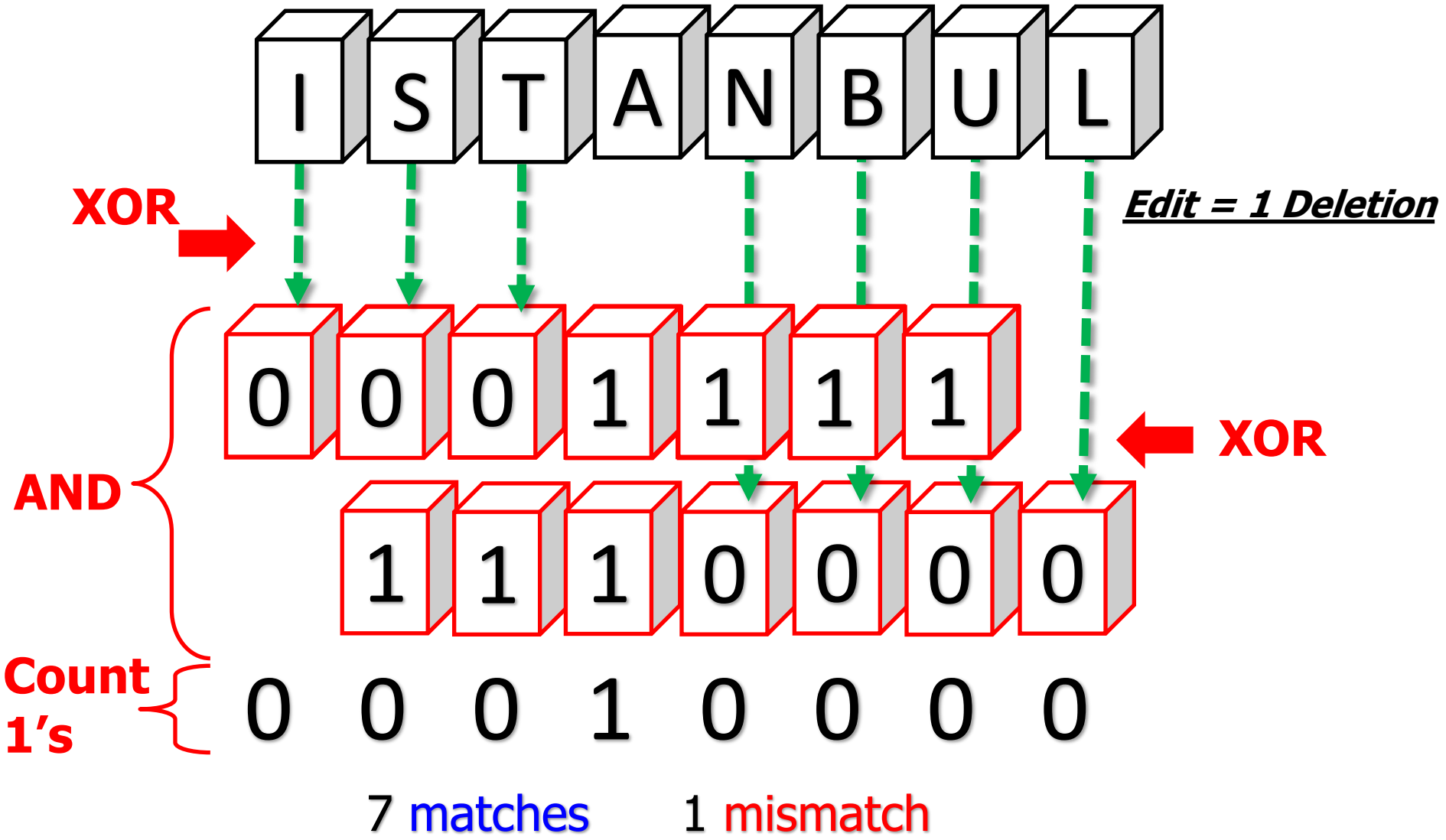
3 matches 5 mismatches



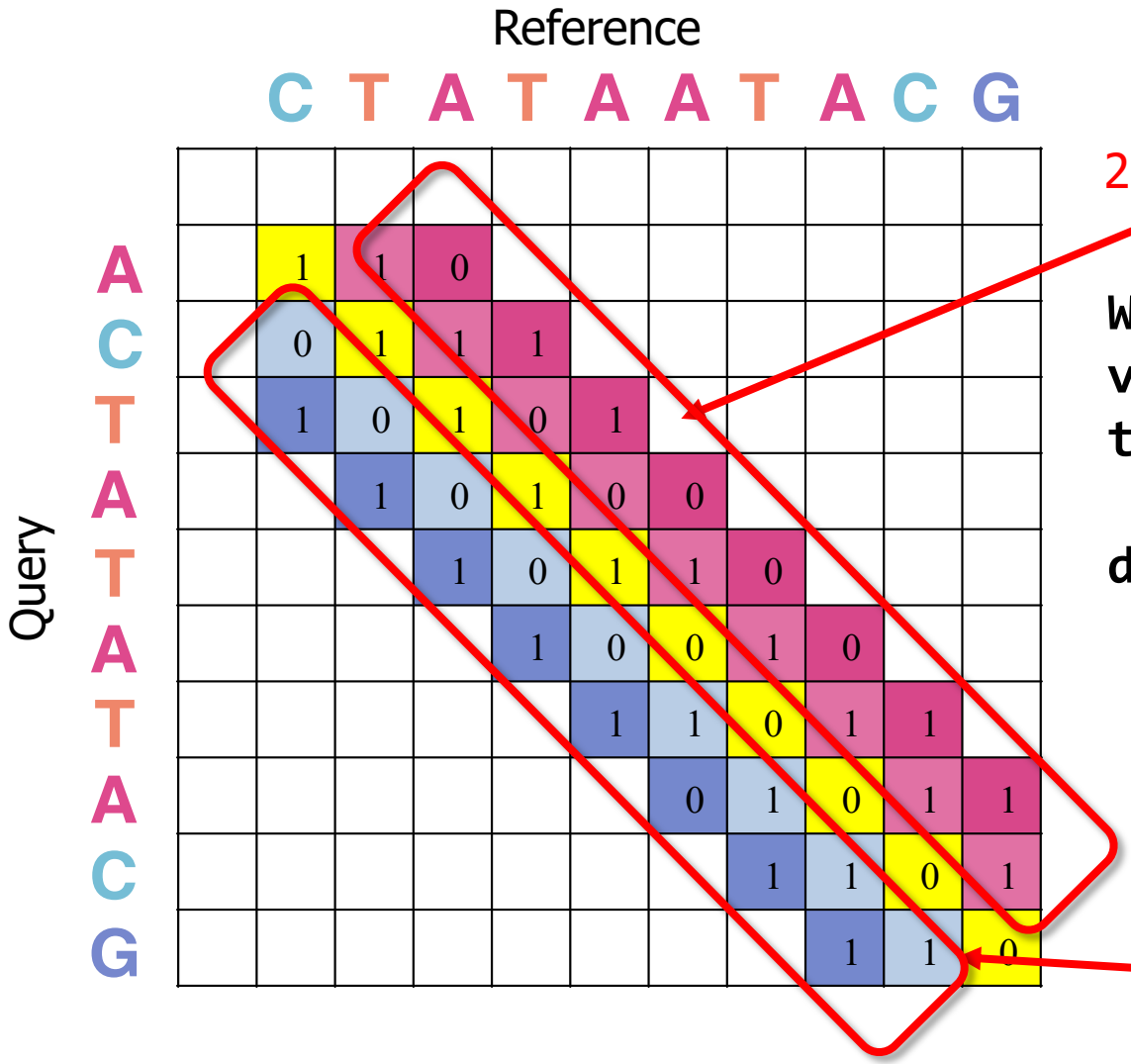
Insight: Shifting a String Helps Similarity Search



Shifted Hamming Distance



Highly Parallel Matrix Computation



We need to compute 2E+1 vectors, E=edit distance threshold

dp[i][j]= 0 if X[i]=Y[j]
1 if X[i]≠Y[j]

No data dependencies!

GateKeeper: FPGA-Based Alignment Filtering

- Mohammed Alser, Hasan Hassan, Hongyi Xin, Oguz Ergin, Onur Mutlu, and Can Alkan
  "GateKeeper: A New Hardware Architecture for Accelerating Pre-Alignment in DNA Short Read Mapping"
  Bioinformatics, [published online, May 31], 2017.
  [Source Code]
  [Online link at Bioinformatics Journal]

GateKeeper: a new hardware architecture for accelerating pre-alignment in DNA short read mapping

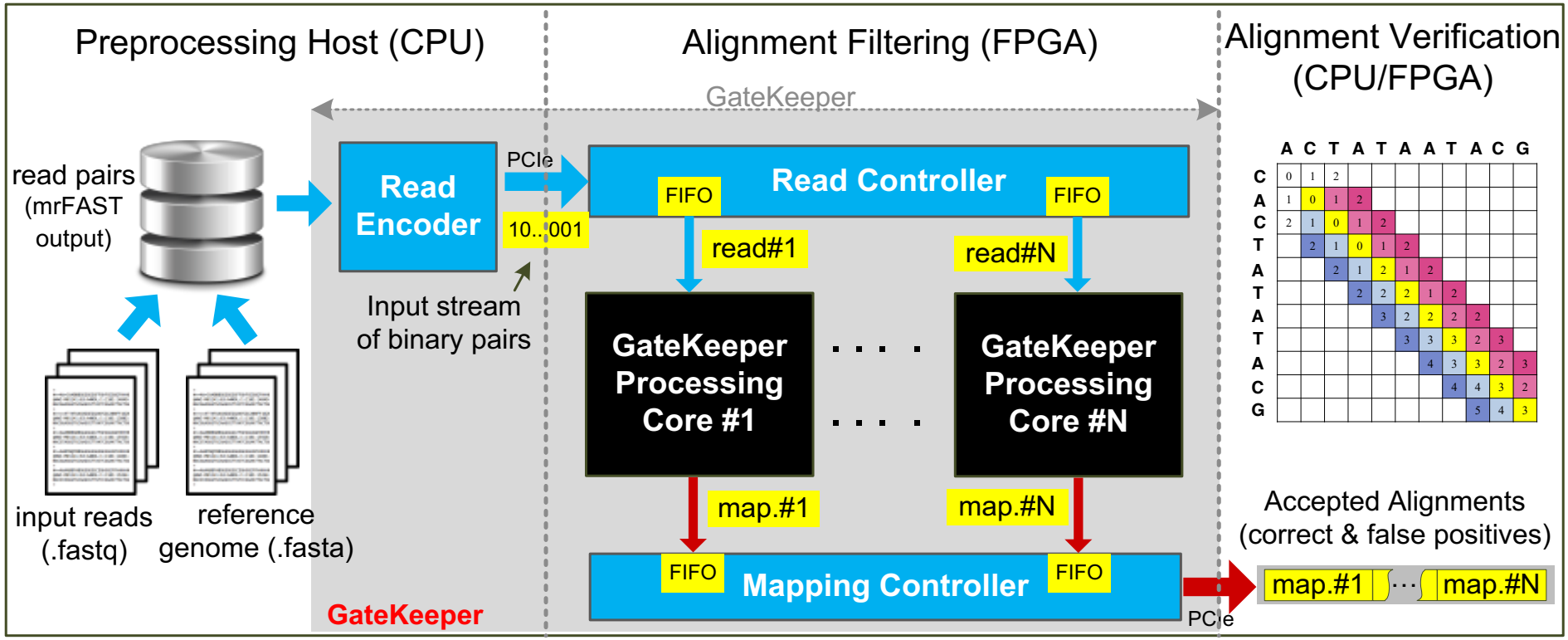
Mohammed Alser ✉, Hasan Hassan, Hongyi Xin, Oğuz Ergin, Onur Mutlu ✉, Can Alkan ✉

Bioinformatics, Volume 33, Issue 21, 1 November 2017, Pages 3355–3363,
https://doi.org/10.1093/bioinformatics/btx342

Published: 31 May 2017 **Article history** ▾

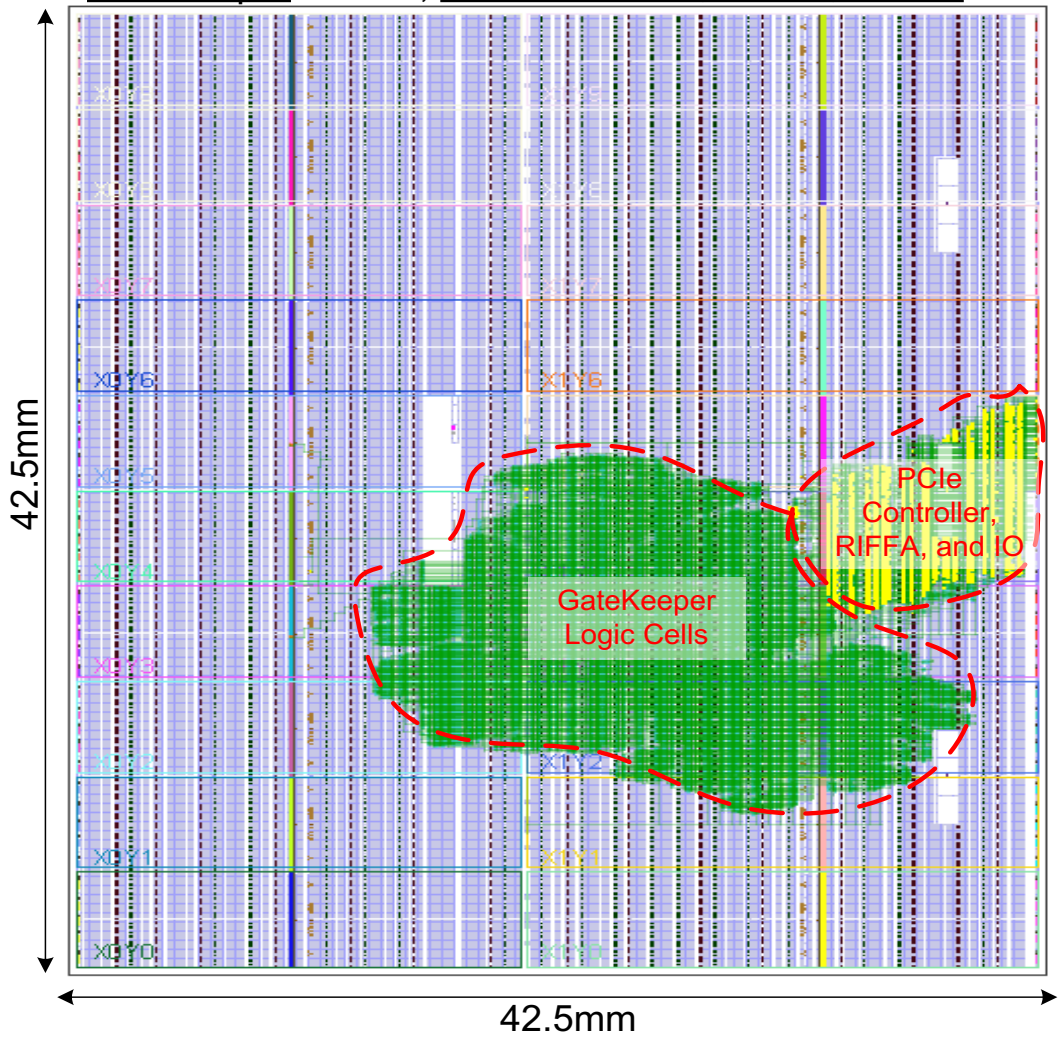
GateKeeper Accelerator Architecture

- **Maximum data throughput** =~13.3 billion bases/sec
- Can examine **8 (300 bp) or 16 (100 bp) mappings concurrently** at 250 MHz
- **Occupies 50%** (100 bp) to **91%** (300 bp) of the FPGA slice LUTs and registers



FPGA Chip Layout

GateKeeper: 17.6%, PCIe Controller, RIFFA, and IO: 5%



Read length:

300 bp

Error threshold:

E=15

GateKeeper: Speed & Accuracy Results

90x-130x faster filter

than SHD (Xin et al., 2015) and the Adjacency Filter (Xin et al., 2013)

4x lower false accept rate

than the Adjacency Filter (Xin et al., 2013)

10x speedup in read mapping

with the addition of GateKeeper to the mrFAST mapper (Alkan et al., 2009)

Freely available online

github.com/BilkentCompGen/GateKeeper

GateKeeper Conclusions

- FPGA-based pre-alignment greatly speeds up read mapping
  - 10x speedup of a state-of-the-art mapper (mrFAST)

- FPGA-based pre-alignment can be integrated with the sequencer
  - It can help to hide the complexity and details of the FPGA
  - Enables **real-time filtering** while sequencing
  - Paves the way to **on-device genome analysis**

More on GateKeeper

- Mohammed Alser, Hasan Hassan, Hongyi Xin, Oguz Ergin, Onur Mutlu, and Can Alkan
  "GateKeeper: A New Hardware Architecture for Accelerating Pre-Alignment in DNA Short Read Mapping"
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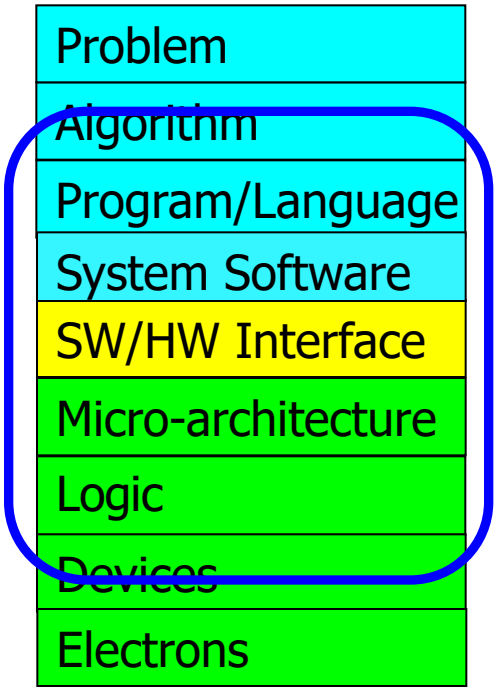
https://doi.org/10.1093/bioinformatics/btx342
Published: 31 May 2017 **Article history** ▾

Algorithm-Arch-Device Co-Design is Critical

Computer Architecture (expanded view)



Shouji (障子) [Alser+, Bioinformatics 2019]

Mohammed Alser, Hasan Hassan, Akash Kumar, Onur Mutlu, and Can Alkan,
"Shouji: A Fast and Efficient Pre-Alignment Filter for Sequence Alignment"
Bioinformatics, [published online, March 28], 2019.
[Source Code]
[Online link at Bioinformatics Journal]

Bioinformatics, 2019, 1–9
doi: 10.1093/bioinformatics/btz234
Advance Access Publication Date: 28 March 2019
Original Paper

OXFORD

Sequence alignment

Shouji: a fast and efficient pre-alignment filter for sequence alignment

Mohammed Alser[1,2,3,*], Hasan Hassan[1], Akash Kumar[2], Onur Mutlu[1,3,*] and Can Alkan[3,*]

[1]Computer Science Department, ETH Zürich, Zürich 8092, Switzerland, [2]Chair for Processor Design, Center For Advancing Electronics Dresden, Institute of Computer Engineering, Technische Universität Dresden, 01062 Dresden, Germany and [3]Computer Engineering Department, Bilkent University, 06800 Ankara, Turkey

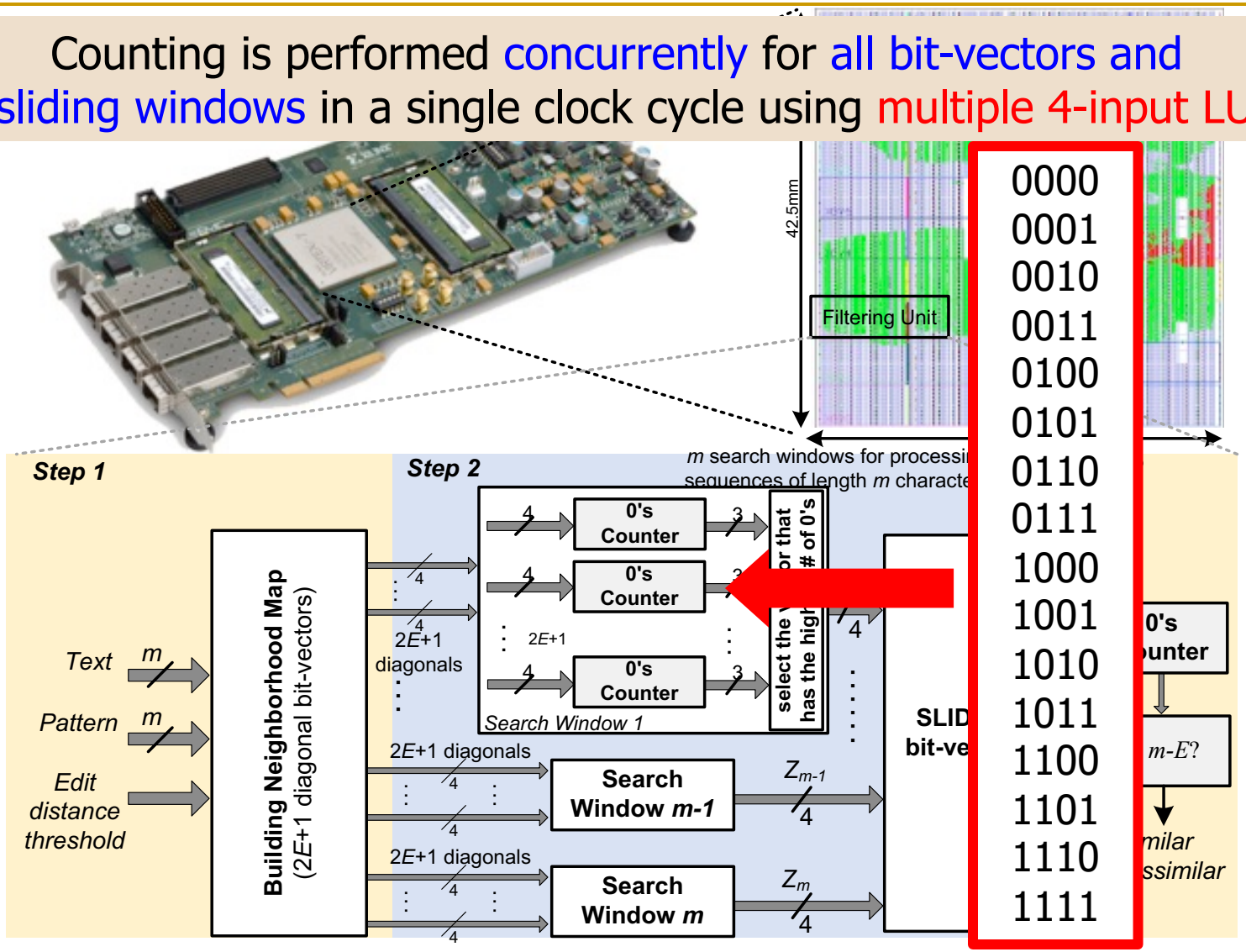
*To whom correspondence should be addressed.

Associate Editor: Inanc Birol

Received on September 13, 2018; revised on February 27, 2019; editorial decision on March 7, 2019; accepted on March 27, 2019

Hardware Implementation

Counting is performed concurrently for all bit-vectors and all sliding windows in a single clock cycle using multiple 4-input LUTs



SneakySnake [Alser+, Bioinformatics 2020]

Mohammed Alser, Taha Shahroodi, Juan-Gomez Luna, Can Alkan, and Onur Mutlu,
"SneakySnake: A Fast and Accurate Universal Genome Pre-Alignment Filter for CPUs, GPUs, and FPGAs"
Bioinformatics, to appear in 2020.
[Source Code]
[Online link at Bioinformatics Journal]

Bioinformatics
doi.10.1093/bioinformatics/xxxxxx
Advance Access Publication Date: Day Month Year
Manuscript Category

Subject Section

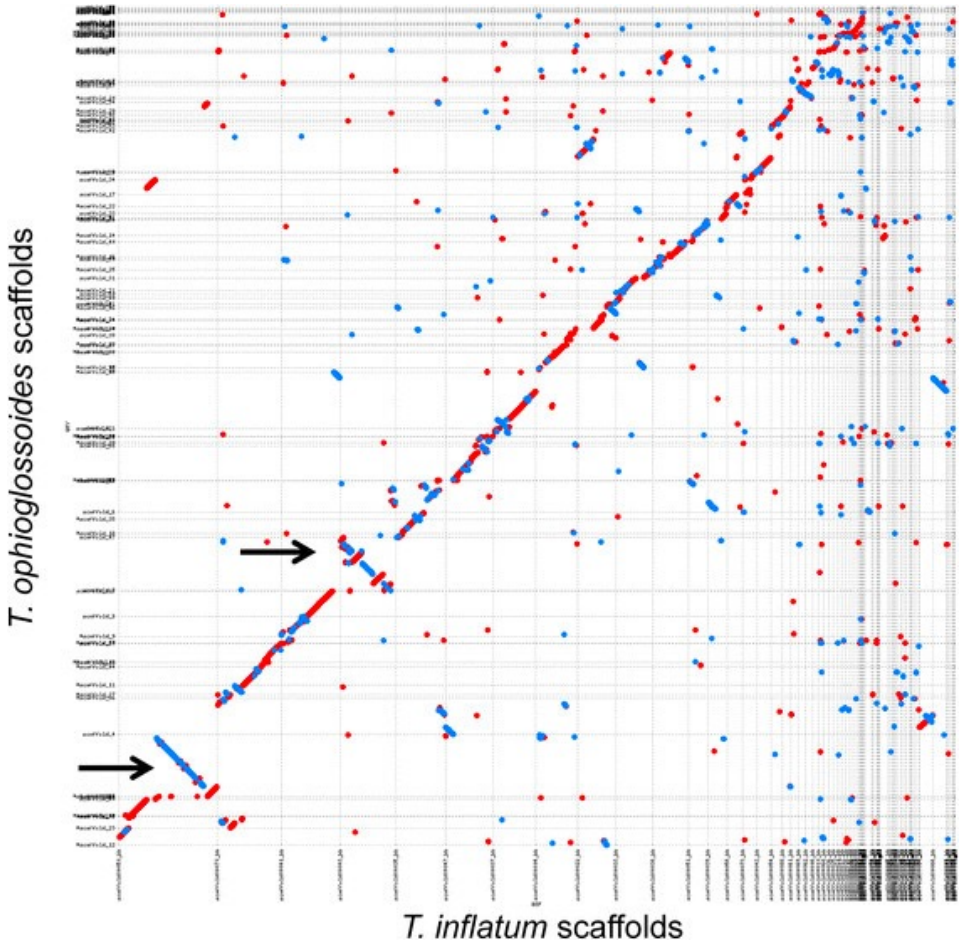
SneakySnake: A Fast and Accurate Universal Genome Pre-Alignment Filter for CPUs, GPUs, and FPGAs

Mohammed Alser [1,2,*], Taha Shahroodi [1], Juan Gómez-Luna [1,2], Can Alkan [4,*], and Onur Mutlu [1,2,3,4,*]

[1] Department of Computer Science, ETH Zurich, Zurich 8006, Switzerland
[2] Department of Information Technology and Electrical Engineering, ETH Zurich, Zurich 8006, Switzerland
[3] Department of Electrical and Computer Engineering, Carnegie Mellon University, Pittsburgh 15213, PA, USA
[4] Department of Computer Engineering, Bilkent University, Ankara 06800, Turkey

SneakySnake

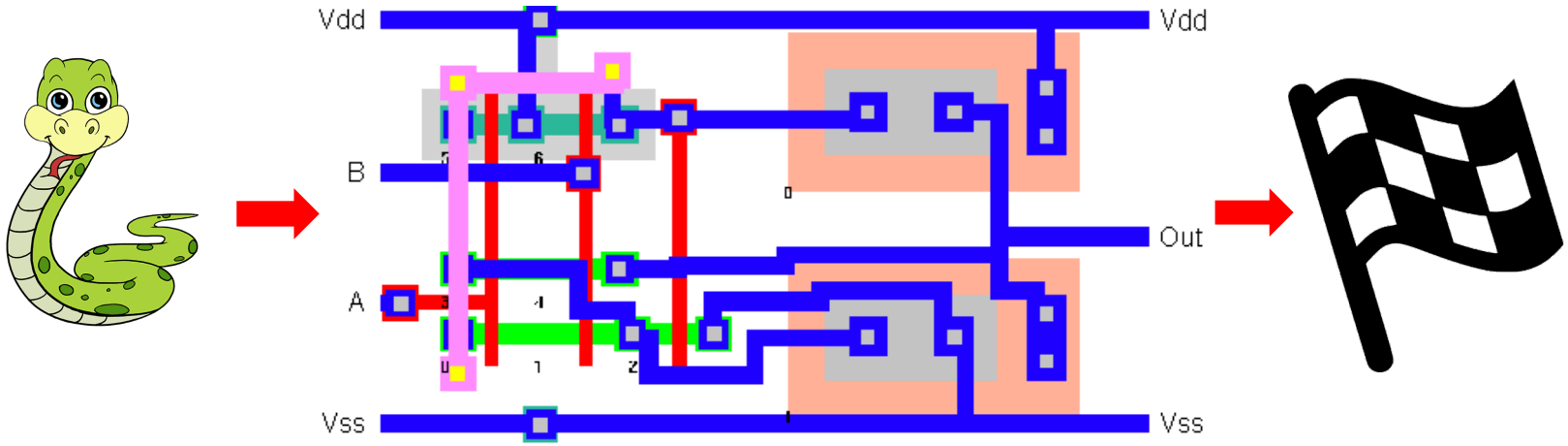
- **Key observation:**
  - Correct alignment is a sequence of non-overlapping long matches



Dot plot, dot matrix
(Lipman and Pearson, 1985)

SneakySnake

- **Key observation:**
  - Correct alignment is a sequence of non-overlapping long matches
- **Key idea:**
  - Reduce the approximate string matching problem to the Single Net Routing problem in VLSI chip layout



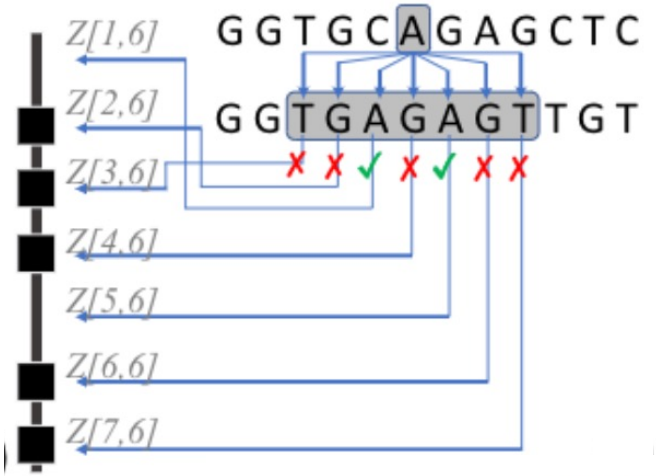
VLSI chip layout

SneakySnake

- **Key observation:**
  - Correct alignment is a sequence of non-overlapping long matches
- **Key idea:**
  - Reduce the approximate string matching problem to the Single Net Routing problem in VLSI chip layout
- **Key result:**
  - SneakySnake is up to four orders of magnitude more accurate than Shouji (Bioinformatics'19) and GateKeeper (Bioinformatics'17)
  - SneakySnake greatly accelerates state-of-the-art CPU sequence aligners, Edlib (Bioinformatics'17) and Parasail (BMC Bioinformatics'16)
    - by up to 37.7× and 43.9× (>12× on average), on CPUs
    - by up to 413× and 689× (>400× on average) *with FPGAs/GPUs*

SneakySnake Walkthrough

Building Neighborhood Map | Finding the Optimal Routing Path | Examining the Snake Survival



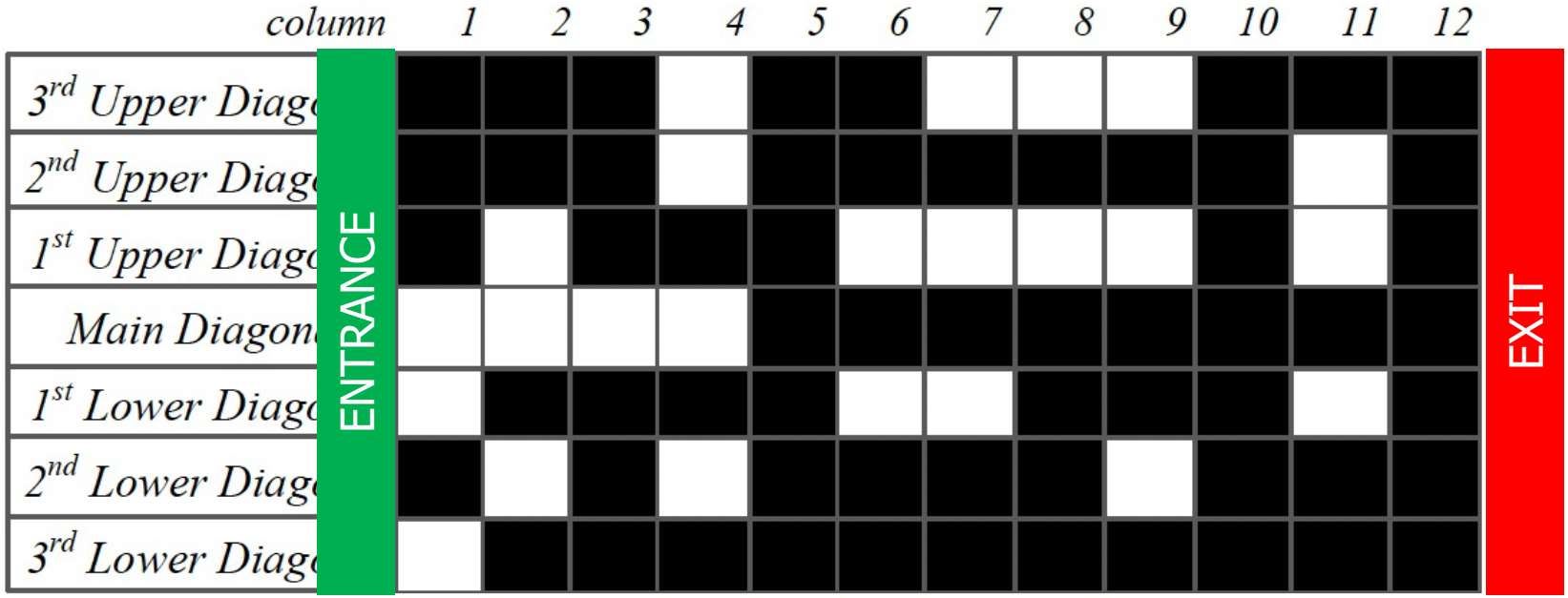
$E = 3$

column	1	2	3	4	5	6	7	8	9	10	11	12
3rd Upper Diagonal	1	1	1	0	1	1	0	0	0	1	1	1
2nd Upper Diagonal	1	1	1	0	1	1	1	1	1	1	0	1
1st Upper Diagonal	1	0	1	1	1	0	0	0	0	1	0	1
Main Diagonal	0	0	0	0	1	1	1	1	1	1	1	1
1st Lower Diagonal	0	1	1	1	1	0	0	1	1	1	0	1
2nd Lower Diagonal	1	0	1	0	1	1	1	1	0	1	1	1
3rd Lower Diagonal	0	1	1	1	1	1	1	1	1	1	1	1

SneakySnake Walkthrough

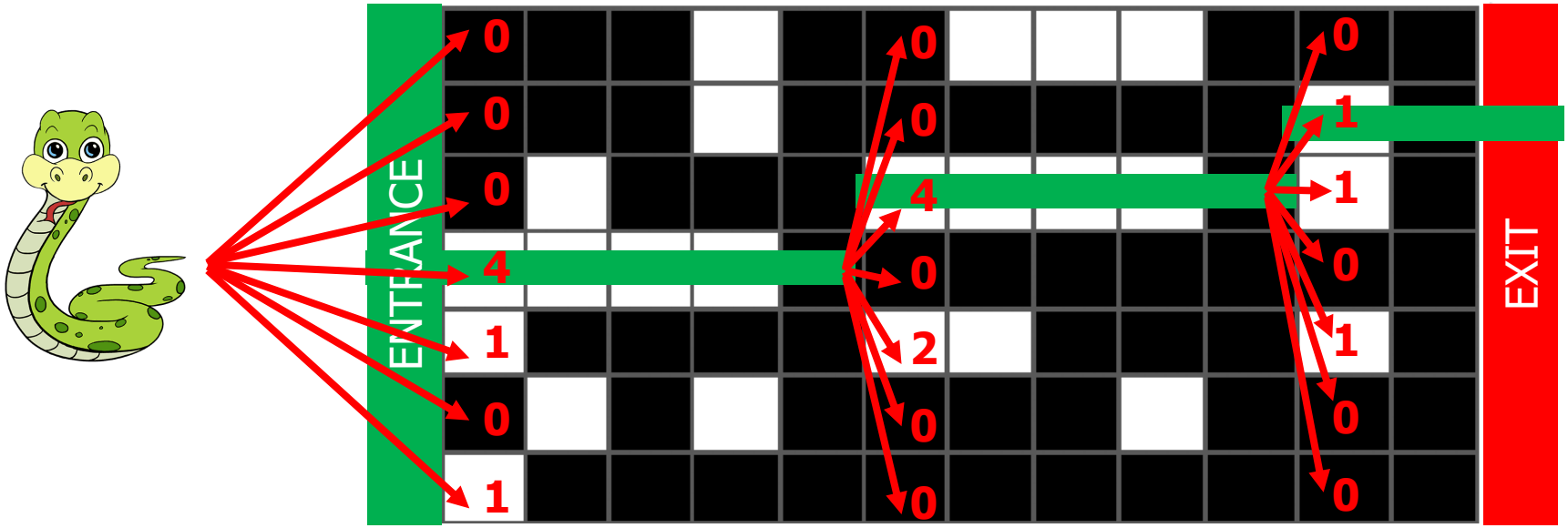
Building Neighborhood Map | Finding the Optimal Routing Path | Examining the Snake Survival

$E = 3$



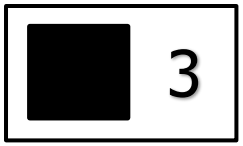
SneakySnake Walkthrough

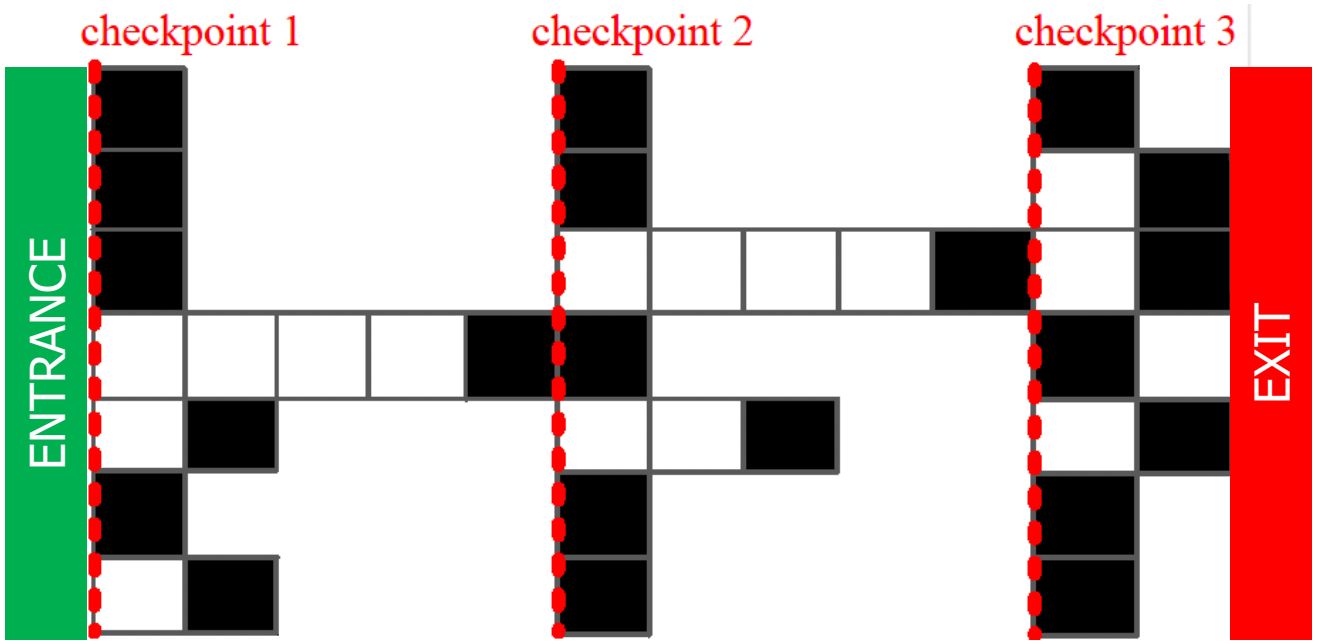
Building Neighborhood Map | Finding the Optimal Routing Path | Examining the Snake Survival



SneakySnake Walkthrough

This is what you actually need to build and it can be done on-the-fly!





FPGA Resource Analysis

- FPGA resource usage for a single filtering unit of GateKeeper, Shouji, and Snake-on-Chip for a sequence length of 100 and under different edit distance thresholds (E).

	E (bp)	Slice LUT	Slice Register	No. of Filtering Units
GateKeeper	2	0.39%	0.01%	16
	5	0.71%	0.01%	16
Shouji	2	0.69%	0.08%	16
	5	1.72%	0.16%	16
Snake-on-Chip	2	0.68%	0.16%	16
	5	1.42%	0.34%	16

Key Results of SneakySnake

- SneakySnake is up to four orders of magnitude more accurate than Shouji (Bioinformatics'19) and GateKeeper (Bioinformatics'17)

- Short reads:
  - SneakySnake accelerates Edlib (Bioinformatics'17) and Parasail (BMC Bioinformatics'16) by
  - up to 37.7× and 43.9× (>12× on average), on CPUs
  - up to 413× and 689× (>400× on average) using *FPGAs/GPUs*

- Long reads:
  - SneakySnake accelerates Parasail and KSW2 by 140.1× and 17.1× on average, respectively, on CPUs

More on SneakySnake [Alser+, Bioinformatics 2020]

Mohammed Alser, Taha Shahroodi, Juan-Gomez Luna, Can Alkan, and Onur Mutlu,
"SneakySnake: A Fast and Accurate Universal Genome Pre-Alignment Filter for CPUs, GPUs, and FPGAs"
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Bioinformatics
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Advance Access Publication Date: Day Month Year
Manuscript Category

OXFORD

Subject Section

SneakySnake: A Fast and Accurate Universal Genome Pre-Alignment Filter for CPUs, GPUs, and FPGAs

Mohammed Alser [1,2,*], Taha Shahroodi [1], Juan Gómez-Luna [1,2], Can Alkan [4,*], and Onur Mutlu [1,2,3,4,*]

[1] Department of Computer Science, ETH Zurich, Zurich 8006, Switzerland
[2] Department of Information Technology and Electrical Engineering, ETH Zurich, Zurich 8006, Switzerland
[3] Department of Electrical and Computer Engineering, Carnegie Mellon University, Pittsburgh 15213, PA, USA
[4] Department of Computer Engineering, Bilkent University, Ankara 06800, Turkey

GenASM Framework [MICRO 2020]

- Damla Senol Cali, Gurpreet S. Kalsi, Zulal Bingol, Can Firtina, Lavanya Subramanian, Jeremie S. Kim, Rachata Ausavarungnirun, Mohammed Alser, Juan Gomez-Luna, Amirali Boroumand, Anant Nori, Allison Scibisz, Sreenivas Subramoney, Can Alkan, Saugata Ghose, and Onur Mutlu, **"GenASM: A High-Performance, Low-Power Approximate String Matching Acceleration Framework for Genome Sequence Analysis"**
  *Proceedings of the 53rd International Symposium on Microarchitecture (**MICRO**)*, Virtual, October 2020.
  [Lighting Talk Video (1.5 minutes)]
  [Lightning Talk Slides (pptx) (pdf)]
  [Talk Video (18 minutes)]
  [Slides (pptx) (pdf)]

GenASM: A High-Performance, Low-Power Approximate String Matching Acceleration Framework for Genome Sequence Analysis

Damla Senol Cali[†⋈] Gurpreet S. Kalsi[⋈] Zülal Bingöl[▽] Can Firtina[◇] Lavanya Subramanian[‡] Jeremie S. Kim[◇†]
Rachata Ausavarungnirun[⊙] Mohammed Alser[◇] Juan Gomez-Luna[◇] Amirali Boroumand[†] Anant Nori[⋈]
Allison Scibisz[†] Sreenivas Subramoney[⋈] Can Alkan[▽] Saugata Ghose[⋆†] Onur Mutlu[◇†▽]

[†]*Carnegie Mellon University* [⋈]*Processor Architecture Research Lab, Intel Labs* [▽]*Bilkent University* [◇]*ETH Zürich*
[‡]*Facebook* [⊙]*King Mongkut's University of Technology North Bangkok* [⋆]*University of Illinois at Urbana–Champaign*

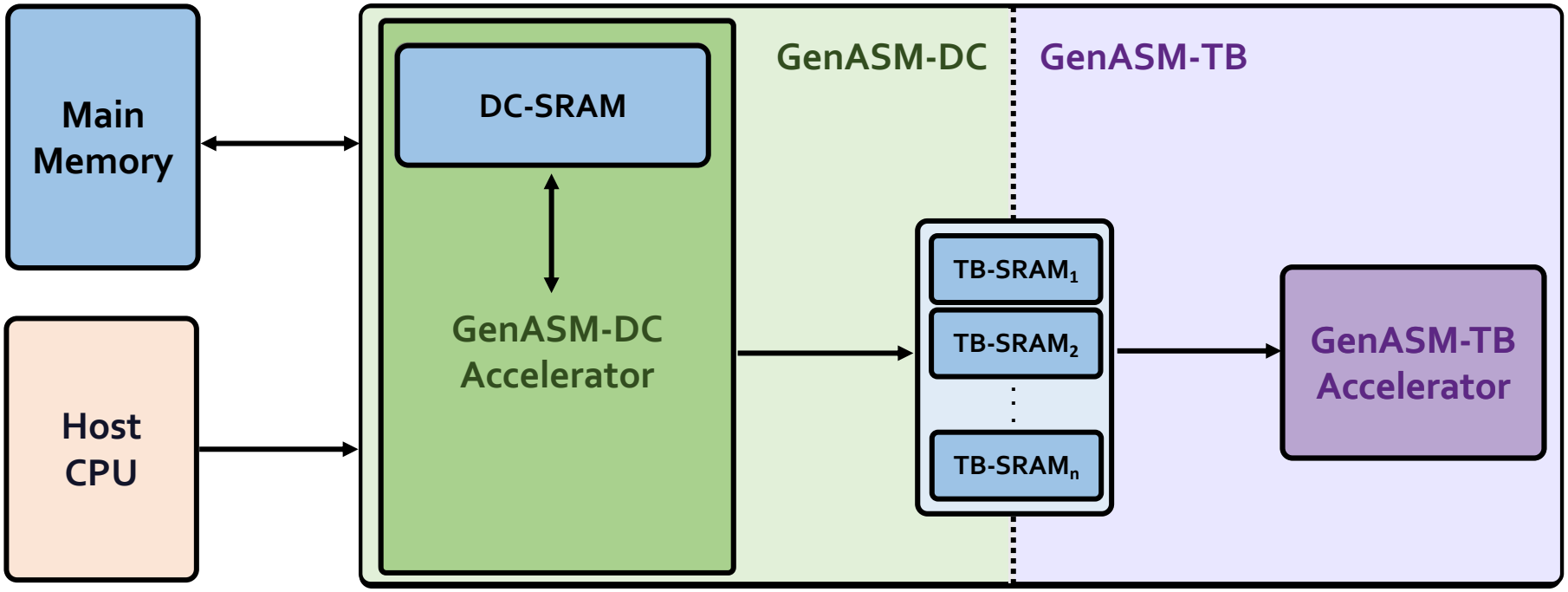
GenASM: ASM Framework for GSA

Our Goal:

Accelerate approximate string matching
by designing a fast and flexible framework,
which can accelerate *multiple steps* of genome sequence analysis

- **GenASM:** *First* ASM acceleration framework for GSA
  - Based on the *Bitap* algorithm
    - Uses fast and simple bitwise operations to perform ASM
  - Modified and extended ASM algorithm
    - Highly-parallel Bitap with long read support
    - Bitvector-based novel algorithm to perform *traceback*
  - Co-design of our modified scalable and memory-efficient algorithms with low-power and area-efficient hardware accelerators

GenASM: Hardware Design

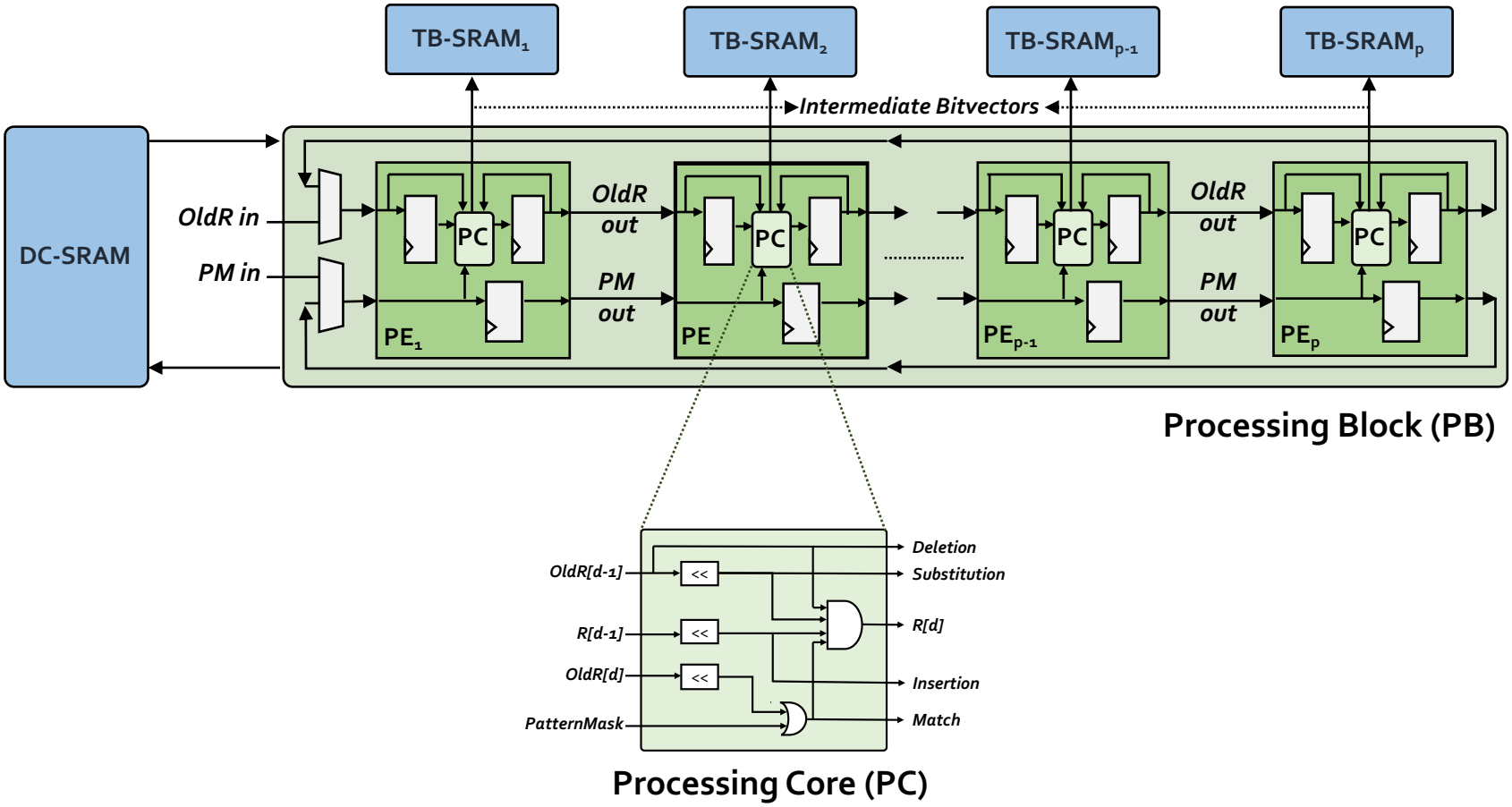


GenASM-DC:
generates bitvectors and performs edit **D**istance **C**alculation

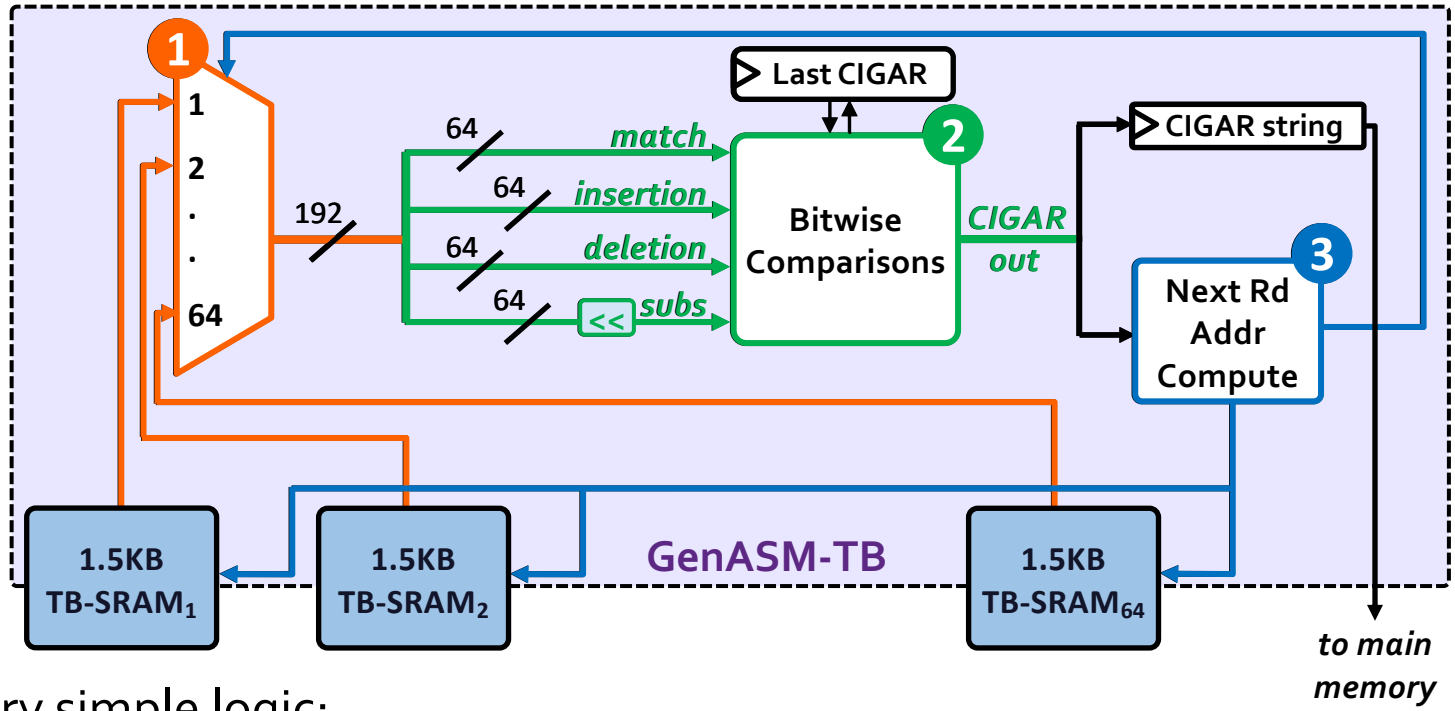
GenASM-TB:
performs **T**race**B**ack and assembles the optimal alignment

GenASM-DC: Hardware Design

- **Linear cyclic systolic array** based accelerator
  - Designed to maximize parallelism and minimize memory bandwidth and memory footprint



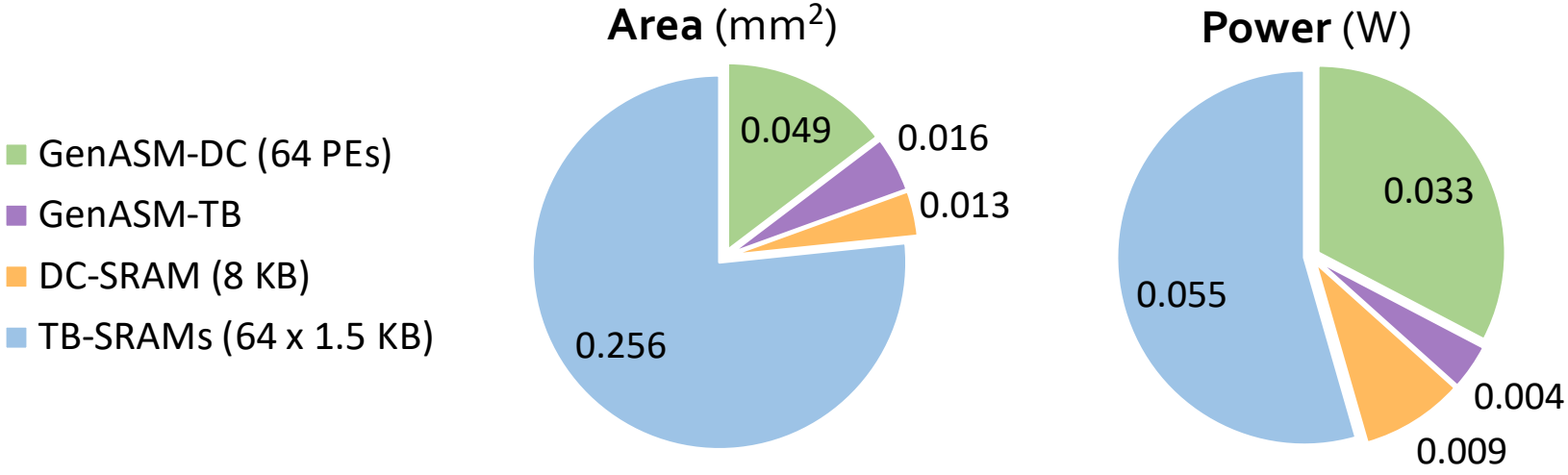
GenASM-TB: Hardware Design



- Very simple logic:
  - 1 Reads the bitvectors from one of the TB-SRAMs using the computed address
  - 2 Performs the required bitwise comparisons to find the traceback output for the current position
  - 3 Computes the next TB-SRAM address to read the new set of bitvectors

Key Results – Area and Power

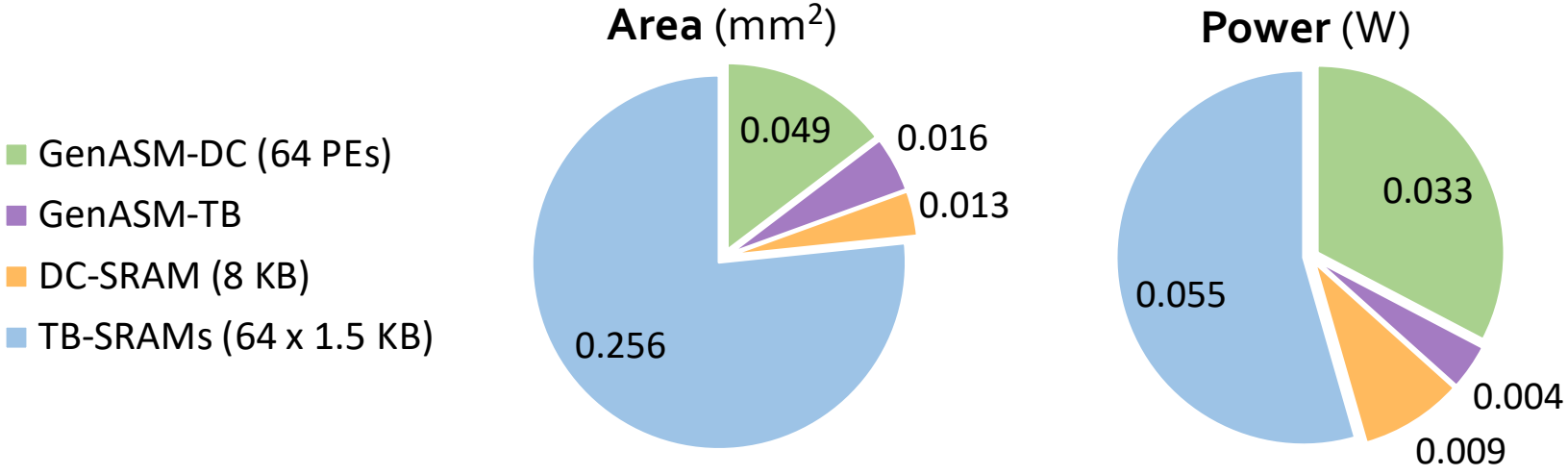
- Based on our **synthesis** of **GenASM-DC** and **GenASM-TB** accelerator datapaths using the Synopsys Design Compiler with a **28nm** LP process:
  - Both GenASM-DC and GenASM-TB operate **@ 1GHz**



Total (1 vault):	0.334 mm^2	0.101 W
Total (32 vaults):	10.69 mm^2	3.23 W
% of a Xeon CPU core:	**1%**	**1%**

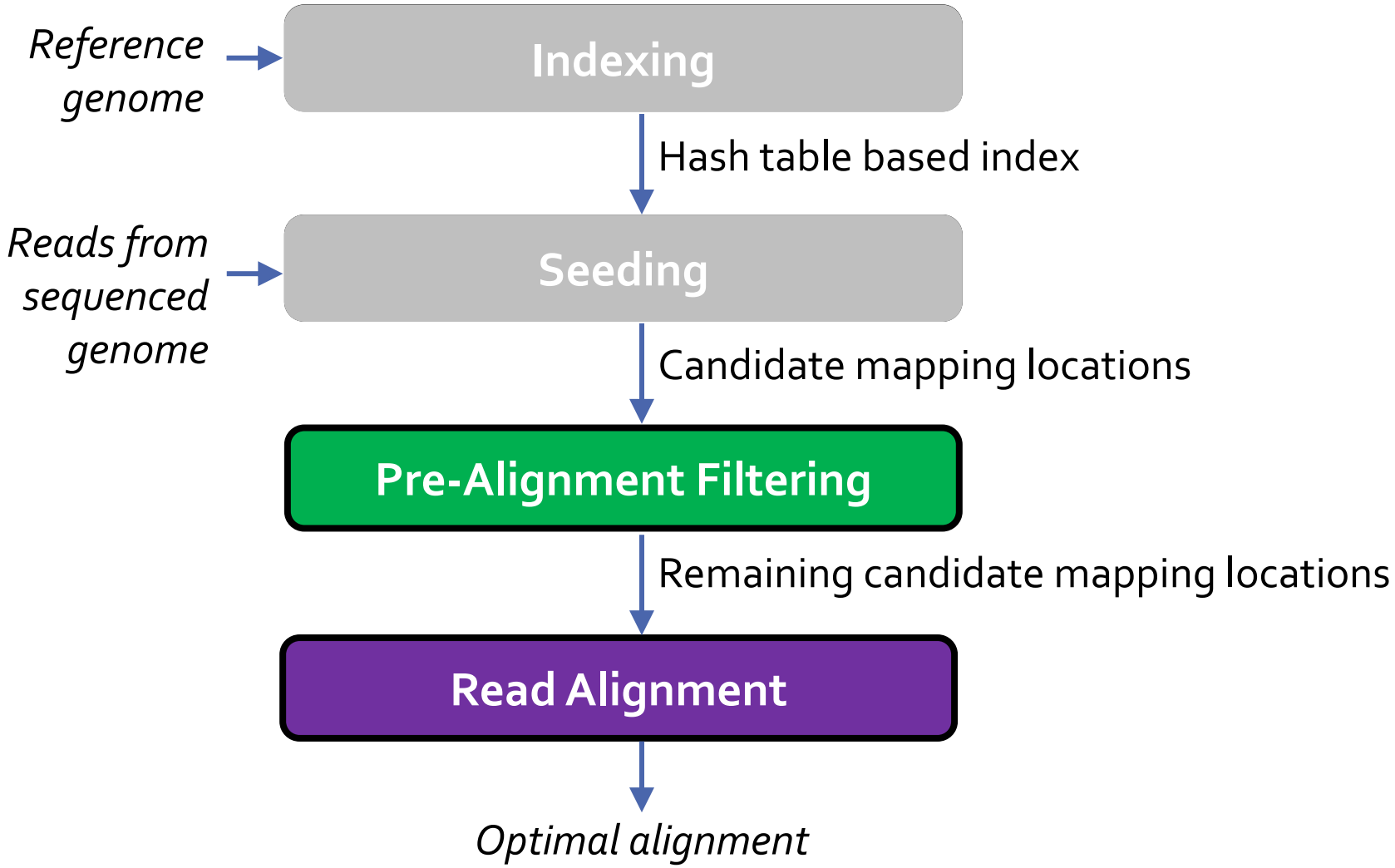
Key Results – Area and Power

- Based on our **synthesis** of **GenASM-DC** and **GenASM-TB** accelerator datapaths using the Synopsys Design Compiler with a **28nm** LP process:
  - Both GenASM-DC and GenASM-TB operate **@ 1GHz**



GenASM has low area and power overheads

Use Cases of GenASM



Use Cases of GenASM (cont'd.)

(1) Read Alignment Step of Read Mapping

- Find the optimal alignment of how reads map to candidate reference regions

(2) Pre-Alignment Filtering for Short Reads

- Quickly identify and filter out the unlikely candidate reference regions for each read

(3) Edit Distance Calculation

- Measure the similarity or distance between two sequences

- We also discuss other possible use cases of GenASM in our paper:
  - Read-to-read overlap finding, hash-table based indexing, whole genome alignment, generic text search

Key Results

(1) Read Alignment

- **116×** speedup, **37×** less power than **Minimap2** (state-of-the-art **SW**)
- **111×** speedup, **33×** less power than **BWA-MEM** (state-of-the-art **SW**)
- **3.9×** better throughput, **2.7×** less power than **Darwin** (state-of-the-art **HW**)
- **1.9×** better throughput, **82%** less logic power than **GenAx** (state-of-the-art **HW**)

(2) Pre-Alignment Filtering

- **3.7×** speedup, **1.7×** less power than **Shouji** (state-of-the-art **HW**)

(3) Edit Distance Calculation

- **22–12501×** speedup, **548–582×** less power than **Edlib** (state-of-the-art **SW**)
- **9.3–400×** speedup, **67×** less power than **ASAP** (state-of-the-art **HW**)

More on GenASM Framework [MICRO 2020]

- Damla Senol Cali, Gurpreet S. Kalsi, Zulal Bingol, Can Firtina, Lavanya Subramanian, Jeremie S. Kim, Rachata Ausavarungnirun, Mohammed Alser, Juan Gomez-Luna, Amirali Boroumand, Anant Nori, Allison Scibisz, Sreenivas Subramoney, Can Alkan, Saugata Ghose, and Onur Mutlu, **"GenASM: A High-Performance, Low-Power Approximate String Matching Acceleration Framework for Genome Sequence Analysis"**
  *Proceedings of the 53rd International Symposium on Microarchitecture (**MICRO**)*, Virtual, October 2020.
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  [Slides (pptx) (pdf)]

GenASM: A High-Performance, Low-Power Approximate String Matching Acceleration Framework for Genome Sequence Analysis

Damla Senol Cali[†⋈] Gurpreet S. Kalsi[⋈] Zülal Bingöl[▽] Can Firtina[◇] Lavanya Subramanian[‡] Jeremie S. Kim[◇†]
Rachata Ausavarungnirun[⊙] Mohammed Alser[◇] Juan Gomez-Luna[◇] Amirali Boroumand[†] Anant Nori[⋈]
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[†]*Carnegie Mellon University* [⋈]*Processor Architecture Research Lab, Intel Labs* [▽]*Bilkent University* [◇]*ETH Zürich*
[‡]*Facebook* [⊙]*King Mongkut's University of Technology North Bangkok* [⋆]*University of Illinois at Urbana–Champaign*

Scrooge: Faster Approximate String Matching

- Joël Lindegger, Damla Senol Cali, Mohammed Alser, Juan Gómez-Luna, Nika Mansouri Ghiasi, and Onur Mutlu,
  "Scrooge: A Fast and Memory-Frugal Genomic Sequence Aligner for CPUs, GPUs, and ASICs"
  Bioinformatics, [published online on] 24 March 2023.
  [Online link at Bioinformatics Journal]
  [arXiv preprint]
  [Scrooge Source Code]

Scrooge: A Fast and Memory-Frugal Genomic Sequence Aligner for CPUs, GPUs, and ASICs

Joël Lindegger[§] Damla Senol Cali[†] Mohammed Alser[§]
Juan Gómez-Luna[§] Nika Mansouri Ghiasi[§] Onur Mutlu[§]

[§]*ETH Zürich* [†]*Bionano Genomics*

https://github.com/cmu-safari/scrooge

Our Goals

Build a practical and efficient implementation of the GenASM algorithm for multiple computing platforms

Compete with state-of-the-art pairwise sequence aligners like Edlib, KSW2, and BiWFA

Scrooge

Three novel algorithmic improvements
which address inefficiencies in the GenASM algorithm

Efficient open-source implementations
for CPUs and GPUs

Key Results

Scrooge consistently outperforms GenASM
- 2.1x speedup over GenASM on CPU
- 5.9x speedup over GenASM on GPU
- 3.6x better area efficiency and 3.6x less power than GenASM as an ASIC

Scrooge consistently outperforms state-of-the-art CPU and GPU baselines, including KSW2, Edlib, and BiWFA

SAFARI

Scrooge on GitHub

README.md

Scrooge: A fast and memory-frugal genomic sequence aligner for CPUs, GPUs and ASICs

Scrooge is a fast pairwise genomic sequence aligner. It efficiently aligns short and long genomic sequence pairs on multiple computing platforms. It is based on the GenASM algorithm (Senol Cali+, 2020), and adds multiple algorithmic improvements that significantly improve the throughput and resource efficiency for CPUs, GPUs and ASICs. For long reads, the CPU version of Scrooge achieves a 20.1x, 1.7x, and 2.1x speedup over KSW2, Edlib, and a CPU implementation of GenASM, respectively. The GPU version of Scrooge achieves a 4.0x 80.4x, 6.8x, 12.6x and 5.9x speedup over the CPU version of Scrooge, KSW2, Edlib, Darwin-GPU, and a GPU implementation of GenASM, respectively. We estimate an ASIC implementation of Scrooge to use 3.6x less chip area and 2.1x less power than a GenASM ASIC while maintaining the same throughput.

This repository contains Scrooge's CPU and GPU implementations, and several evaluation scripts. We describe Scrooge in our paper on arXiv and in Bioinformatics.

3 forks

Report repository

Releases

No releases published

Create a new release

Packages

No packages published

Publish your first package

Languages

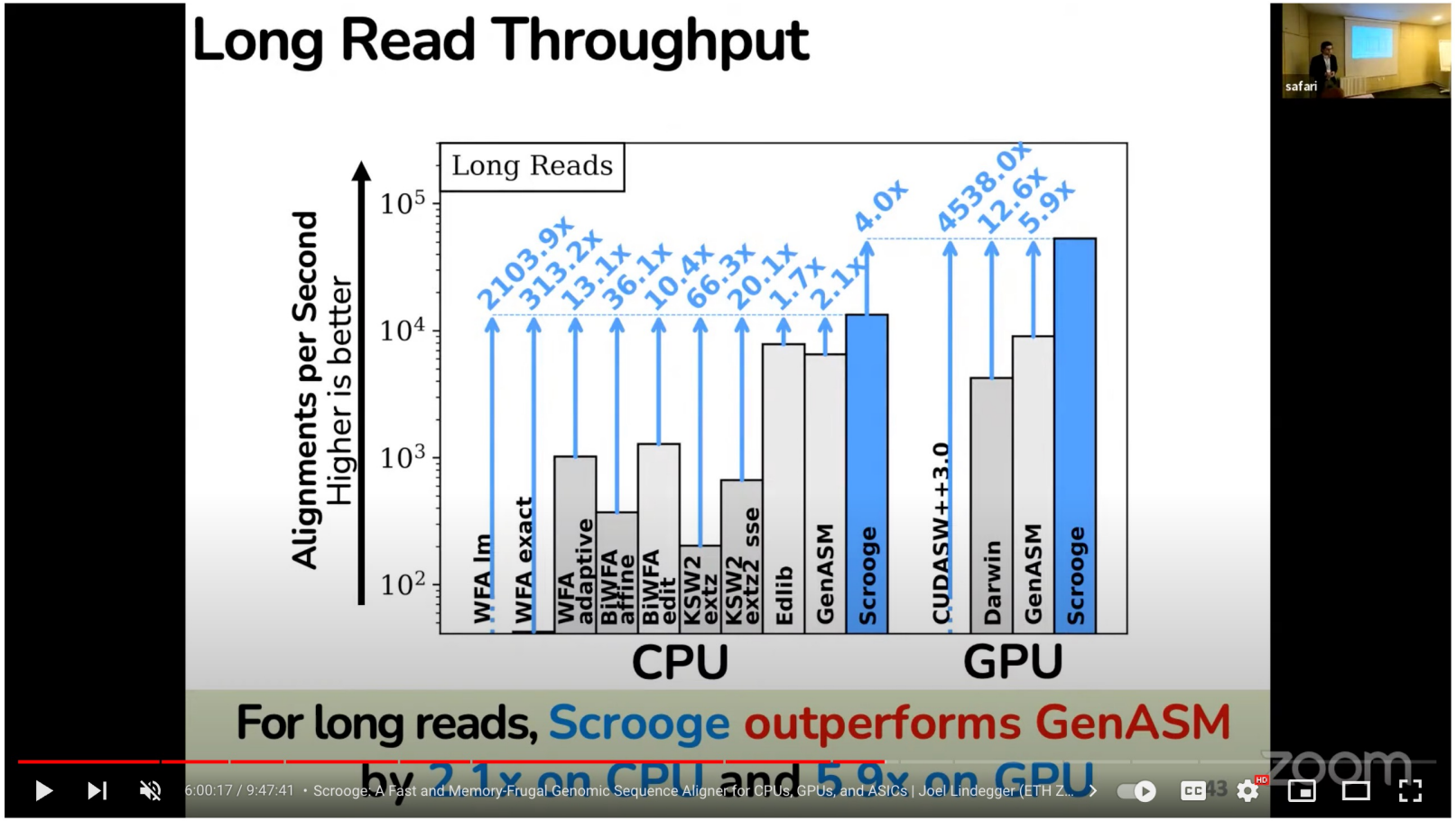
C 33.5% C++ 32.4%

Python 18.1% Cuda 14.5%

Makefile 0.9% Shell 0.6%

Scrooge on GitHub

Scrooge Talk Video



BIO-Arch: Workshop on Hardware Acceleration of Bioinformatics Workloads

Onur Mutlu Lectures
32.9K subscribers

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1,447 views Streamed live on Apr 14, 2023
BIO-Arch: Workshop on Hardware Acceleration of Bioinformatics Workloads
https://safari.ethz.ch/recomb23-arch-...

https://www.youtube.com/watch?v=2rCsb4-nLmg&t=20313s

Accelerating Sequence-to-Graph Mapping

- Damla Senol Cali, Konstantinos Kanellopoulos, Joel Lindegger, Zulal Bingol, Gurpreet S. Kalsi, Ziyi Zuo, Can Firtina, Meryem Banu Cavlak, Jeremie Kim, Nika MansouriGhiasi, Gagandeep Singh, Juan Gomez-Luna, Nour Almadhoun Alserr, Mohammed Alser, Sreenivas Subramoney, Can Alkan, Saugata Ghose, and Onur Mutlu,
  "SeGraM: A Universal Hardware Accelerator for Genomic Sequence-to-Graph and Sequence-to-Sequence Mapping"
  *Proceedings of the 49th International Symposium on Computer Architecture (**ISCA**)*, New York, June 2022.
  [arXiv version]

SeGraM: A Universal Hardware Accelerator for Genomic Sequence-to-Graph and Sequence-to-Sequence Mapping

Damla Senol Cali[1] Konstantinos Kanellopoulos[2] Joël Lindegger[2] Zülal Bingöl[3]
Gurpreet S. Kalsi[4] Ziyi Zuo[5] Can Firtina[2] Meryem Banu Cavlak[2] Jeremie Kim[2]
Nika Mansouri Ghiasi[2] Gagandeep Singh[2] Juan Gómez-Luna[2] Nour Almadhoun Alserr[2]
Mohammed Alser[2] Sreenivas Subramoney[4] Can Alkan[3] Saugata Ghose[6] Onur Mutlu[2]

[1]Bionano Genomics [2]ETH Zürich [3]Bilkent University [4]Intel Labs
[5]Carnegie Mellon University [6]University of Illinois Urbana-Champaign

Genome Sequence Analysis

- Mapping the reads to a reference genome (i.e., ***read mapping***) is a *critical step* in genome sequence analysis

Linear Reference: ACGTACGT

Read: ACGG

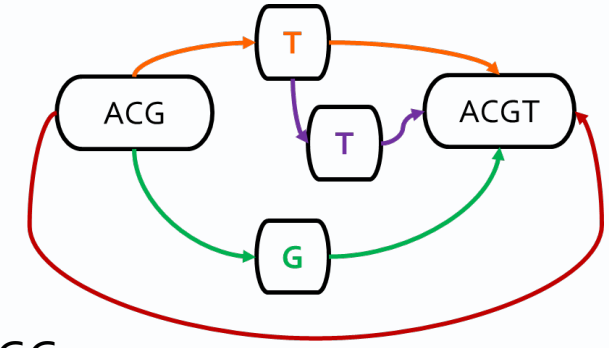
Alternative Sequence: ACGGACGT

Alternative Sequence: ACGTTACGT

Alternative Sequence: ACG–ACGT

Sequence-to-Sequence (S2S) Mapping

Graph-based Reference:



Read: ACGG

Sequence-to-Graph (S2G) Mapping

Sequence-to-graph mapping results in **notable quality improvements.**

However, it is a **more difficult** computational problem,

with **no prior hardware design.**

SeGraM: First Graph Mapping Accelerator

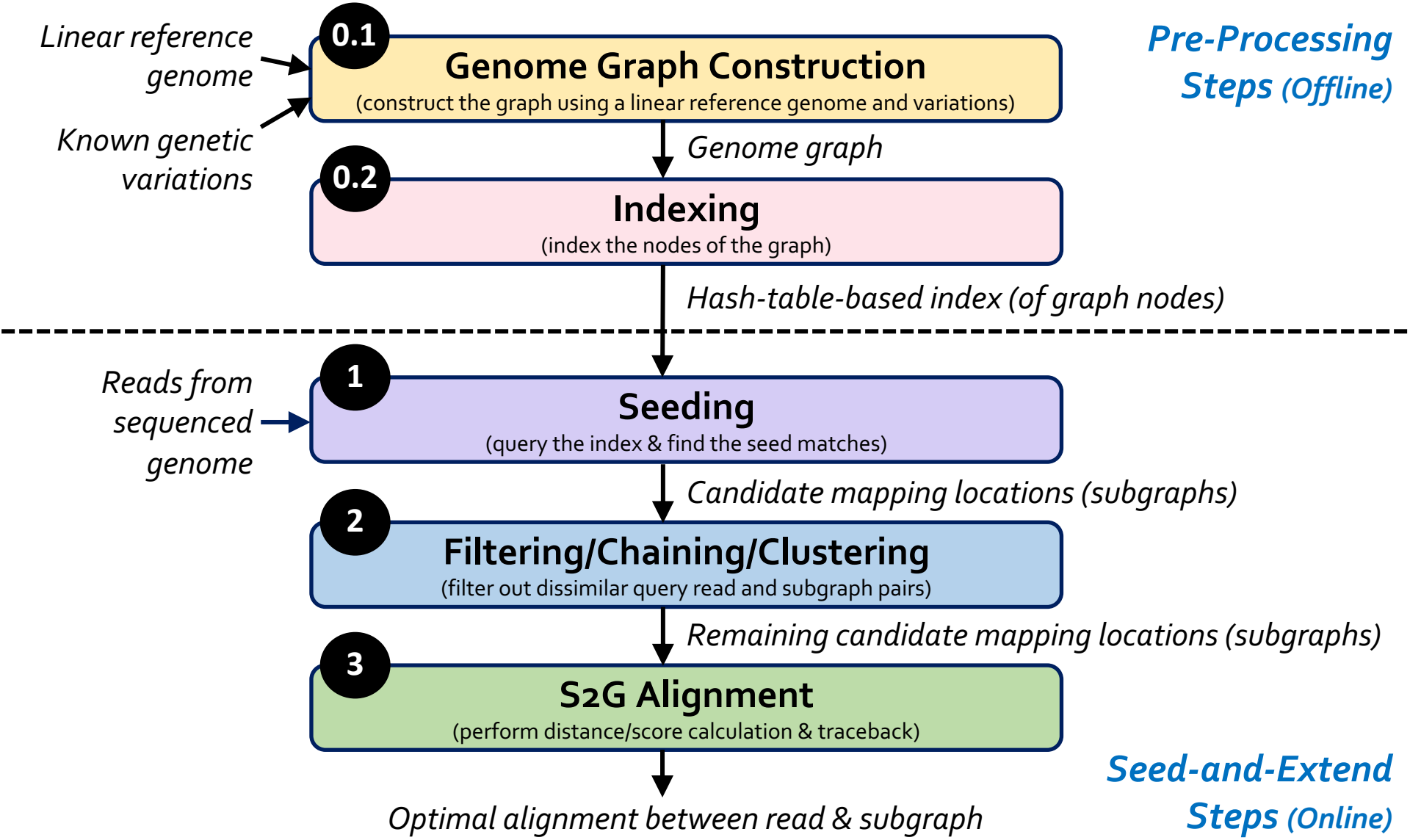
Our Goal:

Specialized, high-performance, scalable, and low-cost algorithm/hardware co-design that alleviates bottlenecks in **multiple steps** of sequence-to-graph mapping

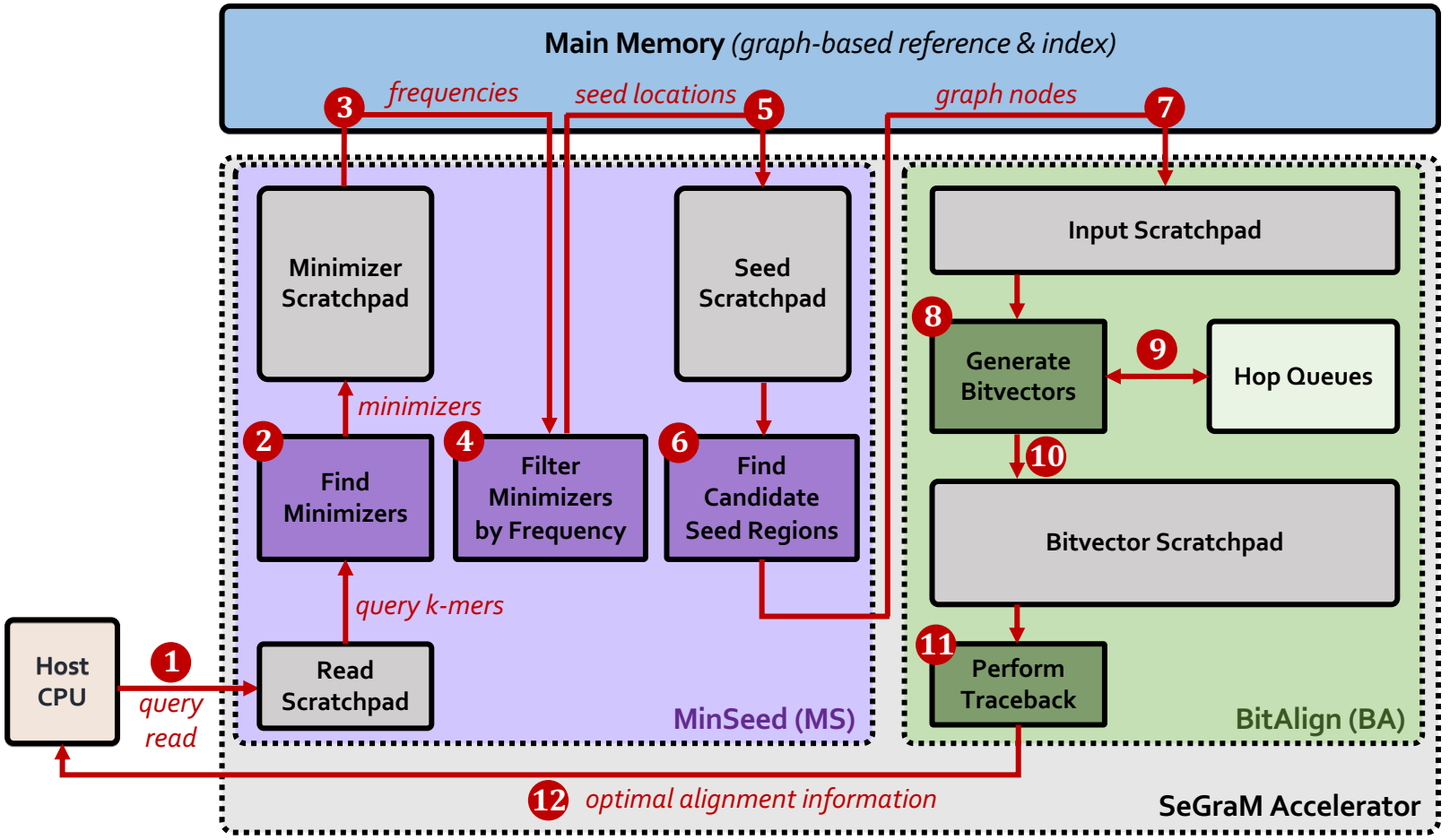
SeGraM: *First universal algorithm/hardware co-designed genomic mapping accelerator* that can effectively and efficiently support:

- Sequence-to-graph mapping
- Sequence-to-sequence mapping
- Both short and long reads

Sequence-to-Graph Mapping Pipeline



SeGraM Hardware Design



MinSeed: *first* hardware accelerator for **Min**imizer-based **Seed**ing

BitAlign: *first* hardware accelerator for (**Bit**vector-based) sequence-to-graph **Align**ment

Use Cases & Key Results

(1) Sequence-to-Graph (S2G) Mapping

- **5.9×/106×** speedup, **4.1×/3.0×** less power than **GraphAligner** for long and short reads, respectively (state-of-the-art **SW**)
- **3.9×/742×** speedup, **4.4×/3.2×** less power than **vg** for long and short reads, respectively (state-of-the-art **SW**)

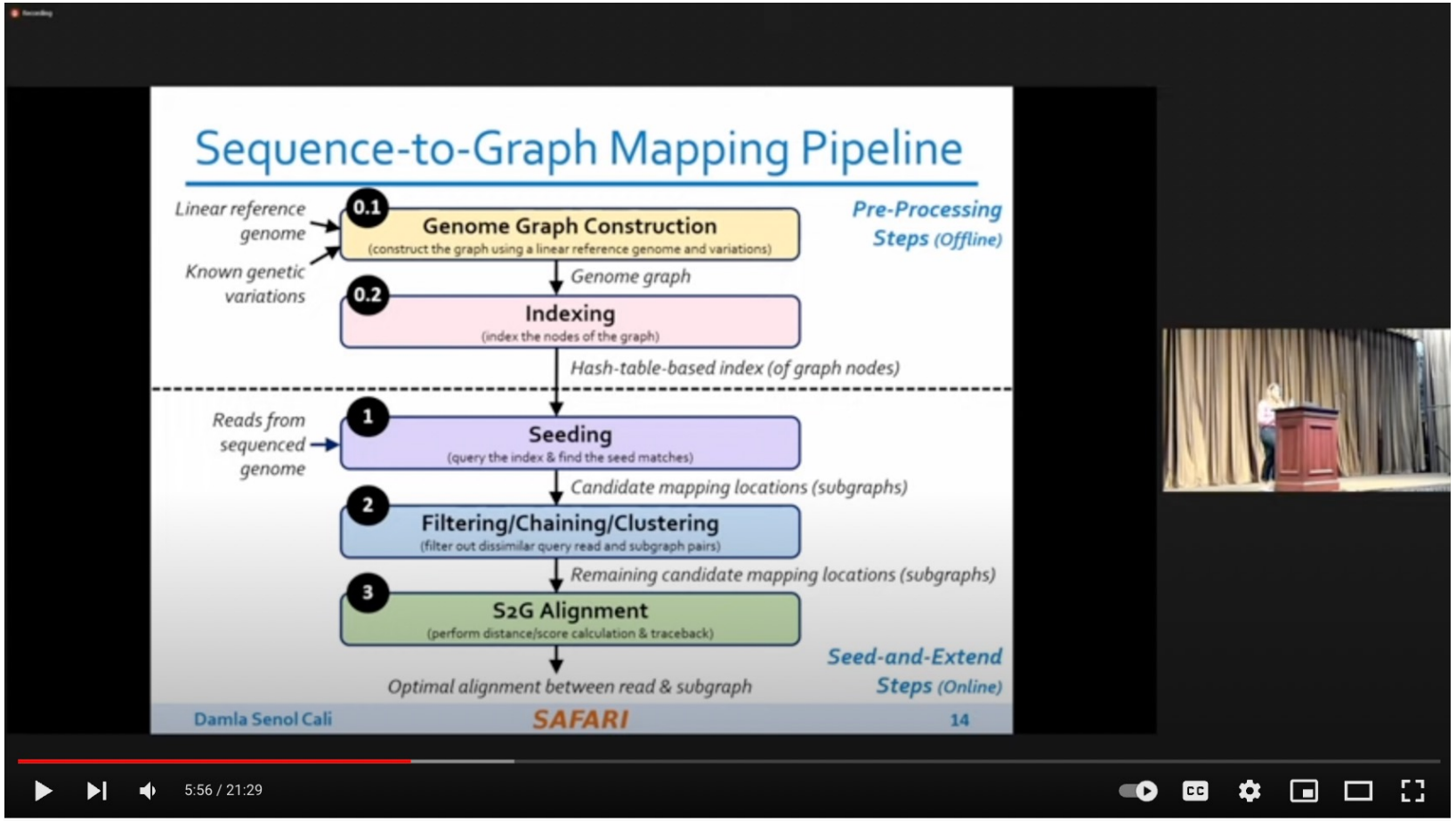
(2) Sequence-to-Graph (S2G) Alignment

- **41×–539×** speedup over **PaSGAL** with AVX-512 support (state-of-the-art **SW**)

(3) Sequence-to-Sequence (S2S) Alignment

- **1.2×/4.8×** higher throughput than **GenASM** and **GACT of Darwin** for long reads (state-of-the-art **HW**)
- **1.3×/2.4×** higher throughput than **GenASM** and **SillaX of GenAX** for short reads (state-of-the-art **HW**)

SeGraM Talk Video



https://www.youtube.com/watch?v=gyjqYoyDP9s

Accelerating Sequence-to-Graph Mapping

- Damla Senol Cali, Konstantinos Kanellopoulos, Joel Lindegger, Zulal Bingol, Gurpreet S. Kalsi, Ziyi Zuo, Can Firtina, Meryem Banu Cavlak, Jeremie Kim, Nika MansouriGhiasi, Gagandeep Singh, Juan Gomez-Luna, Nour Almadhoun Alserr, Mohammed Alser, Sreenivas Subramoney, Can Alkan, Saugata Ghose, and Onur Mutlu,
  "SeGraM: A Universal Hardware Accelerator for Genomic Sequence-to-Graph and Sequence-to-Sequence Mapping"
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  [arXiv version]

SeGraM: A Universal Hardware Accelerator for Genomic Sequence-to-Graph and Sequence-to-Sequence Mapping

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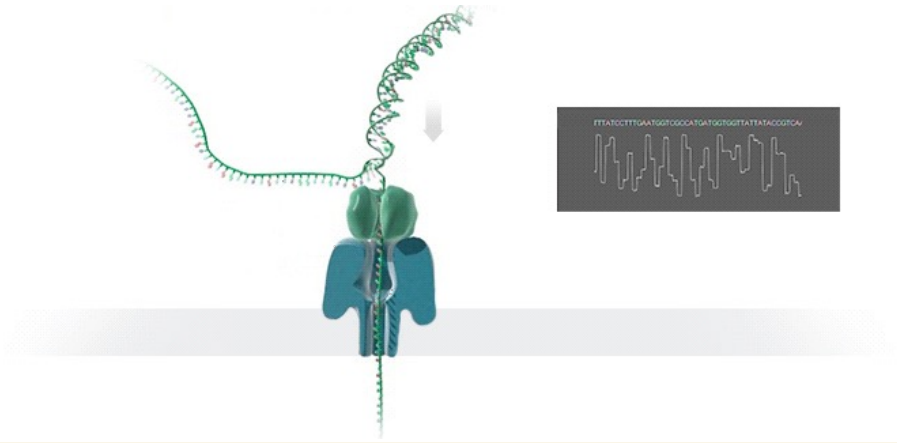
[1]Bionano Genomics [2]ETH Zürich [3]Bilkent University [4]Intel Labs
[5]Carnegie Mellon University [6]University of Illinois Urbana-Champaign

Designing & Accelerating Basecallers

A Framework for Designing Efficient Deep Learning-Based Genomic Basecallers

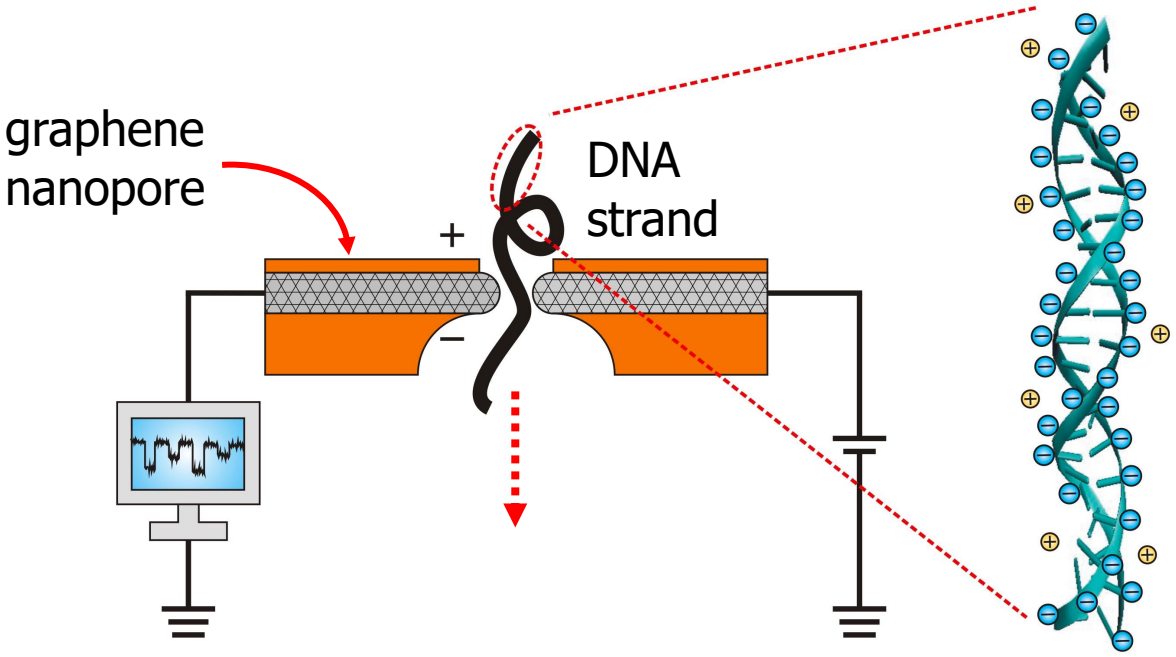
Gagandeep Singh[a] Mohammed Alser*[a] Alireza Khodamoradi*[b]
Kristof Denolf[b] Can Firtina[a] Meryem Banu Cavlak[a]
Henk Corporaal[c] Onur Mutlu[a]
[a]ETH Zürich [b]AMD [c]Eindhoven University of Technology

Nanopore sequencing is a widely-used high-throughput genome sequencing technology that can sequence long fragments of a genome. Nanopore sequencing generates noisy electrical signals that need to be converted into a standard string of DNA nucleotide bases (i.e., A, C, G, T) using a computational step called *basecalling*. The accuracy and speed of basecalling have critical implications for every subsequent step in genome analysis. Currently, basecallers are developed mainly based on deep learning techniques to provide high sequencing accuracy without considering the compute demands of such tools. We observe that state-of-the-art basecallers (i.e., Guppy, Bonito, Fast-Bonito) are slow, inefficient, and memory-hungry



https://arxiv.org/pdf/2211.03079.pdf

How Does a Nanopore Machine Work?



- **Nanopore** is a nano-scale hole (<20nm).
- In nanopore sequencers, an **ionic current** passes through the nanopores
- When the DNA strand passes through the nanopore, the sequencer measures the the **change in current**
- This change is used to identify the bases in the strand with the help of **different electrochemical structures** of the different bases

Figure is adapted from: https://phys.org/news/2013-12-gene-sequencing-future.html

Accelerating Basecallers: Software Methods

- M. Banu Cavlak, Gagandeep Singh, Mohammed Alser, Can Firtina, Joel Lindegger, Mohammad Sadrosadati, Nika Mansouri Ghiasi, Can Alkan, and Onur Mutlu, **"TargetCall: Eliminating the Wasted Computation in Basecalling via Pre-Basecalling Filtering"**
  Proceedings of the 21st Asia Pacific Bioinformatics Conference (***APBC***), Changsha, China, April 2023.
  [TargetCall Source Code]
  [arxiv.org Version]
  [Talk Video at BIO-Arch 2023 Workshop]

TargetCall: Eliminating the Wasted Computation in Basecalling via Pre-Basecalling Filtering

Meryem Banu Cavlak[1] Gagandeep Singh[1] Mohammed Alser[1] Can Firtina[1] Joël Lindegger[1]
Mohammad Sadrosadati[1] Nika Mansouri Ghiasi[1] Can Alkan[2] Onur Mutlu[1]
[1]*ETH Zürich* [2]*Bilkent University*

New Frontiers: Raw Signal Analysis

- Can Firtina, Nika Mansouri Ghiasi, Joel Lindegger, Gagandeep Singh, Meryem Banu Cavlak, Haiyu Mao, and Onur Mutlu,
  "RawHash: Enabling Fast and Accurate Real-Time Analysis of Raw Nanopore Signals for Large Genomes"
  *Proceedings of the 31st Annual Conference on Intelligent Systems for Molecular Biology and the 22nd European Conference on Computational Biology (**ISMB/ECCB**)*, Lyon, France, July 2023.
  [RawHash Source Code]

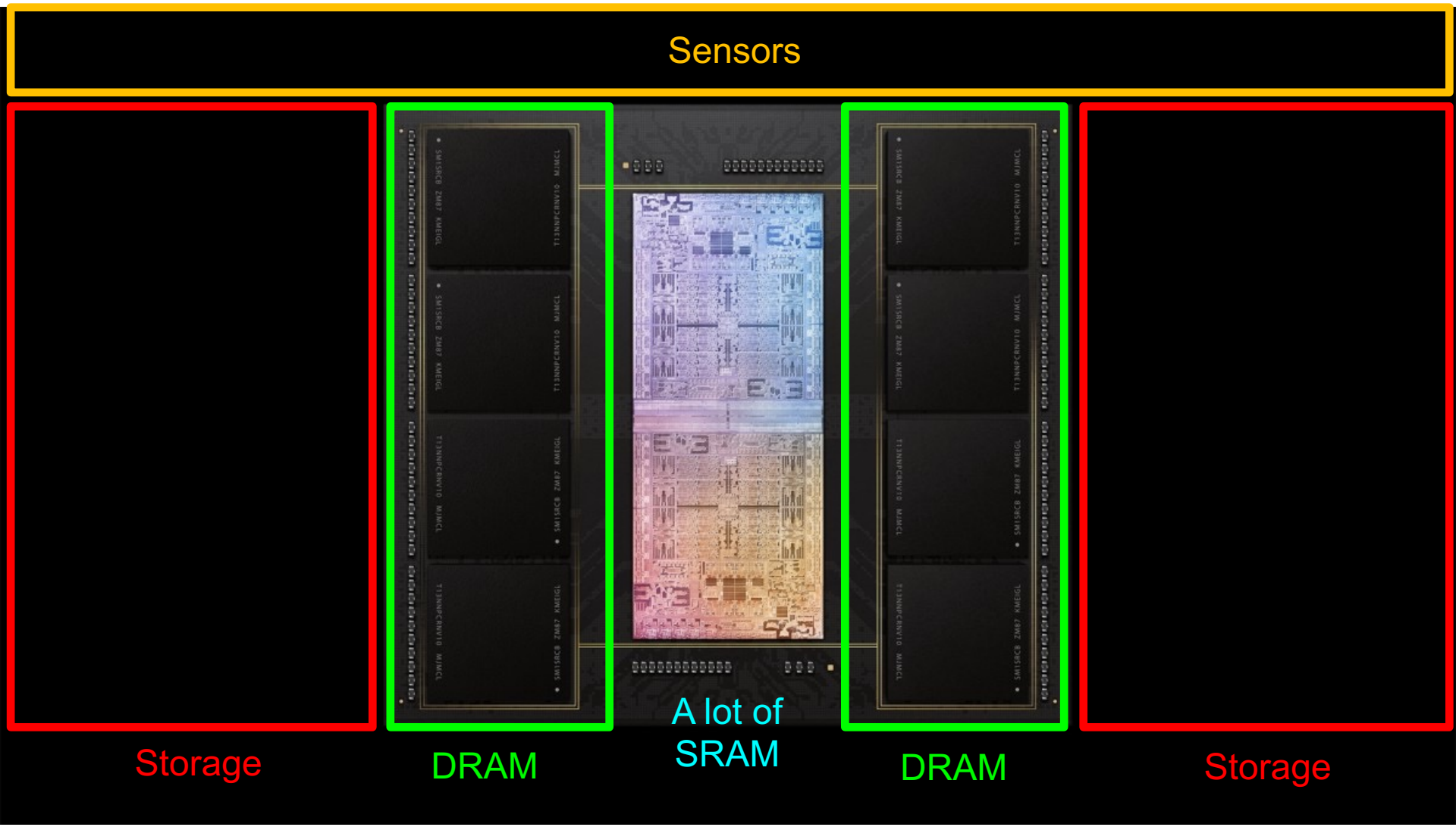
RawHash: Enabling Fast and Accurate Real-Time Analysis of Raw Nanopore Signals for Large Genomes

Can Firtina[1] Nika Mansouri Ghiasi[1] Joel Lindegger[1] Gagandeep Singh[1]
Meryem Banu Cavlak[1] Haiyu Mao[1] Onur Mutlu[1]
[1]*ETH Zurich*

Agenda

- The Problem: DNA Read Mapping
  - State-of-the-art Read Mapper Design
- Algorithmic Acceleration
  - Exploiting Structure of the Genome
  - Exploiting SIMD Instructions
- Hardware Acceleration
  - Specialized Architectures
  - Processing in Memory & Storage
- Future Opportunities: New Technologies & Applications

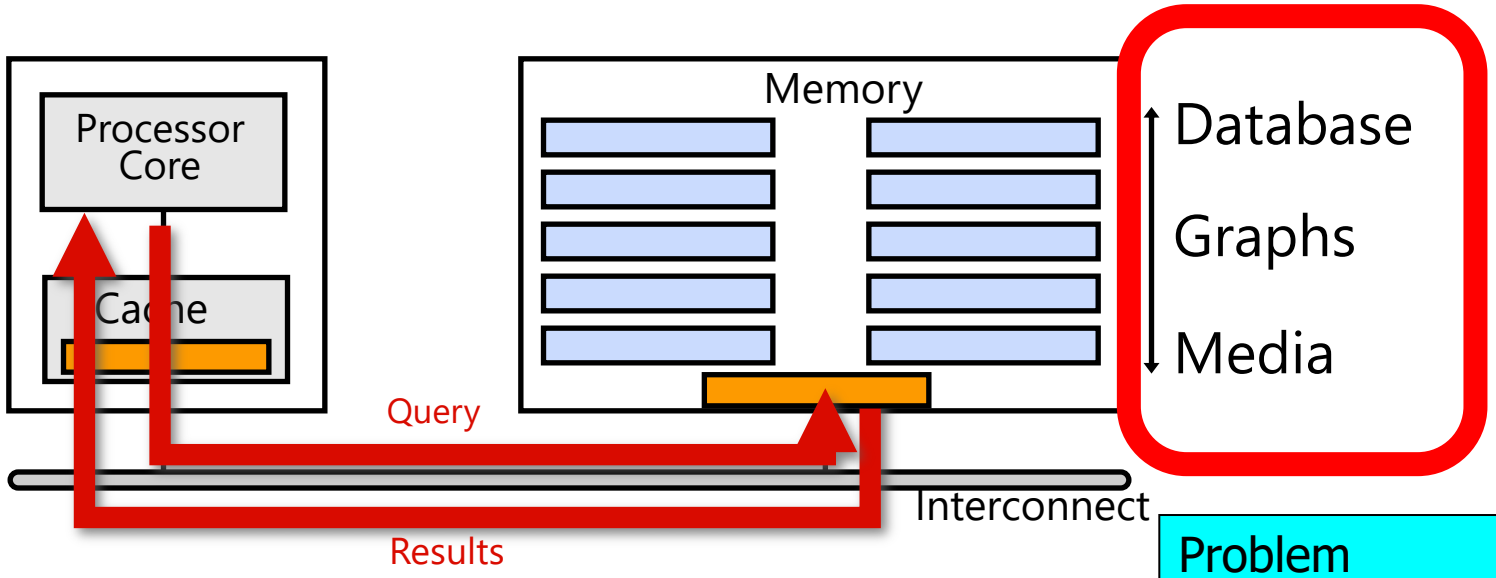
Process Data Where It Makes Sense



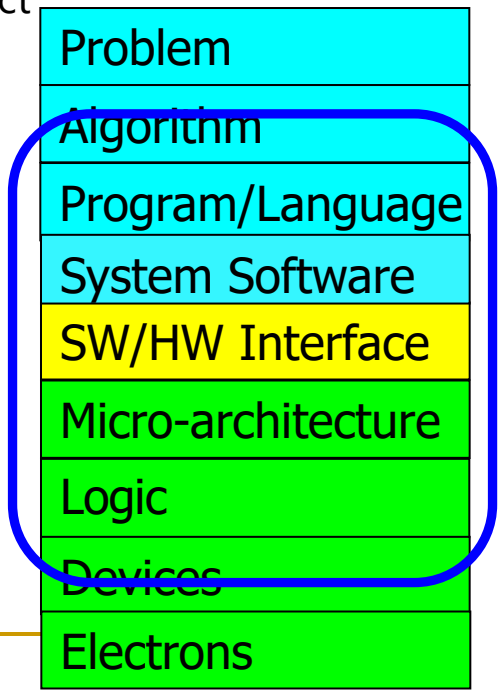
Apple M1 Ultra System (2022)

https://www.gsmarena.com/apple_announces_m1_ultra_with_20core_cpu_and_64core_gpu-news-53481.php

Goal: Processing Inside Memory



- Many questions … How do we design the:
  - compute-capable memory & controllers?
  - processors & communication units?
  - software & hardware interfaces?
  - system software, compilers, languages?
  - algorithms & theoretical foundations?



Read Mapping & Filtering in Memory

We need to design

mapping & filtering algorithms

that fit processing-in-memory

Near-Memory Pre-Alignment Filtering

Gagandeep Singh, Mohammed Alser, Damla Senol Cali, Dionysios Diamantopoulos, Juan Gomez-Luna, Henk Corporaal, Onur Mutlu,
"**FPGA-Based Near-Memory Acceleration of Modern Data-Intensive Applications**"
IEEE Micro, 2021.
[Source Code]

Previous | Next

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IEEE Micro

FPGA-Based Near-Memory Acceleration of Modern Data-Intensive Applications

July-Aug. 2021, pp. 39-48, vol. 41
DOI Bookmark: 10.1109/MM.2021.3088396

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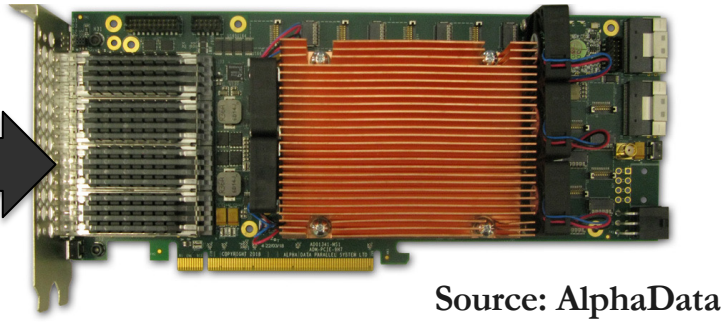
Juan Gomez-Luna, ETH Zürich, Zürich, Switzerland
Henk Corporaal, Eindhoven University of Technology, Eindhoven, The Netherlands
Onur Mutlu, ETH Zürich, Zürich, Switzerland

Near-Memory SneakySnake

- Problem: Read mapping is heavily bottlenecked by data movement from main memory
- Solution: Perform read mapping near where data resides using specialized logic
- We carefully redesign the accelerator logic of SneakySnake to exploit near-memory computation capability on real FPGA boards that use HBM (high-bandwidth memory)
- **Near-memory SneakySnake** improves **performance** and **energy efficiency** by 27.4× and 133×, respectively, over a 16-core (64-thread) IBM POWER9 CPU

Near-Memory Acceleration using FPGAs

IBM POWER9 CPU

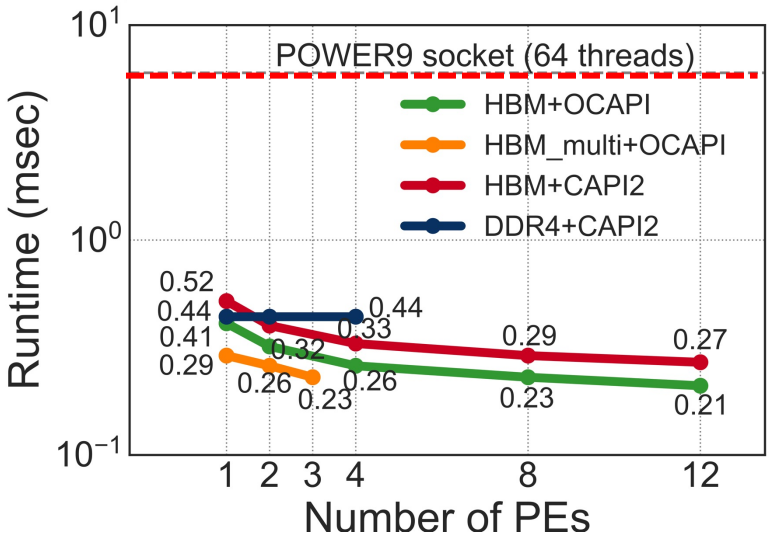


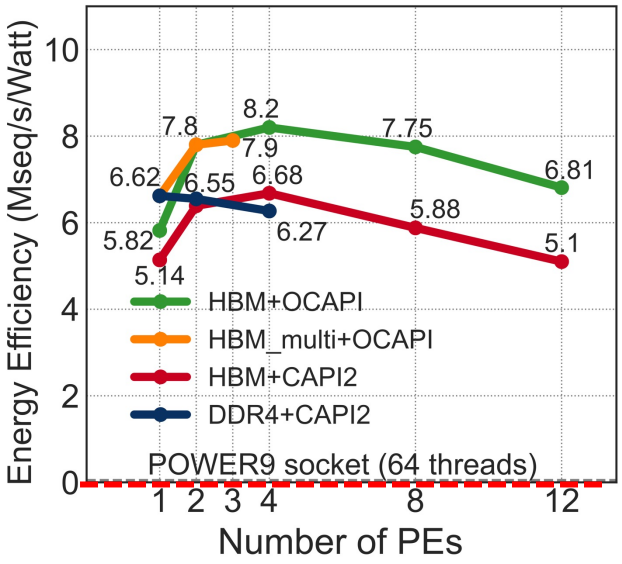
HBM-based FPGA board

Near-HBM FPGA-based accelerator

Two communication technologies: **CAPI2** and **OCAPI**
Two memory technologies: **DDR4** and **HBM**
Two workloads: **Weather Modeling** and **Genome Analysis**

Performance & Energy Greatly Improve





5-27× performance vs. a 16-core (64-thread) IBM POWER9 CPU

12-133× energy efficiency vs. a 16-core (64-thread) IBM POWER9 CPU

HBM alleviates memory bandwidth contention vs. DDR4

More On Near-Memory SneakySnake

Gagandeep Singh, Mohammed Alser, Damla Senol Cali, Dionysios Diamantopoulos, Juan Gomez-Luna, Henk Corporaal, Onur Mutlu,
"**FPGA-Based Near-Memory Acceleration of Modern Data-Intensive Applications**"
IEEE Micro, 2021.
[Source Code]

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IEEE Micro

FPGA-Based Near-Memory Acceleration of Modern Data-Intensive Applications

July-Aug. 2021, pp. 39-48, vol. 41
DOI Bookmark: 10.1109/MM.2021.3088396

Authors

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Damla Senol Cali, Carnegie Mellon University, Pittsburgh, PA, USA
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Juan Gomez-Luna, ETH Zürich, Zürich, Switzerland
Henk Corporaal, Eindhoven University of Technology, Eindhoven, The Netherlands
Onur Mutlu, ETH Zürich, Zürich, Switzerland

Location Filtering in 3D-Stacked PIM

- Jeremie S. Kim, Damla Senol Cali, Hongyi Xin, Donghyuk Lee, Saugata Ghose, Mohammed Alser, Hasan Hassan, Oguz Ergin, Can Alkan, and Onur Mutlu,
  "GRIM-Filter: Fast Seed Location Filtering in DNA Read Mapping Using Processing-in-Memory Technologies"
  BMC Genomics, 2018.
  *Proceedings of the 16th Asia Pacific Bioinformatics Conference (**APBC**)*, Yokohama, Japan, January 2018.
  [Slides (pptx) (pdf)]
  [Source Code]
  [arxiv.org Version (pdf)]
  [Talk Video at AACBB 2019]

Research | Open Access | Published: 09 May 2018

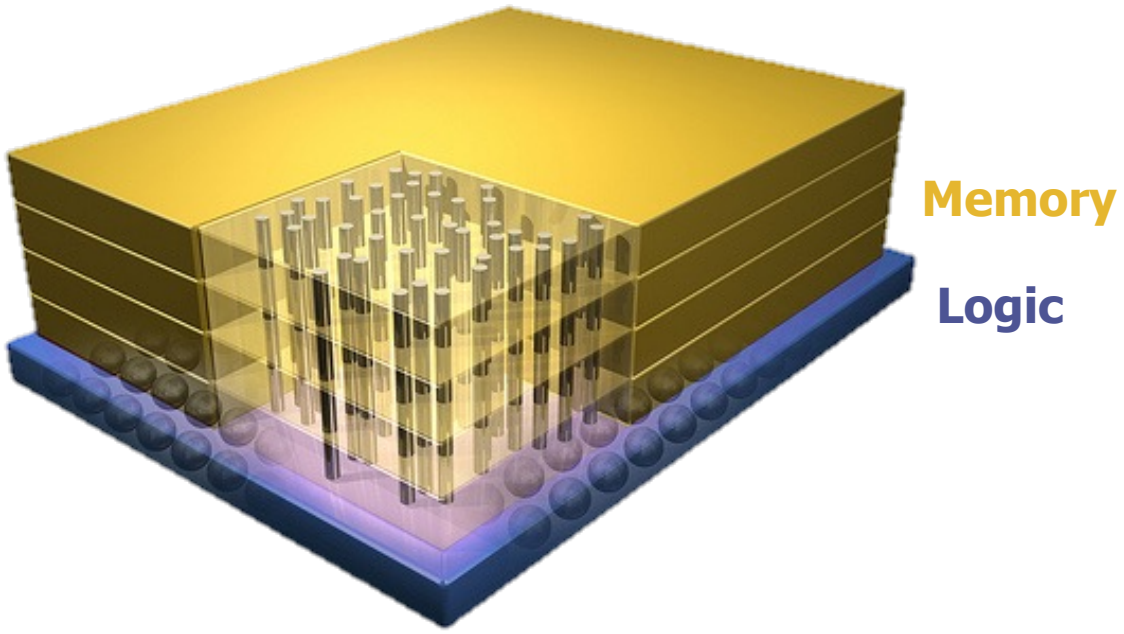
GRIM-Filter: Fast seed location filtering in DNA read mapping using processing-in-memory technologies

Jeremie S. Kim, Damla Senol Cali, Hongyi Xin, Donghyuk Lee, Saugata Ghose, Mohammed Alser, Hasan Hassan, Oguz Ergin, Can Alkan & Onur Mutlu

BMC Genomics **19**, Article number: 89 (2018) | Cite this article

4340 Accesses | **39** Citations | **9** Altmetric | Metrics

Opportunity: 3D-Stacked Logic+Memory



Other "True 3D" technologies under development

In-Storage Genome Filtering [ASPLOS 2022]

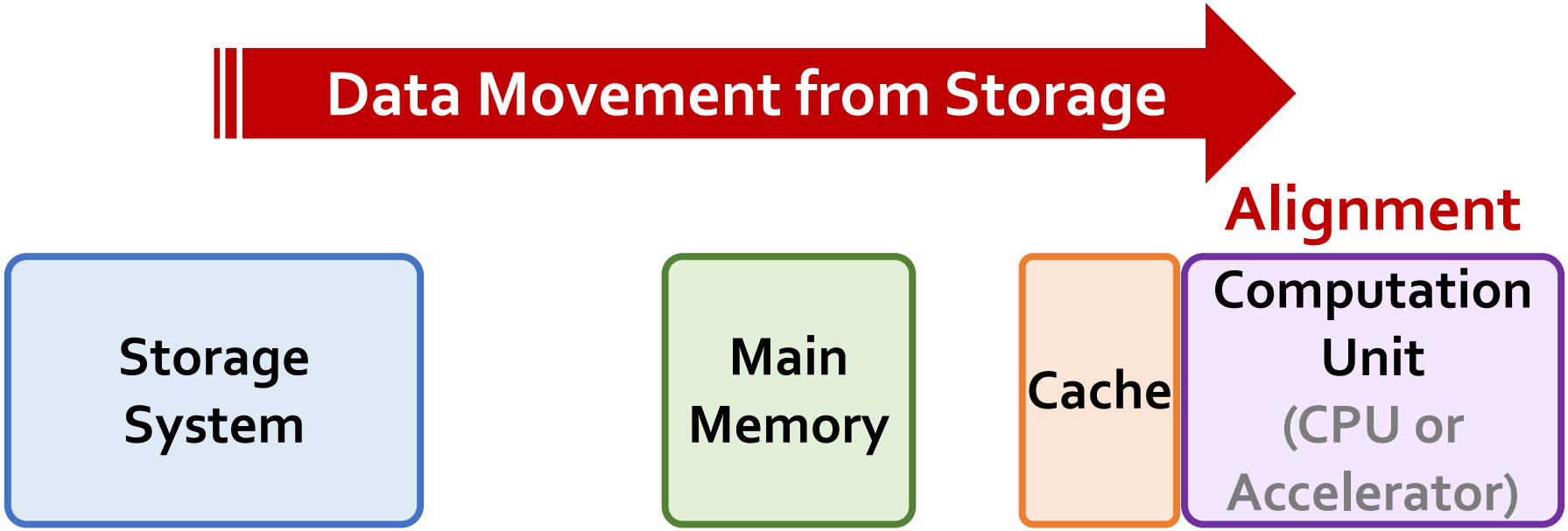
- Nika Mansouri Ghiasi, Jisung Park, Harun Mustafa, Jeremie Kim, Ataberk Olgun, Arvid Gollwitzer, Damla Senol Cali, Can Firtina, Haiyu Mao, Nour Almadhoun Alserr, Rachata Ausavarungnirun, Nandita Vijaykumar, Mohammed Alser, and Onur Mutlu,
  "GenStore: A High-Performance and Energy-Efficient In-Storage Computing System for Genome Sequence Analysis"
  *Proceedings of the 27th International Conference on Architectural Support for Programming Languages and Operating Systems (**ASPLOS**)*, Virtual, February-March 2022.
  [Lightning Talk Slides (pptx) (pdf)]
  [Lightning Talk Video (90 seconds)]

GenStore: A High-Performance In-Storage Processing 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

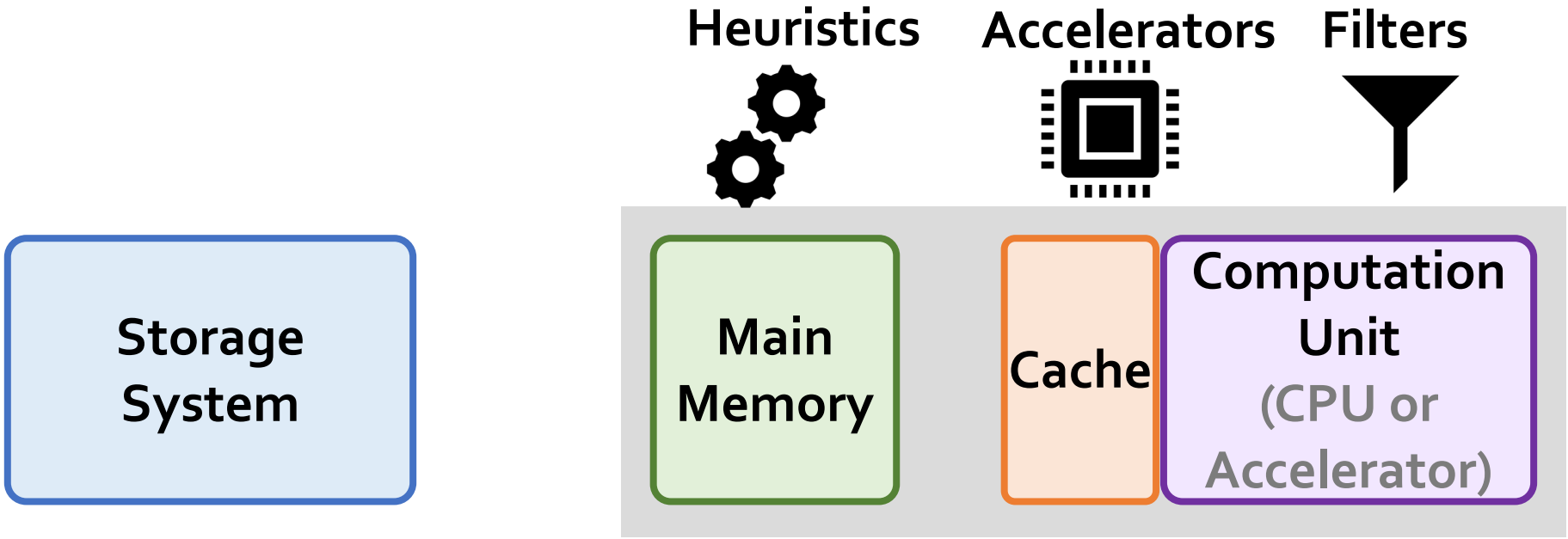
Genome Sequence Analysis



✗ Computation overhead

✗ Data movement overhead

Accelerating Genome Sequence Analysis

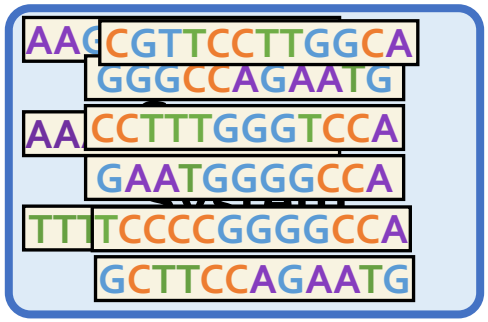


✓ Computation overhead

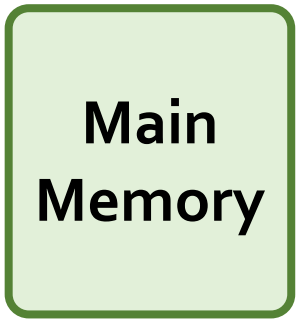
✗ Data movement overhead

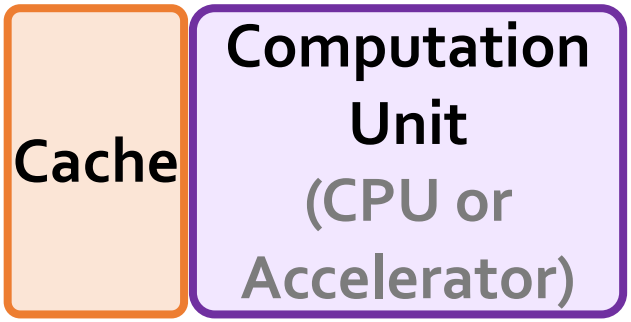
Key Idea

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

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

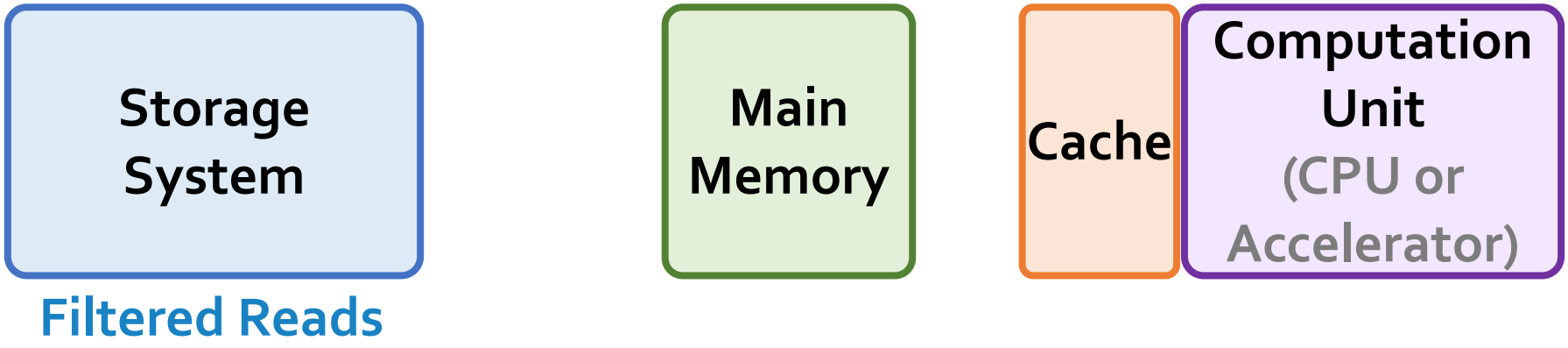
Non-matching reads

Do not have potential matching locations, so they skip alignment

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

Challenges

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

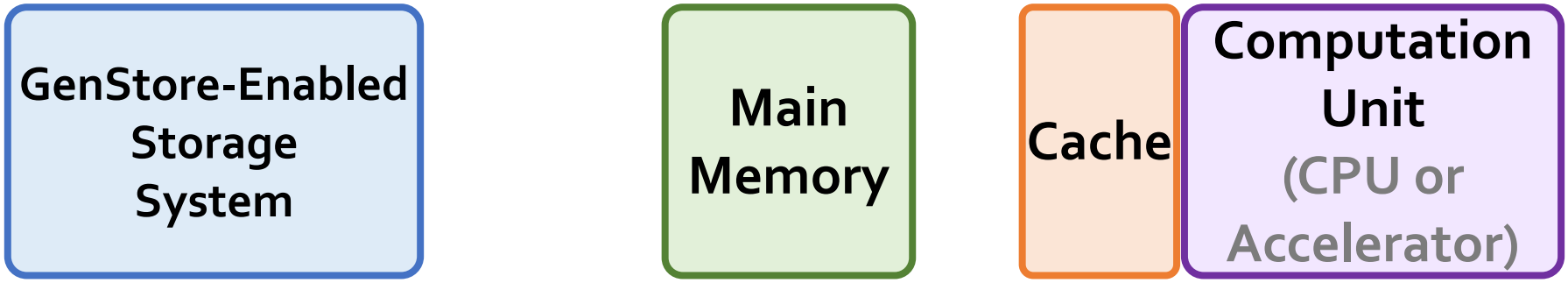


Read mapping workloads can exhibit different behavior

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

In-Storage Genome Filtering [ASPLOS 2022]

- 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,
  "GenStore: A High-Performance and Energy-Efficient In-Storage Computing System for Genome Sequence Analysis"
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[1]ETH Zürich [2]Bionano Genomics [3]KMUTNB [4]University of Toronto

PIM Review and Open Problems

A Modern Primer on Processing in Memory

Onur Mutlu[a,b], Saugata Ghose[b,c], Juan Gómez-Luna[a], Rachata Ausavarungnirun[d]

SAFARI Research Group

[a] *ETH Zürich*
[b] *Carnegie Mellon University*
[c] *University of Illinois at Urbana-Champaign*
[d] *King Mongkut's University of Technology North Bangkok*

Onur Mutlu, Saugata Ghose, Juan Gomez-Luna, and Rachata Ausavarungnirun,
"A Modern Primer on Processing in Memory"
Invited Book Chapter in ***Emerging Computing: From Devices to Systems - Looking Beyond Moore and Von Neumann***, Springer, to be published in 2021.

https://arxiv.org/pdf/1903.03988.pdf

PIM Review and Open Problems (II)

A Workload and Programming Ease Driven Perspective of Processing-in-Memory

Saugata Ghose[†] Amirali Boroumand[†] Jeremie S. Kim[†§] Juan Gómez-Luna[§] Onur Mutlu[§†]

[†]*Carnegie Mellon University* [§]*ETH Zürich*

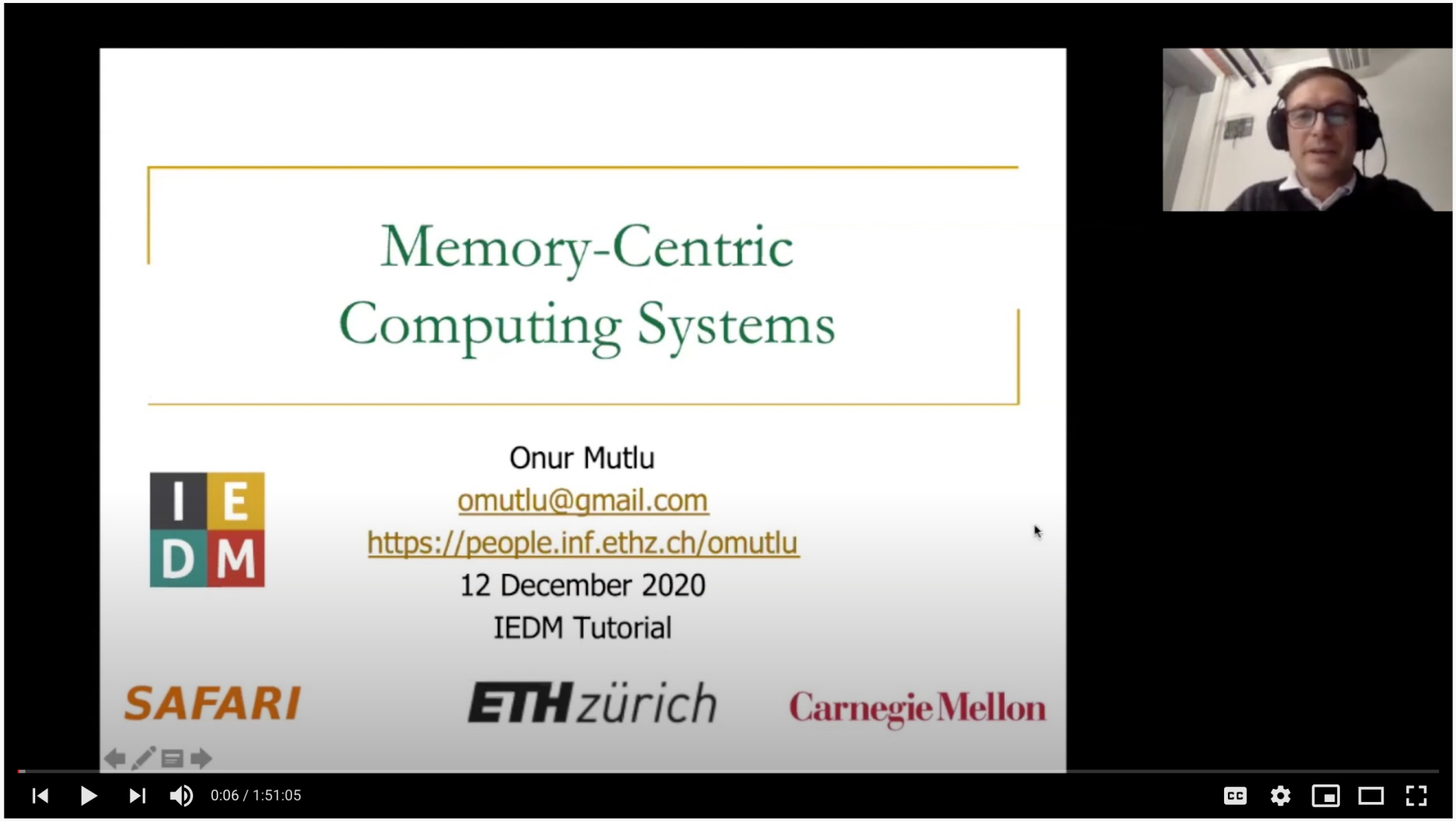
Saugata Ghose, Amirali Boroumand, Jeremie S. Kim, Juan Gomez-Luna, and Onur Mutlu,
"Processing-in-Memory: A Workload-Driven Perspective"
Invited Article in IBM Journal of Research & Development, Special Issue on Hardware for Artificial Intelligence, to appear in November 2019.
[Preliminary arXiv version]

https://arxiv.org/pdf/1907.12947.pdf

More on Processing-in-Memory

- Onur Mutlu,
  "Memory-Centric Computing Systems"
  Invited Tutorial at *66th International Electron Devices Meeting (**IEDM**)*, Virtual, 12 December 2020.
  [Slides (pptx) (pdf)]
  [Executive Summary Slides (pptx) (pdf)]
  [Tutorial Video (1 hour 51 minutes)]
  [Executive Summary Video (2 minutes)]
  [Abstract and Bio]
  [Related Keynote Paper from VLSI-DAT 2020]
  [Related Review Paper on Processing in Memory]

https://www.youtube.com/watch?v=H3sEaINPBOE



IEDM 2020 Tutorial: Memory-Centric Computing Systems, Onur Mutlu, 12 December 2020

1,641 views • Dec 23, 2020

48 0 SHARE SAVE

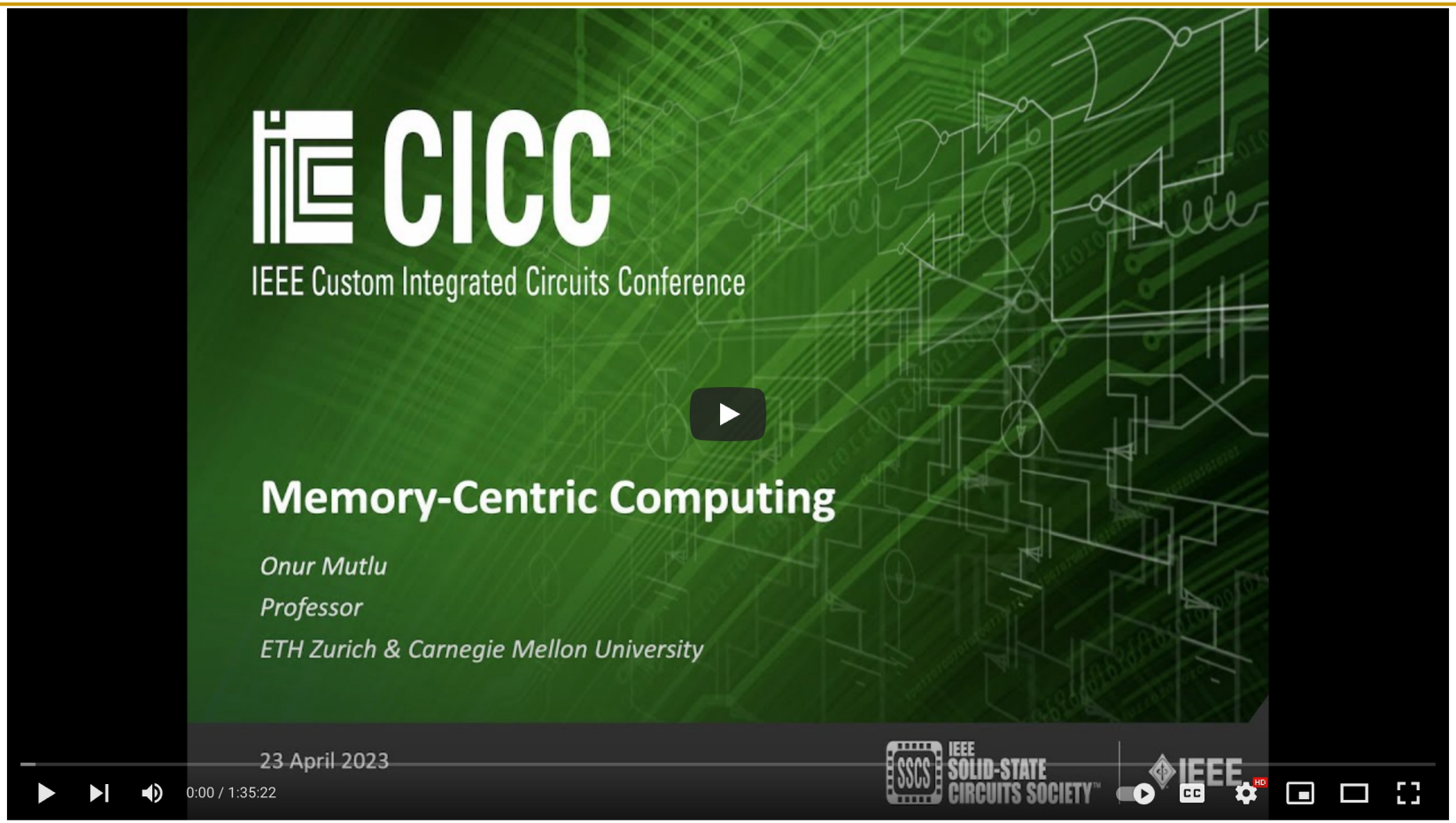
Onur Mutlu Lectures
13.9K subscribers

https://www.youtube.com/watch?v=H3sEaINPBOE

ANALYTICS EDIT VIDEO

https://www.youtube.com/onurmutlulectures

Tutorial on Processing in Memory



IEEE CICC Educational Session Talk on Memory-Centric Computing (Prof. Onur Mutlu)

Onur Mutlu Lectures
32.8K subscribers
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411 views Streamed 2 weeks ago
IEEE CICC Educational Session Talk on Memory-Centric Computing
Presenter: Professor Onur Mutlu (https://people.inf.ethz.ch/omutlu/)

https://www.youtube.com/watch?v=4x9nujJtqjM

https://www.youtube.com/onurmutlulectures

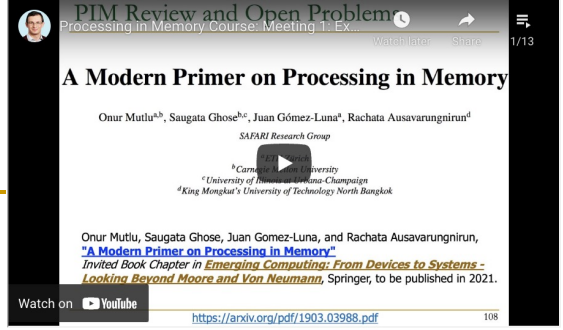
PIM Course (Fall 2022)

- **Fall 2022 Edition:**
  - https://safari.ethz.ch/projects_and_seminars/fall2022/doku.php?id=processing_in_memory
- **Spring 2022 Edition:**
  - https://safari.ethz.ch/projects_and_seminars/spring2022/doku.php?id=processing_in_memory

- **Youtube Livestream (Fall 2022):**
  - https://www.youtube.com/watch?v=QLL0wQ9I4Dw&list=PL5Q2soXY2Zi8KzG2CQYRNQOVD0GOBrnKy
- **Youtube Livestream (Spring 2022):**
  - https://www.youtube.com/watch?v=9e4Chnwdovo&list=PL5Q2soXY2Zi-841fUYYUK9EsXKhQKRPyX

- Project course
  - Taken by Bachelor's/Master's students
  - Processing-in-Memory lectures
  - Hands-on research exploration
  - Many research readings

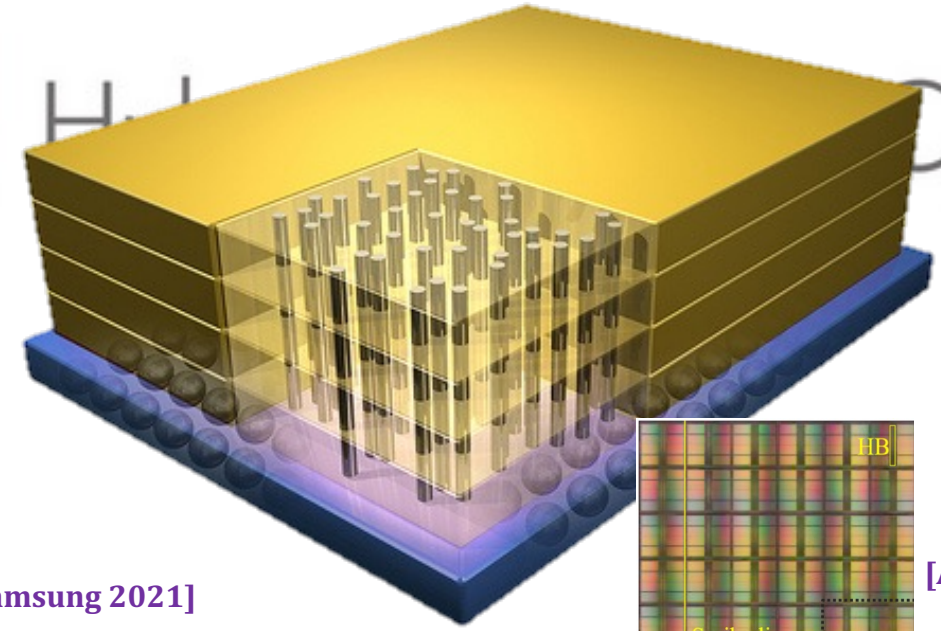
https://www.youtube.com/onurmutlulectures

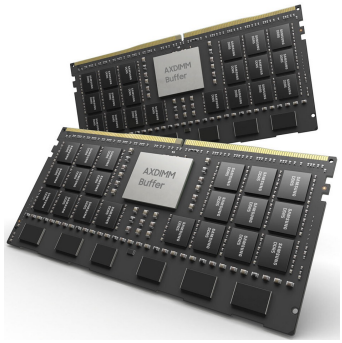


Spring 2022 Meetings/Schedule

Week	Date	Livestream	Meeting	Learning Materials	Assignments
W1	10.03 Thu.	YouTube Live	M1: P&S PIM Course Presentation (PDF) (PPT)	Required Materials Recommended Materials	HW 0 Out
W2	15.03 Tue.		Hands-on Project Proposals		
	17.03 Thu.	YouTube Premiere	M2: Real-world PIM: UPMEM PIM (PDF) (PPT)		
W3	24.03 Thu.	YouTube Live	M3: Real-world PIM: Microbenchmarking of UPMEM PIM (PDF) (PPT)		
W4	31.03 Thu.	YouTube Live	M4: Real-world PIM: Samsung HBM-PIM (PDF) (PPT)		
W5	07.04 Thu.	YouTube Live	M5: How to Evaluate Data Movement Bottlenecks (PDF) (PPT)		
W6	14.04 Thu.	YouTube Live	M6: Real-world PIM: SK Hynix AiM (PDF) (PPT)		
W7	21.04 Thu.	YouTube Premiere	M7: Programming PIM Architectures (PDF) (PPT)		
W8	28.04 Thu.	YouTube Premiere	M8: Benchmarking and Workload Suitability on PIM (PDF) (PPT)		
W9	05.05 Thu.	YouTube Premiere	M9: Real-world PIM: Samsung AxDIMM (PDF) (PPT)		
W10	12.05 Thu.	YouTube Premiere	M10: Real-world PIM: Alibaba HB-PNM (PDF) (PPT)		
W11	19.05 Thu.	YouTube Live	M11: SpMV on a Real PIM Architecture (PDF) (PPT)		
W12	26.05 Thu.	YouTube Live	M12: End-to-End Framework for Processing-using-Memory (PDF) (PPT)		
W13	02.06 Thu.	YouTube Live	M13: Bit-Serial SIMD Processing using DRAM (PDF) (PPT)		
W14	09.06 Thu.	YouTube Live	M14: Analyzing and Mitigating ML Inference Bottlenecks (PDF) (PPT)		
W15	15.06 Thu.	YouTube Live	M15: In-Memory HTAP Databases with HW/SW Co-design (PDF) (PPT)		
W16	23.06 Thu.	YouTube Live	M16: In-Storage Processing for Genome Analysis (PDF) (PPT)		
W17	18.07 Mon.	YouTube Premiere	M17: How to Enable the Adoption of PIM? (PDF) (PPT)		
W18	09.08 Tue.	YouTube Premiere	SS1: ISVLSI 2022 Special Session on PIM (PDF & PPT)		

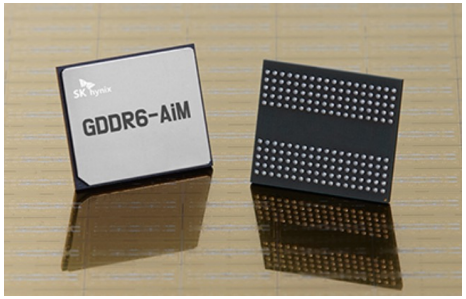
Processing-in-Memory Landscape Today



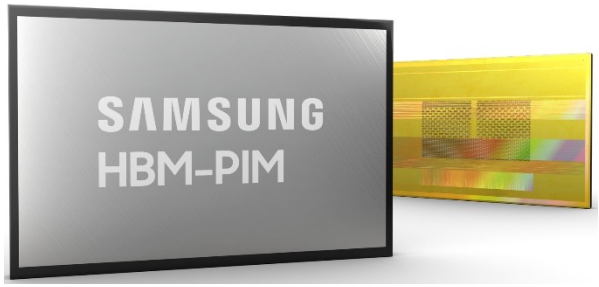


[Samsung 2021]

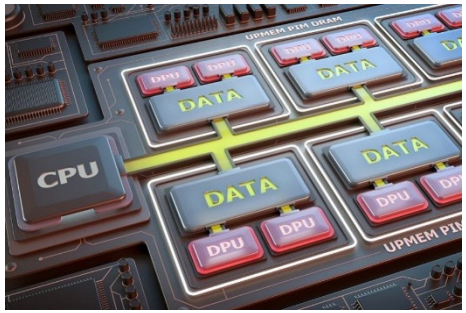
[Alibaba 2022]



[SK Hynix 2022]



[Samsung 2021]

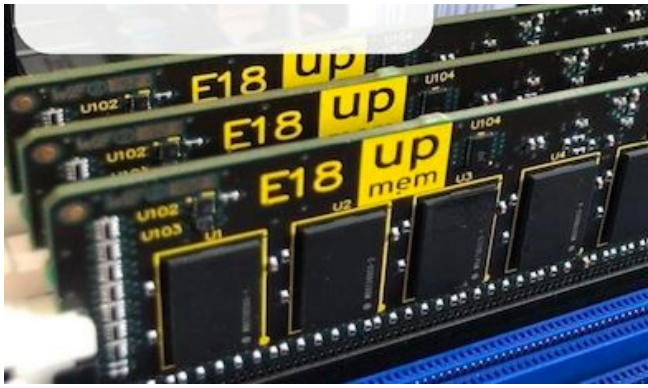


[UPMEM 2019]

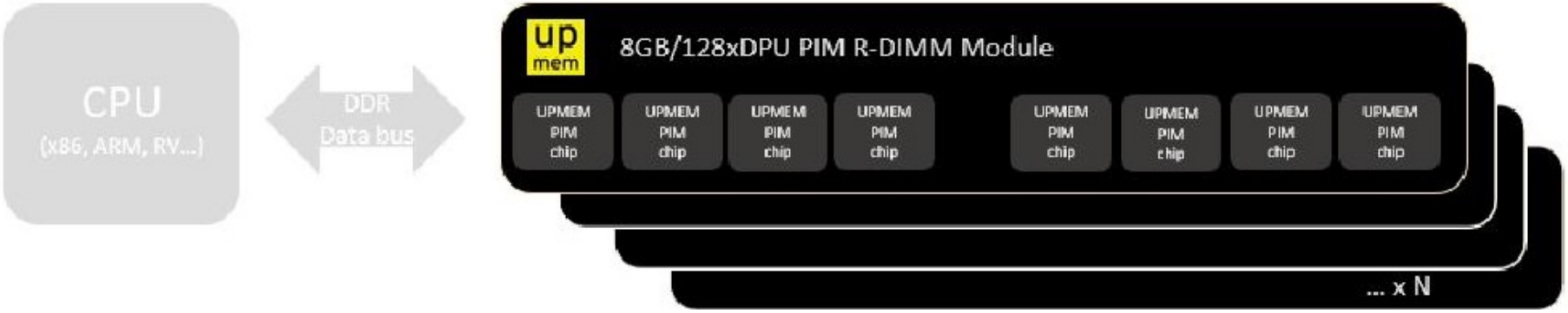
This does not include many experimental chips and startups

UPMEM Processing-in-DRAM Engine (2019)

- Processing in DRAM Engine
- Includes **standard DIMM modules**, with a **large number of DPU processors** combined with DRAM chips.



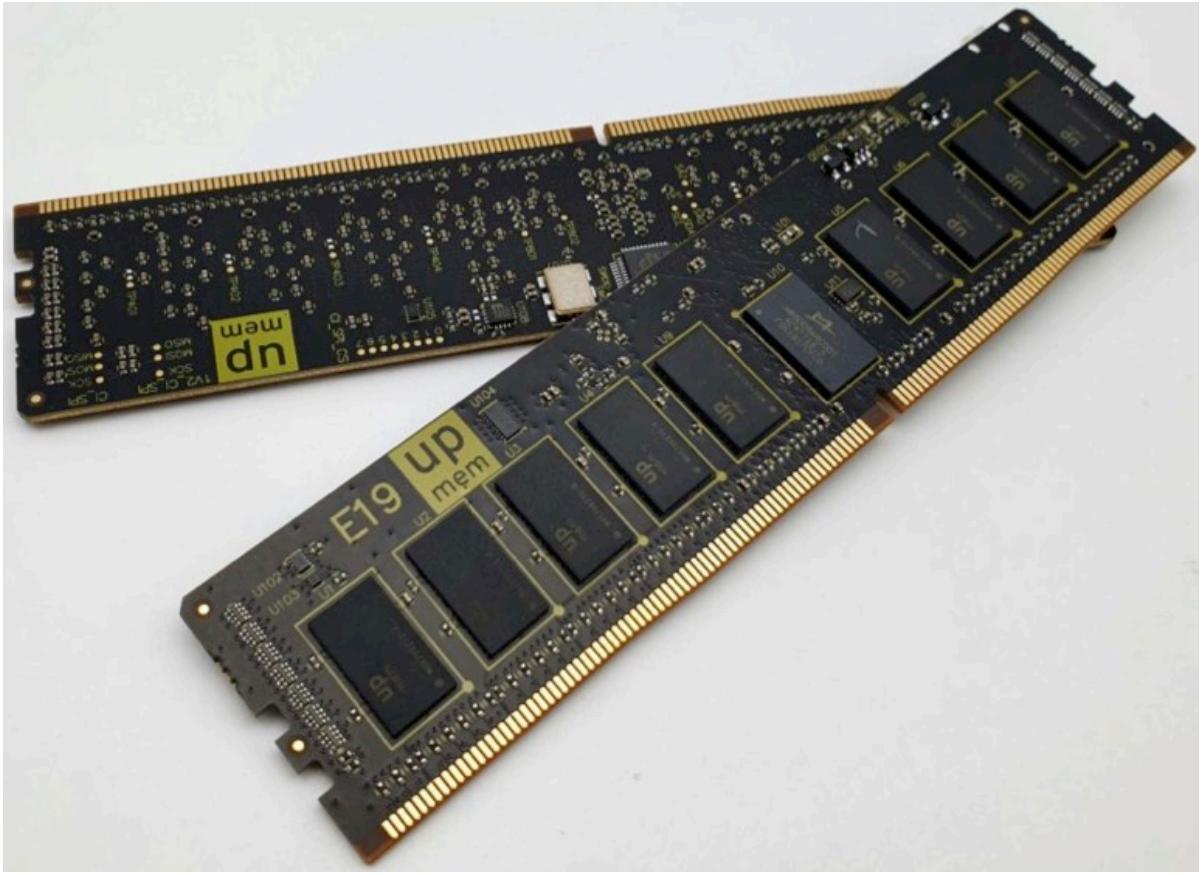
- Replaces **standard** DIMMs
  - DDR4 R-DIMM modules
    - 8GB+128 DPUs (16 PIM chips)
    - Standard 2x-nm DRAM process
  - **Large amounts of** compute & memory bandwidth



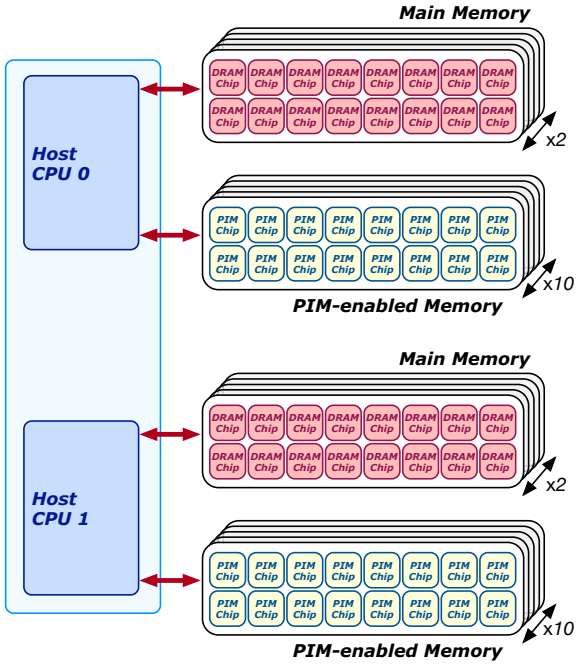
https://www.anandtech.com/show/14750/hot-chips-31-analysis-inmemory-processing-by-upmem
https://www.upmem.com/video-upmem-presenting-its-true-processing-in-memory-solution-hot-chips-2019/

UPMEM Memory Modules

- E19: 8 chips DIMM (1 rank). DPUs @ 267 MHz
- P21: 16 chips DIMM (2 ranks). DPUs @ 350 MHz



2,560-DPU Processing-in-Memory System



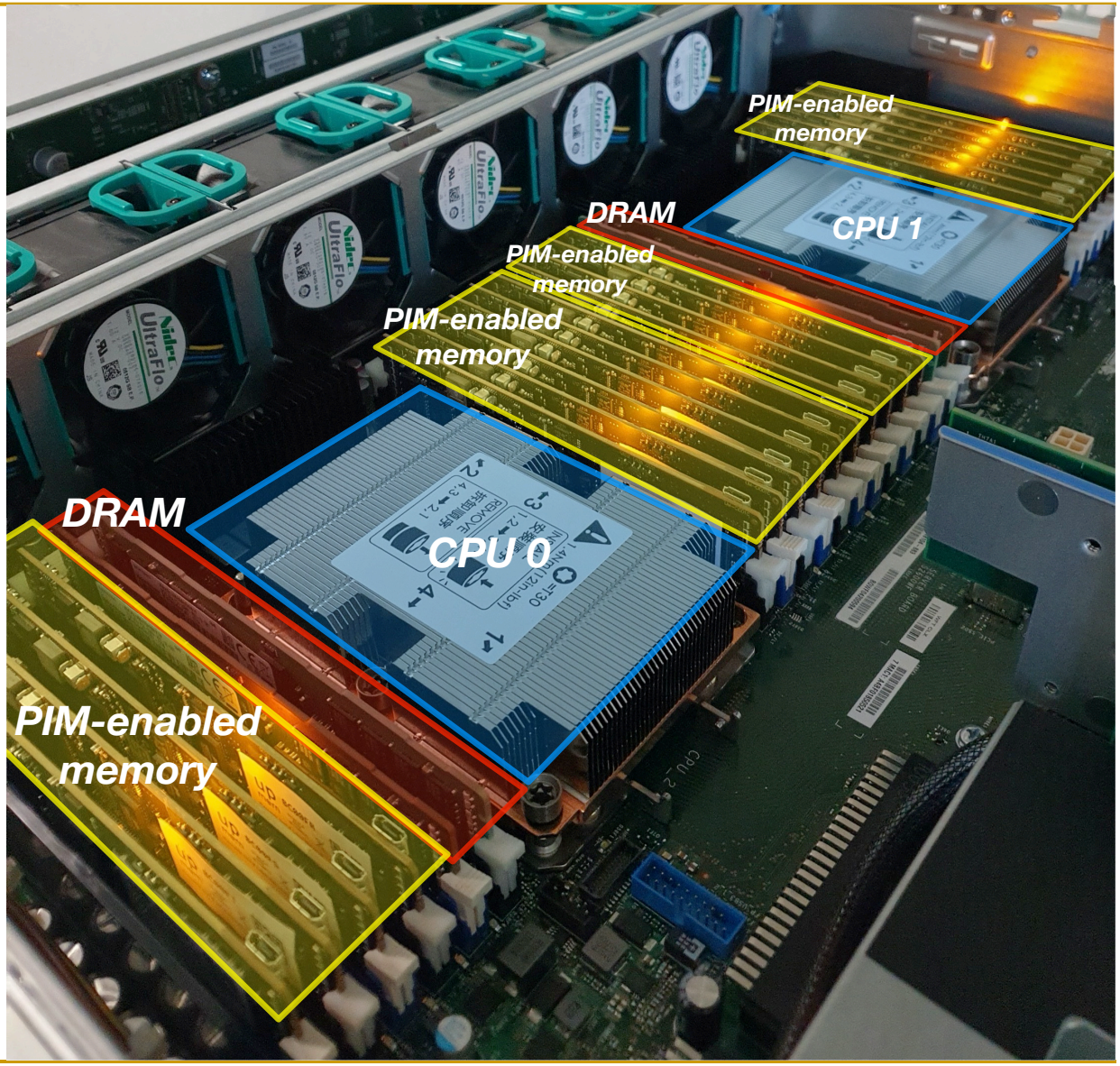
Benchmarking a New Paradigm: An Experimental Analysis of a Real Processing-in-Memory Architecture

JUAN GÓMEZ-LUNA, ETH Zürich, Switzerland
IZZAT EL HAJJ, American University of Beirut, Lebanon
IVAN FERNANDEZ, ETH Zürich, Switzerland and University of Malaga, Spain
CHRISTINA GIANNOULA, ETH Zürich, Switzerland and NTUA, Greece
GERALDO F. OLIVEIRA, ETH Zürich, Switzerland
ONUR MUTLU, ETH Zürich, Switzerland

Many modern workloads, such as neural networks, databases, and graph processing, are fundamentally memory-bound. For such workloads, the data movement between main memory and CPU cores imposes a significant overhead in terms of both latency and energy. A major reason is that this communication happens through a narrow bus with high latency and limited bandwidth, and the low data reuse in memory-bound workloads is insufficient to amortize the cost of main memory access. Fundamentally addressing this *data movement bottleneck* requires a paradigm where the memory system assumes an active role in computing by integrating processing capabilities. This paradigm is known as *processing-in-memory* (*PIM*).

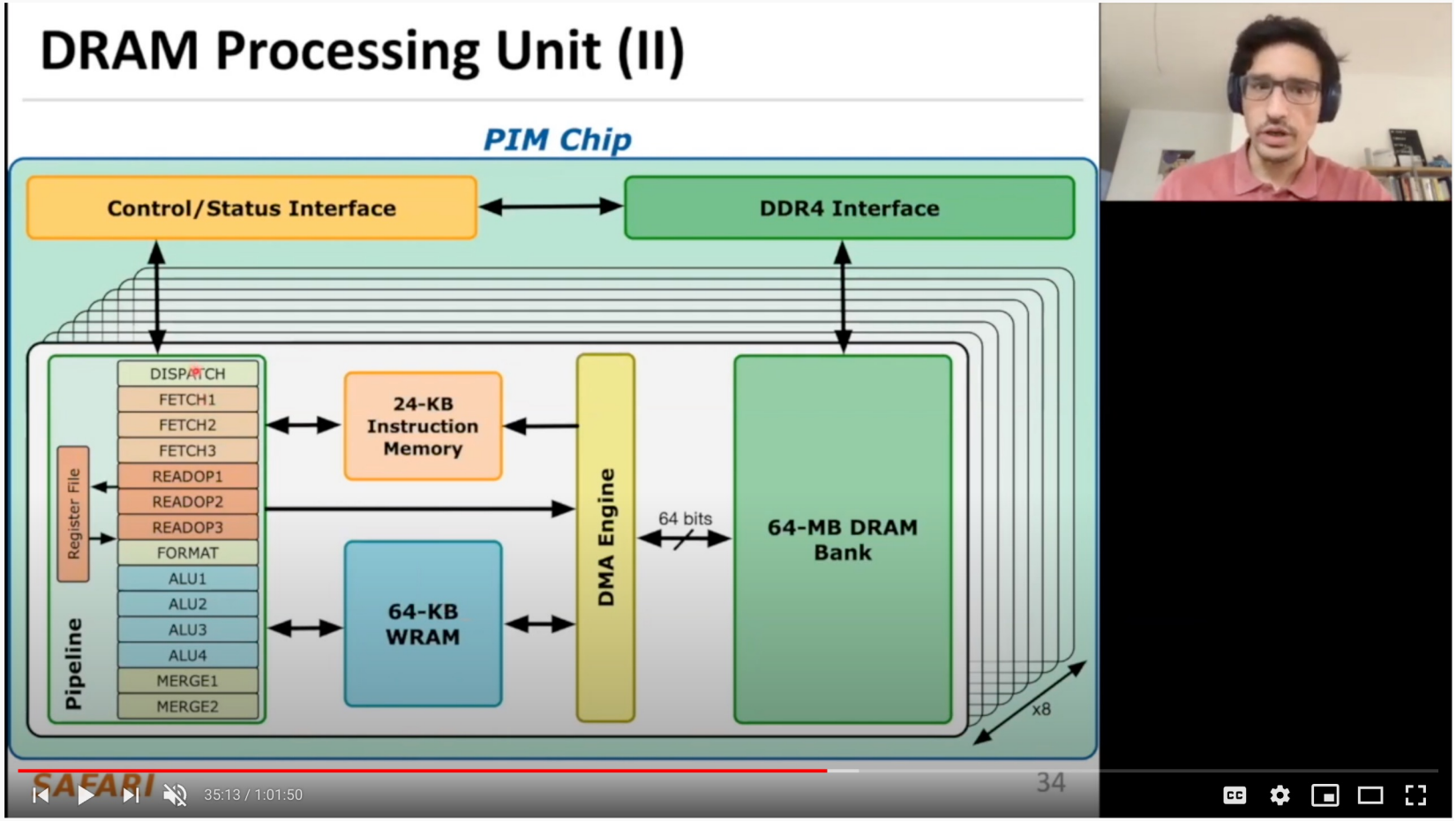
Recent research explores different forms of PIM architectures, motivated by the emergence of new 3D-stacked memory technologies that integrate memory with a logic layer where processing elements can be easily placed. Past works evaluate these architectures in simulation or, at best, with simplified hardware prototypes. In contrast, the UPMEM company has designed and manufactured the first publicly-available real-world PIM architecture. The UPMEM PIM architecture combines traditional DRAM memory arrays with general-purpose in-order cores, called *DRAM Processing Units* (*DPUs*), integrated in the same chip.

This paper provides the first comprehensive analysis of the first publicly-available real-world PIM architecture. We make two key contributions. First, we conduct an experimental characterization of the UPMEM-based PIM system using microbenchmarks to assess various architecture limits such as compute throughput and memory bandwidth, yielding new insights. Second, we present *PrIM* (*Processing-In-Memory benchmarks*), a benchmark suite of 16 workloads from different application domains (e.g., dense/sparse linear algebra, databases, data analytics, graph processing, neural networks, bioinformatics, image processing), which we identify as memory-bound. We evaluate the performance and scaling characteristics of PrIM benchmarks on the UPMEM PIM architecture, and compare their performance and energy consumption to their state-of-the-art CPU and GPU counterparts. Our extensive evaluation conducted on two real UPMEM-based PIM systems with 640 and 2,556 DPUs provides new insights about suitability of different workloads to the PIM system, programming recommendations for software designers, and suggestions and hints for hardware and architecture designers of future PIM systems.



https://arxiv.org/pdf/2105.03814.pdf

More on the UPMEM PIM System



https://www.youtube.com/watch?v=Sscy1Wrr22A&list=PL5Q2soXY2Zi9xidyIgBxUz7xRPS-wisBN&index=26

SRC TECHCON Presentation

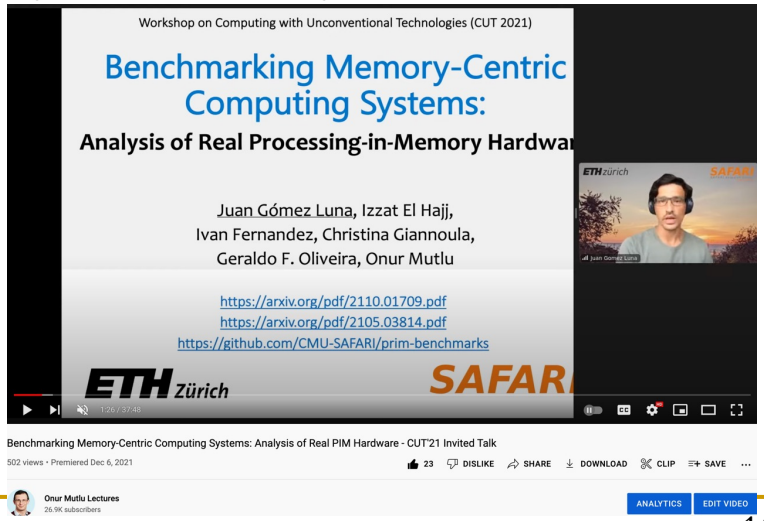
- Dr. Juan Gomez-Luna
  - Benchmarking Memory-Centric Computing Systems: Analysis of Real Processing-in-Memory Hardware
  - Based on two major works
    - https://arxiv.org/pdf/2105.03814.pdf
    - https://arxiv.org/pdf/2207.07886.pdf

Benchmarking Memory-Centric Computing Systems: Analysis of Real Processing-In-Memory Hardware

Year: 2021, Pages: 1-7
DOI Bookmark: 10.1109/IGSC54211.2021.9651614

Authors

Juan Gómez-Luna, ETH Zürich
Izzat El Hajj, American University of Beirut
Ivan Fernandez, University of Malaga
Christina Giannoula, National Technical University of Athens
Geraldo F. Oliveira, ETH Zürich
Onur Mutlu, ETH Zürich



https://www.youtube.com/watch?v=nphV36SrysA

UPMEM PIM System Summary & Analysis

- Juan Gomez-Luna, Izzat El Hajj, Ivan Fernandez, Christina Giannoula, Geraldo F. Oliveira, and Onur Mutlu,
  "Benchmarking Memory-Centric Computing Systems: Analysis of Real Processing-in-Memory Hardware"
  *Invited Paper at Workshop on Computing with Unconventional Technologies (**CUT**)*, Virtual, October 2021.
  [arXiv version]
  [PrIM Benchmarks Source Code]
  [Slides (pptx) (pdf)]
  [Talk Video (37 minutes)]
  [Lightning Talk Video (3 minutes)]

Benchmarking Memory-Centric Computing Systems: Analysis of Real Processing-in-Memory Hardware

Juan Gómez-Luna, *ETH Zürich*
Izzat El Hajj, *American University of Beirut*
Ivan Fernandez, *University of Malaga*
Christina Giannoula, *National Technical University of Athens*
Geraldo F. Oliveira, *ETH Zürich*
Onur Mutlu, *ETH Zürich*

ML Training on Real PIM Systems

- Juan Gómez Luna, Yuxin Guo, Sylvan Brocard, Julien Legriel, Remy Cimadomo, Geraldo F. Oliveira, Gagandeep Singh, and Onur Mutlu,
  "Evaluating Machine Learning Workloads on Memory-Centric Computing Systems"
  *Proceedings of the 2023 IEEE International Symposium on Performance Analysis of Systems and Software (**ISPASS**)*, Raleigh, North Carolina, USA, April 2023.
  [arXiv version, 16 July 2022.]
  [PIM-ML Source Code]
  Best paper session.

An Experimental Evaluation of Machine Learning Training on a Real Processing-in-Memory System

Juan Gómez-Luna[1] Yuxin Guo[1] Sylvan Brocard[2] Julien Legriel[2]
Remy Cimadomo[2] Geraldo F. Oliveira[1] Gagandeep Singh[1] Onur Mutlu[1]
[1]ETH Zürich [2]UPMEM

https://github.com/CMU-SAFARI/pim-ml

https://arxiv.org/pdf/2207.07886.pdf

Sequence Alignment on Real PIM Systems

- Safaa Diab, Amir Nassereldine, Mohammed Alser, Juan Gómez Luna, Onur Mutlu, and Izzat El Hajj,
  "A Framework for High-throughput Sequence Alignment using Real Processing-in-Memory Systems"
  Bioinformatics, [published online on] 27 March 2023.
  [Online link at Bioinformatics Journal]
  [arXiv preprint]
  [AiM Source Code]

A Framework for High-throughput Sequence Alignment using Real Processing-in-Memory Systems

Safaa Diab [1] Amir Nassereldine [1] Mohammed Alser [2] Juan Gómez Luna [2]
Onur Mutlu [2] Izzat El Hajj [1]

[1]American University of Beirut [2]ETH Zürich

https://github.com/CMU-SAFARI/alignment-in-memory

https://arxiv.org/pdf/2208.01243.pdf

Summary

- Sequence alignment on traditional systems is limited by the **memory bandwidth bottleneck**
- **Processing-in-memory (PIM)** overcomes this bottleneck by placing cores near the memory
- Our framework, **Alignment-in-Memory (AIM)**, is a PIM framework that supports multiple alignment algorithms (NW, SWG, GenASM, WFA)
  - Implemented on UPMEM, the first real PIM system
- Results show **substantial speedups over both CPUs (1.8X-28X) and GPUs (1.2X-2.7X)**
- AIM is available at:
  - https://github.com/CMU-SAFARI/alignment-in-memory

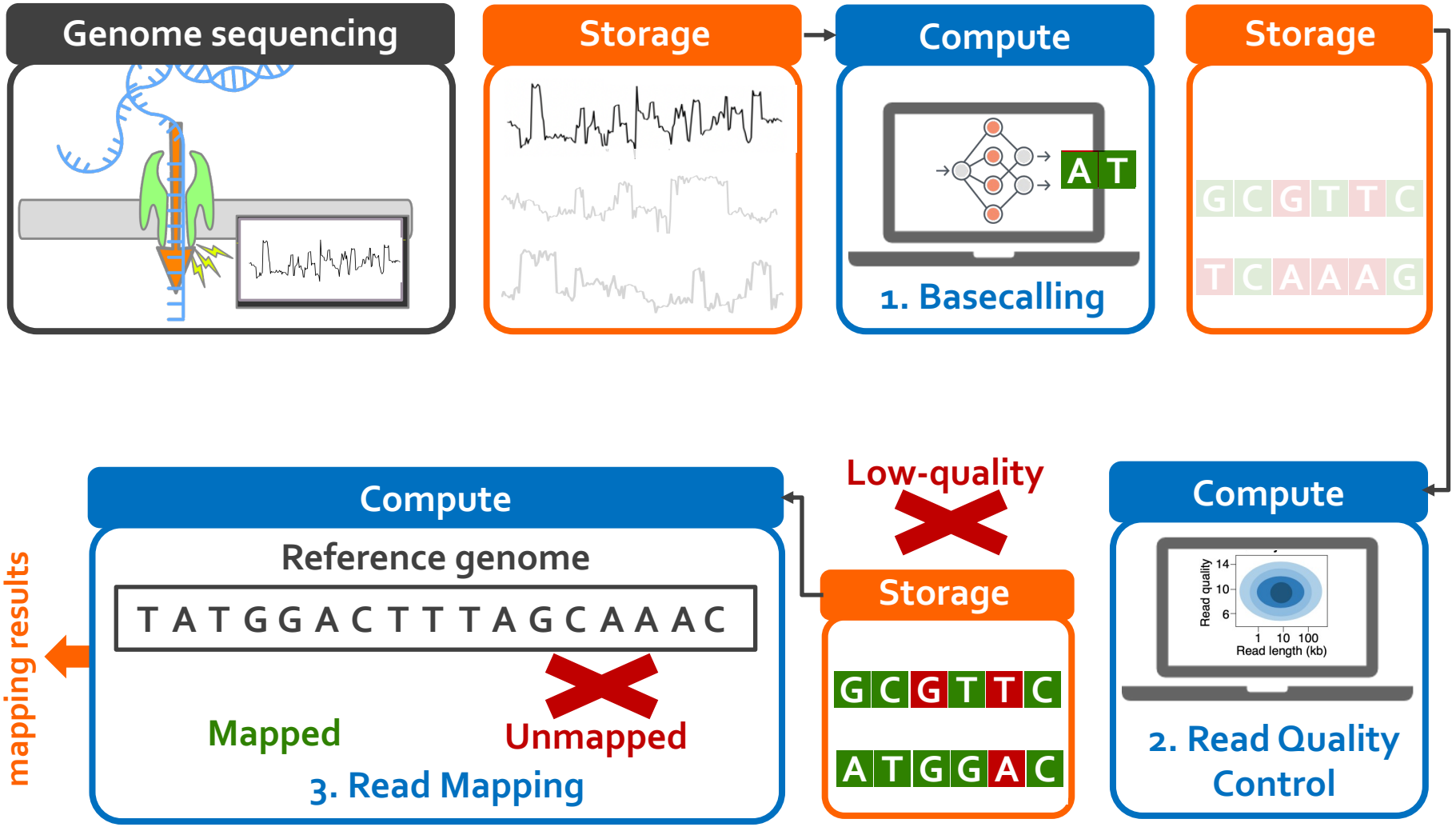
Accelerating Basecalling + Read Mapping via PIM

- Haiyu Mao, Mohammed Alser, Mohammad Sadrosadati, Can Firtina, Akanksha Baranwal, Damla Senol Cali, Aditya Manglik, Nour Almadhoun Alserr, and Onur Mutlu,
  "GenPIP: In-Memory Acceleration of Genome Analysis via Tight Integration of Basecalling and Read Mapping"
  Proceedings of the 55th International Symposium on Microarchitecture (***MICRO***),
  Chicago, IL, USA, October 2022.
  [Slides (pptx) (pdf)]
  [Longer Lecture Slides (pptx) (pdf)]
  [Lecture Video (25 minutes)]
  [arXiv version]

GenPIP: In-Memory Acceleration of Genome Analysis via Tight Integration of Basecalling and Read Mapping

Haiyu Mao[1] Mohammed Alser[1] Mohammad Sadrosadati[1] Can Firtina[1] Akanksha Baranwal[1]
Damla Senol Cali[2] Aditya Manglik[1] Nour Almadhoun Alserr[1] Onur Mutlu[1]
[1]*ETH Zürich* [2]*Bionano Genomics*

Genome Analysis Pipeline



Limitation 1: Large Data Movement

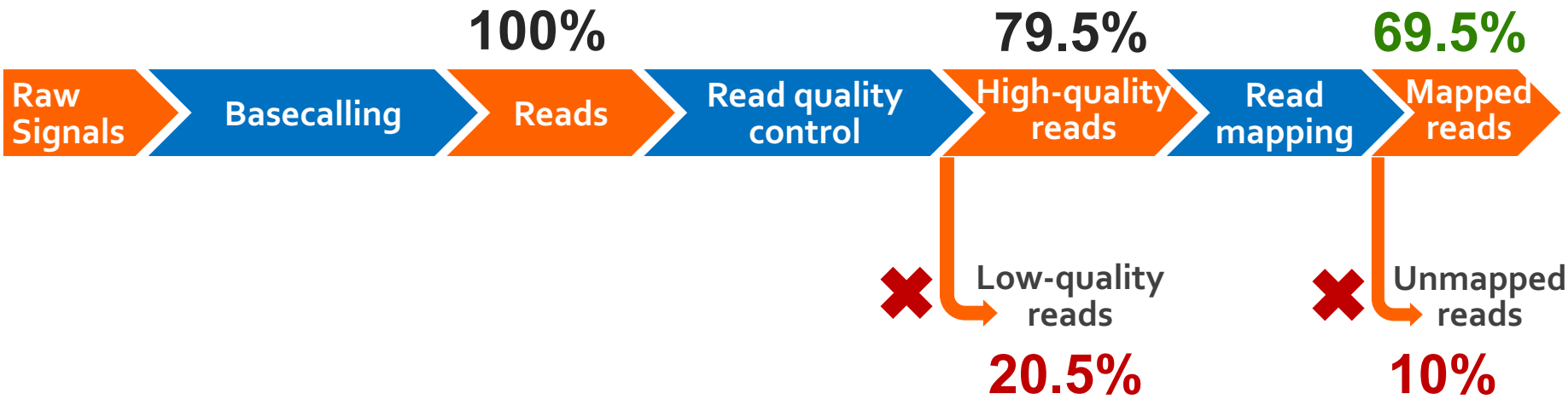
- Using a human dataset in [NC'19] as an example:

Large data movement between genome analysis steps

[NC'19] Rory Bowden, Robert W Davies, Andreas Heger, Alistair T Pagnamenta, Mariateresa de Cesare, Laura E Oikkonen, Duncan Parkes, Colin Freeman, Fatima Dhalla, Smita Y Patel, et al. Sequencing of human genomes with nanopore technology. Nature Communications, 2019.

Limitation 2: Wasted Computation

- Using a human dataset in [NC'19] as an example:



A considerable amount of computation on useless data due to

- **Low-quality reads**
- **Unmapped reads**

[NC'19] Rory Bowden, Robert W Davies, Andreas Heger, Alistair T Pagnamenta, Mariateresa de Cesare, Laura E Oikkonen, Duncan Parkes, Colin Freeman, Fatima Dhalla, Smita Y Patel, et al. Sequencing of human genomes with nanopore technology. Nature Communications, 2019.

Overview: Two Limitations

Multiple steps in genome analysis

Large data movement between multiple steps

A lot of **wasted computation** done on data that is later discovered to be **useless**

Overview: GenPIP

- **GenPIP:** A fast and energy-efficient **in-memory** acceleration system for the Genome analysis PIPeline via **tight integration of genome analysis steps**

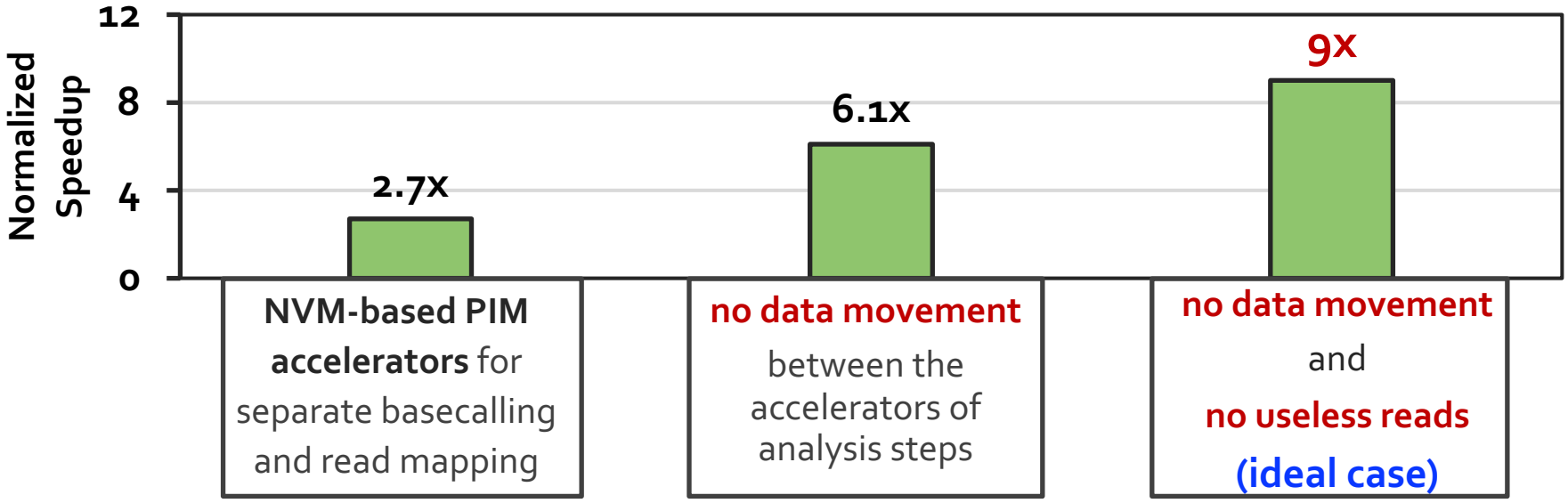
- **GenPIP** has two key techniques
  - **Chunk-based pipeline (CP)**
    - **Provides fine-grained collaboration** of genome analysis steps
  - **Early rejection (ER)**
    - **Timely stops the execution on useless data** by predicting which reads will not be useful

- **GenPIP** outperforms state-of-the-art software & hardware solutions using **CPU**, **GPU**, and **optimistic PIM** by **41.6×**, **8.4x**, and **1.4x**, respectively.

Goal and Opportunities

Goal: Efficiently accelerate the entire genome analysis pipeline while **minimizing data movement and useless computation**

- We perform a study to quantify potential performance benefits
  - Results are normalized to the performance of GPU



Agenda

- The Problem: DNA Read Mapping
  - State-of-the-art Read Mapper Design
- Algorithmic Acceleration
  - Exploiting Structure of the Genome
  - Exploiting SIMD Instructions
- Hardware Acceleration
  - Specialized Architectures
  - Processing in Memory & Storage
- Future Opportunities: New Technologies & Applications

Newer Genome Sequencing Technologies

Nanopore sequencing technology and tools for genome assembly: computational analysis of the current state, bottlenecks and future directions

Damla Senol Cali ✉, Jeremie S Kim, Saugata Ghose, Can Alkan, Onur Mutlu

Briefings in Bioinformatics, bby017, https://doi.org/10.1093/bib/bby017
Published: 02 April 2018 **Article history** ▾

Oxford Nanopore MinION

Senol Cali+, "**Nanopore Sequencing Technology and Tools for Genome Assembly: Computational Analysis of the Current State, Bottlenecks and Future Directions**," Briefings in Bioinformatics, 2018.
[Open arxiv.org version] [Slides (pptx) (pdf)] [Talk Video at AACBB 2019]

New Applications: Graph Genomes

- Damla Senol Cali, Konstantinos Kanellopoulos, Joel Lindegger, Zulal Bingol, Gurpreet S. Kalsi, Ziyi Zuo, Can Firtina, Meryem Banu Cavlak, Jeremie Kim, Nika MansouriGhiasi, Gagandeep Singh, Juan Gomez-Luna, Nour Almadhoun Alserr, Mohammed Alser, Sreenivas Subramoney, Can Alkan, Saugata Ghose, and Onur Mutlu,
  "SeGraM: A Universal Hardware Accelerator for Genomic Sequence-to-Graph and Sequence-to-Sequence Mapping"
  *Proceedings of the 49th International Symposium on Computer Architecture (**ISCA**)*, New York, June 2022.
  [arXiv version]

SeGraM: A Universal Hardware Accelerator for Genomic Sequence-to-Graph and Sequence-to-Sequence Mapping

Damla Senol Cali[1] Konstantinos Kanellopoulos[2] Joël Lindegger[2] Zülal Bingöl[3]
Gurpreet S. Kalsi[4] Ziyi Zuo[5] Can Firtina[2] Meryem Banu Cavlak[2] Jeremie Kim[2]
Nika Mansouri Ghiasi[2] Gagandeep Singh[2] Juan Gómez-Luna[2] Nour Almadhoun Alserr[2]
Mohammed Alser[2] Sreenivas Subramoney[4] Can Alkan[3] Saugata Ghose[6] Onur Mutlu[2]

[1]Bionano Genomics [2]ETH Zürich [3]Bilkent University [4]Intel Labs
[5]Carnegie Mellon University [6]University of Illinois Urbana-Champaign

New Applications: Frequent Reference Updates

- Jeremie S. Kim, Can Firtina, M. Banu Cavlak, Damla Senol Cali, Nastaran Hajinazar, Mohammed Alser, Can Alkan, and Onur Mutlu,
  "AirLift: A Fast and Comprehensive Technique for Remapping Alignments between Reference Genomes"
  Proceedings of the 21st Asia Pacific Bioinformatics Conference ***(APBC)***, Changsha, China, April 2023.
  [AirLift Source Code]
  [arxiv.org Version (pdf)]
  [Talk Video at BIO-Arch 2023 Workshop]

METHOD

AirLift: A Fast and Comprehensive Technique for Remapping Alignments between Reference Genomes

Jeremie S. Kim[1†], Can Firtina[1†], Meryem Banu Cavlak[2], Damla Senol Cali[3], Nastaran Hajinazar[1,4], Mohammed Alser[1], Can Alkan[2] and Onur Mutlu[1,2,3*]

Mapping Constant Regions Between References

- Jeremie S. Kim, Can Firtina, Meryem Banu Cavlak, Damla Senol Cali, Can Alkan, and Onur Mutlu,
  "FastRemap: A Tool for Quickly Remapping Reads between Genome Assemblies"
  Bioinformatics, btac554.
  [FastRemap Source Code]

FastRemap: A Tool for Quickly Remapping Reads between Genome Assemblies

Jeremie S. Kim[1] Can Firtina[1] Meryem Banu Cavlak[1] Damla Senol Cali[2,3]
Can Alkan[4] Onur Mutlu[1,2,4]

[1]*ETH Zürich* [2]*Carnegie Mellon University* [3]*Bionano Genomics* [4]*Bilkent University*

New Frontiers: Raw Signal Analysis

- Can Firtina, Nika Mansouri Ghiasi, Joel Lindegger, Gagandeep Singh, Meryem Banu Cavlak, Haiyu Mao, and Onur Mutlu,
  "RawHash: Enabling Fast and Accurate Real-Time Analysis of Raw Nanopore Signals for Large Genomes"
  *Proceedings of the 31st Annual Conference on Intelligent Systems for Molecular Biology and the 22nd European Conference on Computational Biology (**ISMB/ECCB**)*, Lyon, France, July 2023.
  [RawHash Source Code]

RawHash: Enabling Fast and Accurate Real-Time Analysis of Raw Nanopore Signals for Large Genomes

Can Firtina[1] Nika Mansouri Ghiasi[1] Joel Lindegger[1] Gagandeep Singh[1]
Meryem Banu Cavlak[1] Haiyu Mao[1] Onur Mutlu[1]
[1]*ETH Zurich*

New Frontiers: Raw Signal Analysis

- M. Banu Cavlak, Gagandeep Singh, Mohammed Alser, Can Firtina, Joel Lindegger, Mohammad Sadrosadati, Nika Mansouri Ghiasi, Can Alkan, and Onur Mutlu, **"TargetCall: Eliminating the Wasted Computation in Basecalling via Pre-Basecalling Filtering"**
  Proceedings of the 21st Asia Pacific Bioinformatics Conference (***APBC***), Changsha, China, April 2023.
  [TargetCall Source Code]
  [arxiv.org Version]
  [Talk Video at BIO-Arch 2023 Workshop]

TargetCall: Eliminating the Wasted Computation in Basecalling via Pre-Basecalling Filtering

Meryem Banu Cavlak[1] Gagandeep Singh[1] Mohammed Alser[1] Can Firtina[1] Joël Lindegger[1]
Mohammad Sadrosadati[1] Nika Mansouri Ghiasi[1] Can Alkan[2] Onur Mutlu[1]
[1]*ETH Zürich* [2]*Bilkent University*

A Bright Future for Intelligent Genome Analysis

Mohammed Alser, Zülal Bingöl, Damla Senol Cali, Jeremie Kim, Saugata Ghose, Can Alkan, Onur Mutlu
"Accelerating Genome Analysis: A Primer on an Ongoing Journey" IEEE Micro, August 2020.

MinION from ONT

Accelerating Genome Analysis: A Primer on an Ongoing Journey
Sept.-Oct. 2020, pp. 65-75, vol. 40
DOI Bookmark: 10.1109/MM.2020.3013728

FPGA-Based Near-Memory Acceleration of Modern Data-Intensive Applications
July-Aug. 2021, pp. 39-48, vol. 41
DOI Bookmark: 10.1109/MM.2021.3088396

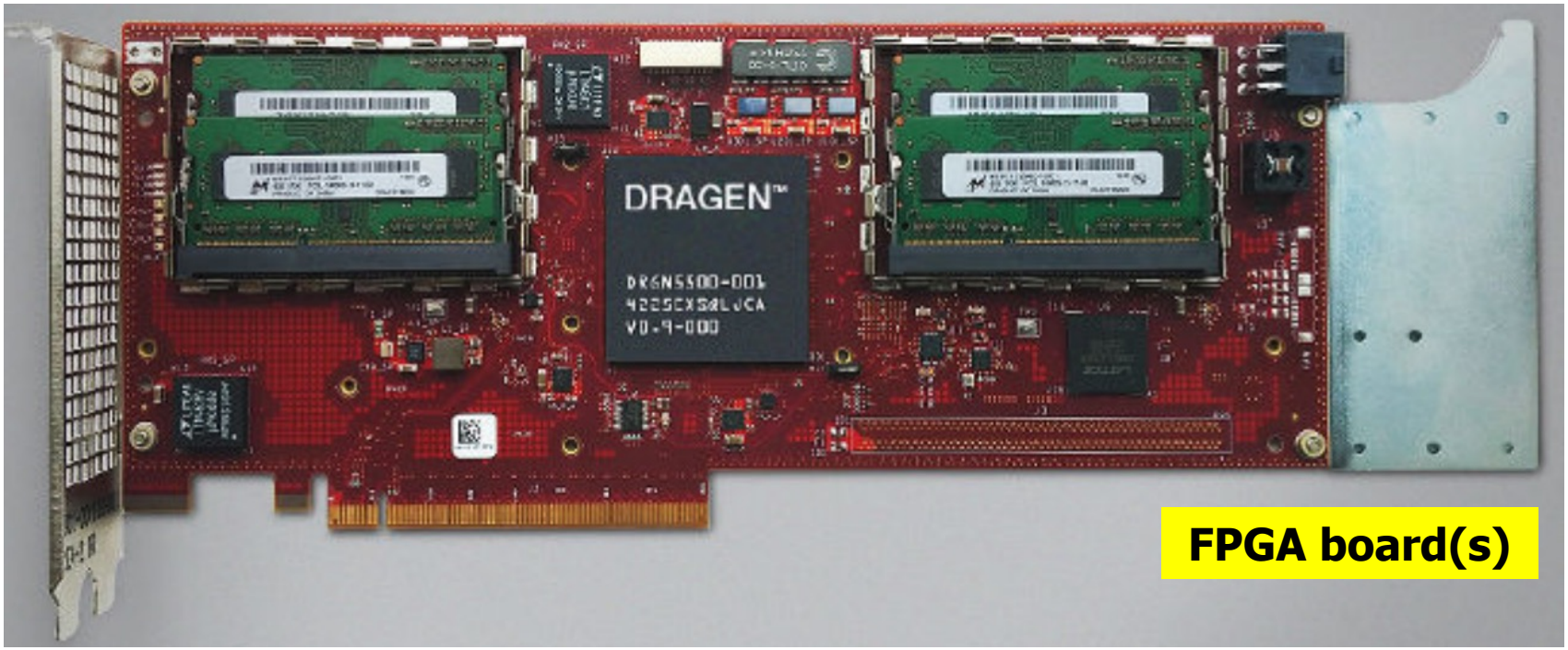
SmidgION from ONT

Conclusion

Things Are Happening In Industry

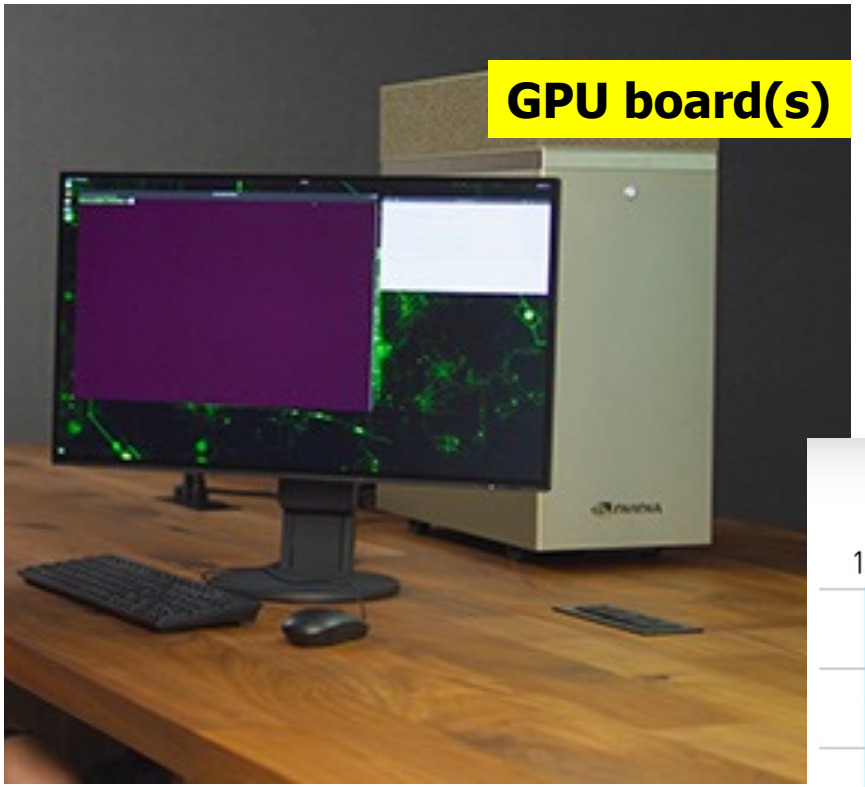
Illumina DRAGEN Bio-IT Platform (2018)

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

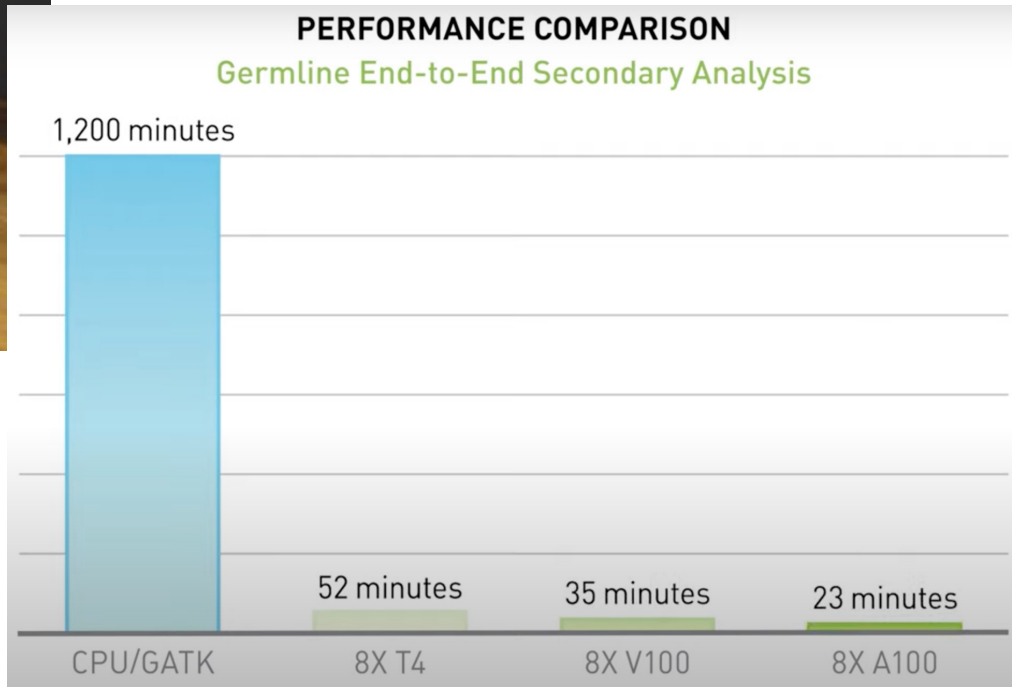


emea.illumina.com/products/by-type/informatics-products/dragen-bio-it-platform.html
emea.illumina.com/company/news-center/press-releases/2018/2349147.html

NVIDIA Clara Parabricks (2020)



A University of Michigan startup in 2018 joined NVIDIA in 2020



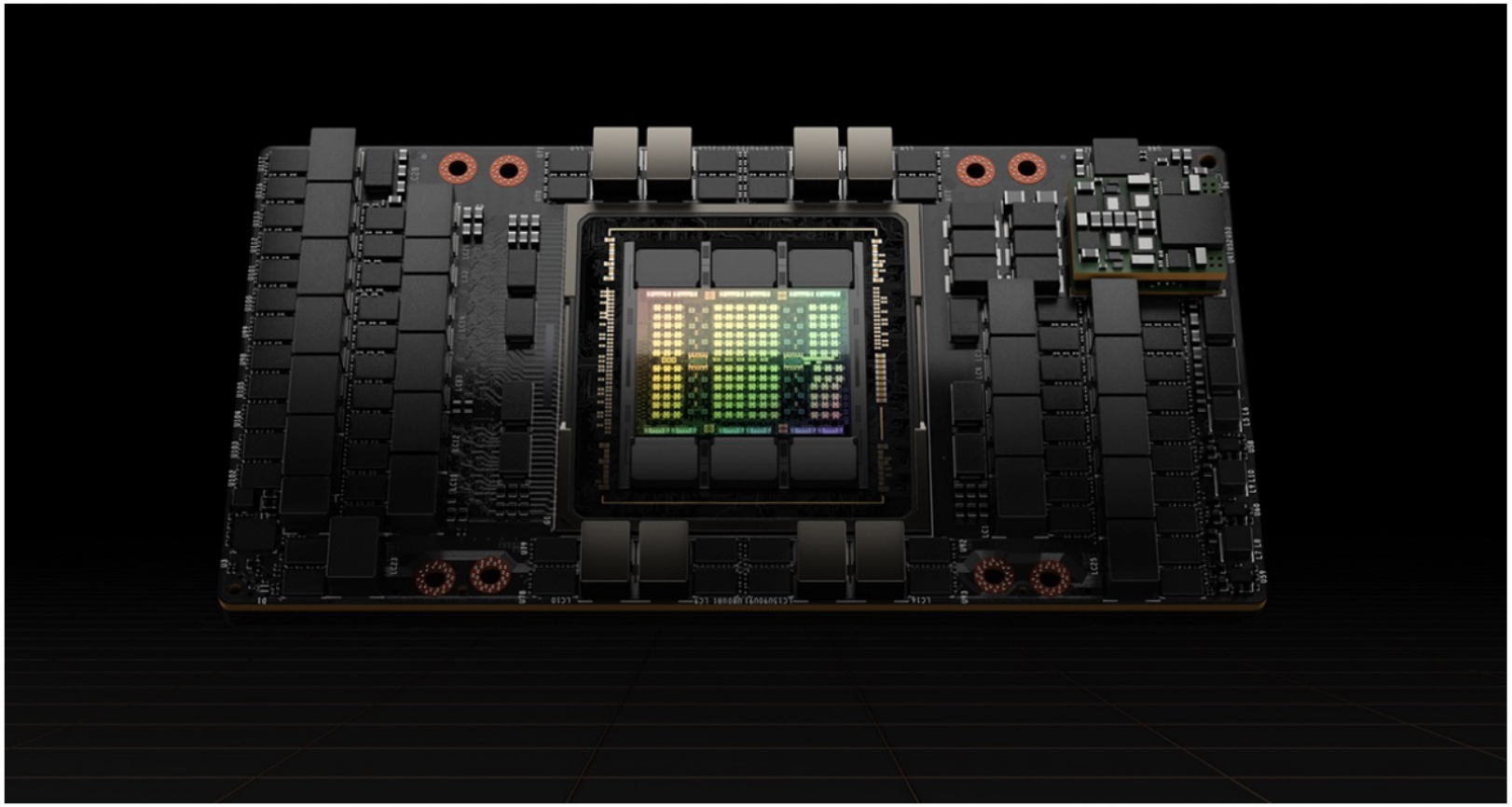
https://developer.nvidia.com/clara-parabricks

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

Analysis of highly complex cancer whole genomes in **less than 2 hours**

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

Recall Our Dream (from 2007)

- An embedded device that can perform comprehensive genome analysis in real time (within a minute)

- Still a long ways to go
  - Energy efficiency
  - Performance (latency)
  - Security & privacy
  - **Huge memory bottleneck**

Conclusion

- System design for bioinformatics is a critical problem
  - It has large scientific, medical, societal, personal implications
- This talk is about accelerating a key step in bioinformatics: genome sequence analysis
  - Especially techniques for read mapping
- We covered various recent ideas to accelerate read mapping
  - My personal journey since September 2006
- **Many future opportunities exist**
  - **Especially with new sequencing technologies**
  - **Especially with new applications and use cases**

A Bright Future for Intelligent Genome Analysis

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MinION from ONT

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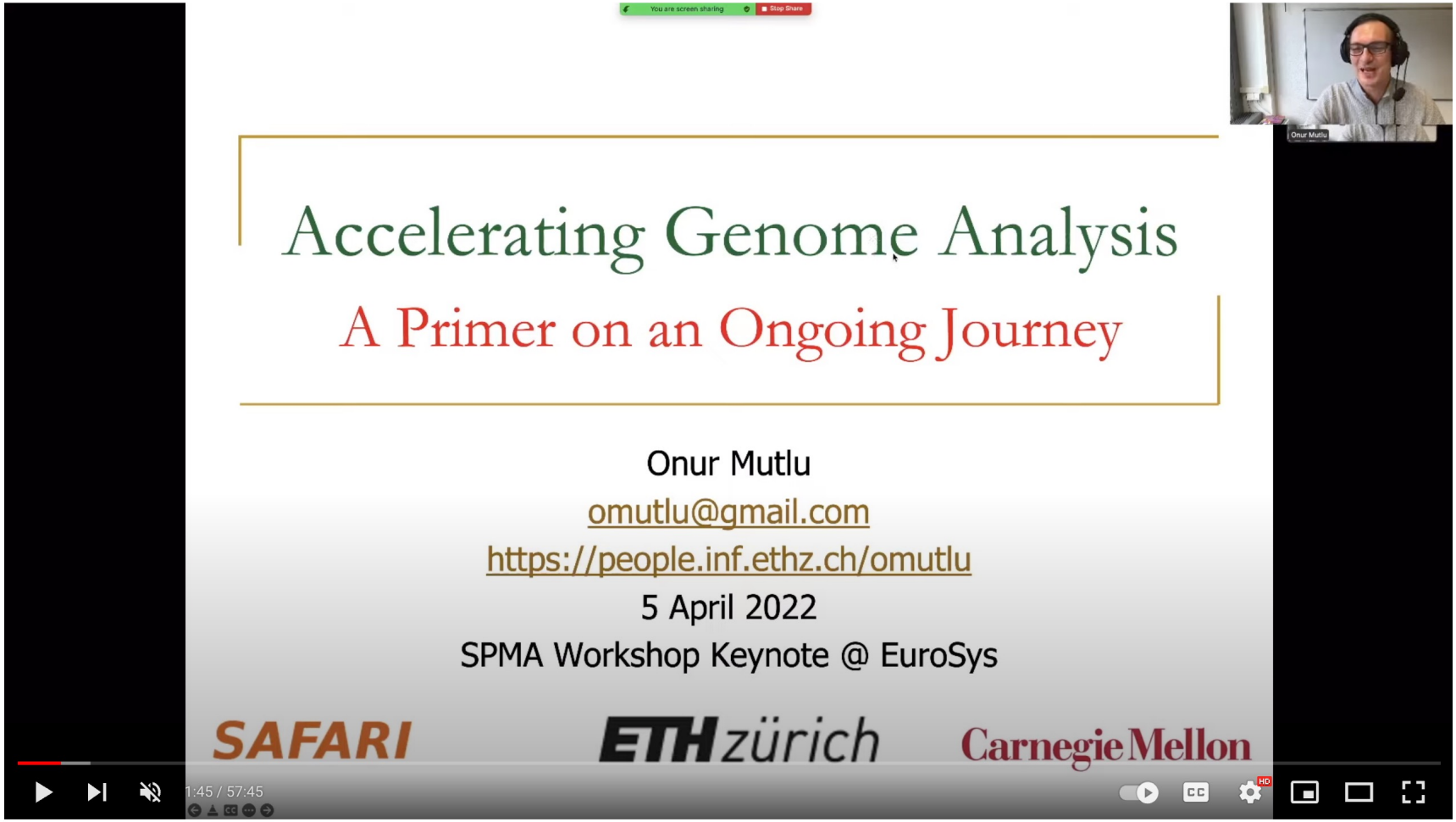
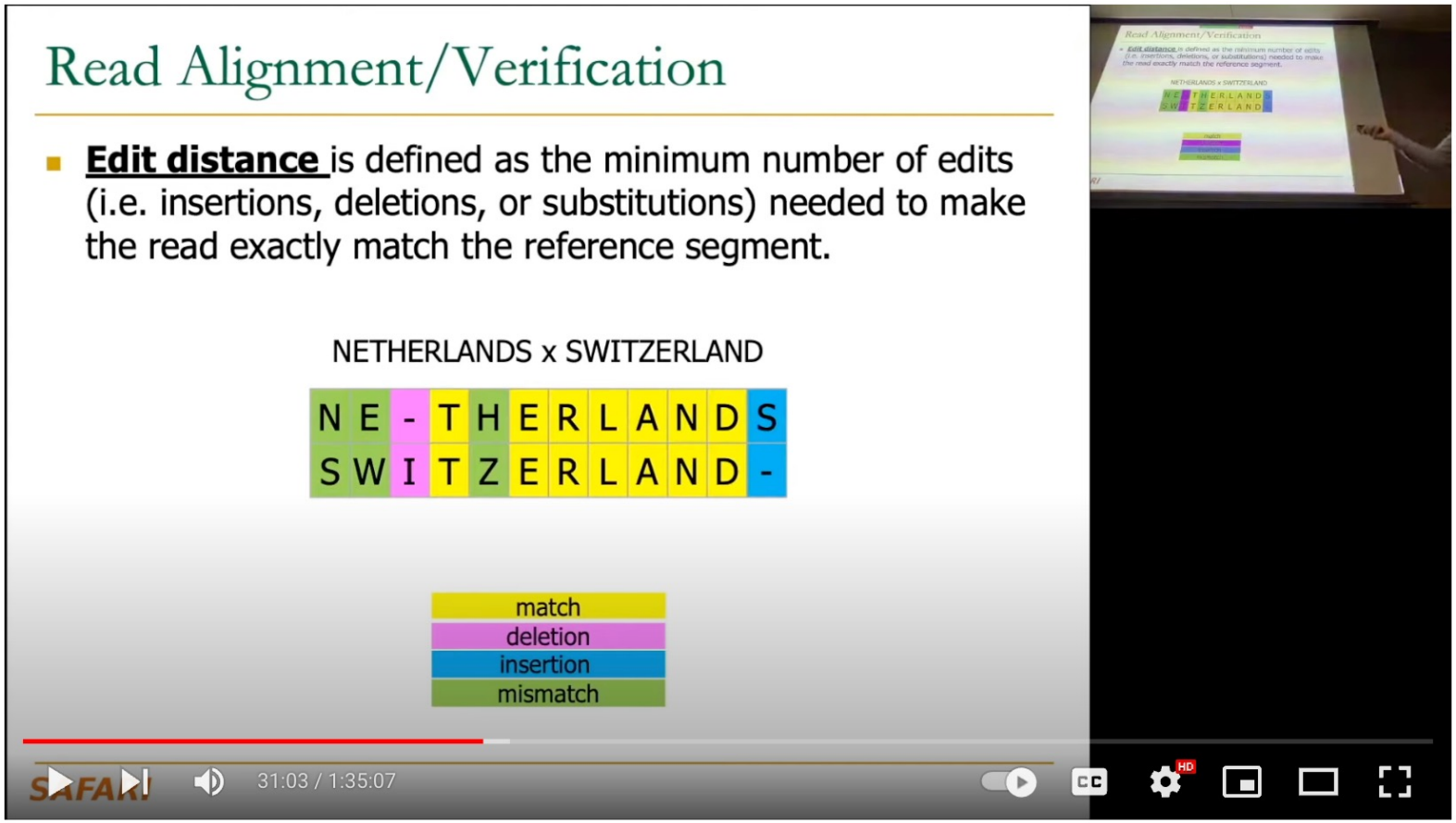
SmidgION from ONT

A Longer Version of This Talk (I)



https://www.youtube.com/watch?v=NCagwf0ivT0

A Longer Version of This Talk (II)



Accelerating Genome Analysis - Onur Mutlu's Invited Talk at the Barcelona Supercomputing Center

Onur Mutlu Lectures
32.3K subscribers
Subscribed
15
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385 views 2 months ago

https://www.youtube.com/watch?v=tVpg0XqU_c4

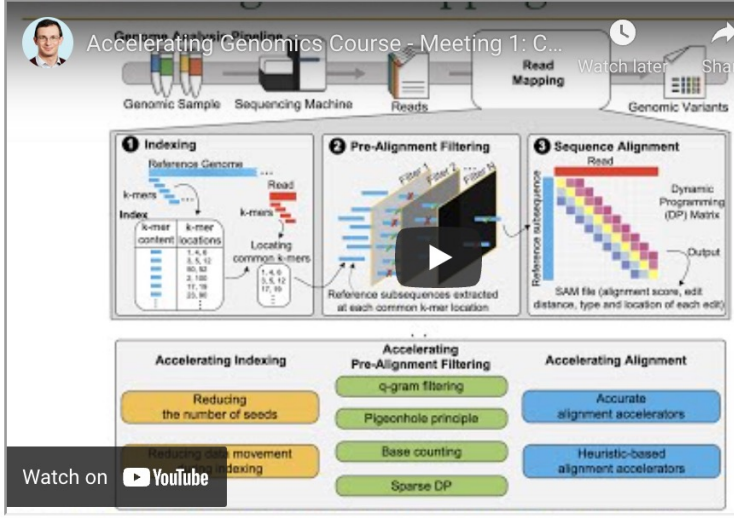
Genomics Course (Fall 2022)

- **Fall 2022 Edition:**
  - https://safari.ethz.ch/projects_and_seminars/fall2022/doku.php?id=bioinformatics
- **Spring 2022 Edition:**
  - https://safari.ethz.ch/projects_and_seminars/spring2022/doku.php?id=bioinformatics

- **Youtube Livestream (Fall 2022):**
  - https://www.youtube.com/watch?v=nA41964-9r8&list=PL5Q2soXY2Zi8tFlQvdxOdizD_EhVAMVQV
- **Youtube Livestream (Spring 2022):**
  - https://www.youtube.com/watch?v=DEL_5A_Y3TI&list=PL5Q2soXY2Zi8NrPDgOR1yRU_Cxxjw-u18

- Project course
  - Taken by Bachelor's/Master's students
  - Genomics lectures
  - Hands-on research exploration
  - Many research readings

https://www.youtube.com/onurmutlulectures



Spring 2022 Meetings/Schedule

Week	Date	Livestream	Meeting	Learning Materials
W1	11.3 Fri.	YouTube Live	M1: P&S Accelerating Genomics Course Introduction & Project Proposals (PDF) (PPT)	Required Materials Recommended Materials
W2	18.3 Fri.	YouTube Live	M2: Introduction to Sequencing (PDF) (PPT)	
W3	25.3 Fri.	YouTube Premiere	M3: Read Mapping (PDF) (PPT)	
W4	01.04 Fri.	YouTube Premiere	M4: GateKeeper (PDF) (PPT)	
W5	08.04 Fri.	YouTube Premiere	M5: MAGNET & Shouji (PDF) (PPT)	
W6	15.4 Fri.	YouTube Premiere	M6: SneakySnake (PDF) (PPT)	
W7	29.4 Fri.	YouTube Premiere	M7: GenStore (PDF) (PPT)	
W8	06.05 Fri.	YouTube Premiere	M8: GRIM-Filter (PDF) (PPT)	
W9	13.05 Fri.	YouTube Premiere	M9: Genome Assembly (PDF) (PPT)	
W10	20.05 Fri.	YouTube Live	M10: Genomic Data Sharing Under Differential Privacy (PDF) (PPT)	
W11	10.06 Fri.	YouTube Premiere	M11: Accelerating Genome Sequence Analysis (PDF) (PPT)	

PIM Course (Fall 2022)

- **Fall 2022 Edition:**
  - https://safari.ethz.ch/projects_and_seminars/fall2022/doku.php?id=processing_in_memory
- **Spring 2022 Edition:**
  - https://safari.ethz.ch/projects_and_seminars/spring2022/doku.php?id=processing_in_memory

- **Youtube Livestream (Fall 2022):**
  - https://www.youtube.com/watch?v=QLL0wQ9I4Dw&list=PL5Q2soXY2Zi8KzG2CQYRNQOVD0GOBrnKy
- **Youtube Livestream (Spring 2022):**
  - https://www.youtube.com/watch?v=9e4Chnwdovo&list=PL5Q2soXY2Zi-841fUYYUK9EsXKhQKRPyX

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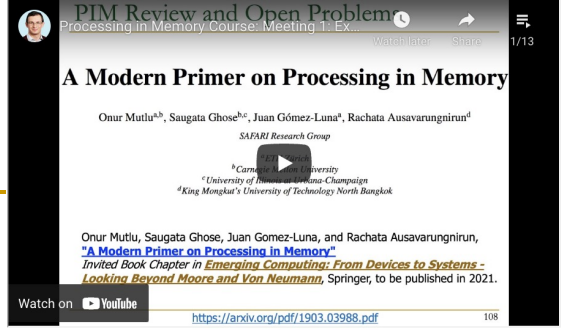


Spring 2022 Meetings/Schedule

Week	Date	Livestream	Meeting	Learning Materials	Assignments
W1	10.03 Thu.	YouTube Live	M1: P&S PIM Course Presentation (PDF) (PPT)	Required Materials Recommended Materials	HW 0 Out
W2	15.03 Tue.		Hands-on Project Proposals		
	17.03 Thu.	YouTube Premiere	M2: Real-world PIM: UPMEM PIM (PDF) (PPT)		
W3	24.03 Thu.	YouTube Live	M3: Real-world PIM: Microbenchmarking of UPMEM PIM (PDF) (PPT)		
W4	31.03 Thu.	YouTube Live	M4: Real-world PIM: Samsung HBM-PIM (PDF) (PPT)		
W5	07.04 Thu.	YouTube Live	M5: How to Evaluate Data Movement Bottlenecks (PDF) (PPT)		
W6	14.04 Thu.	YouTube Live	M6: Real-world PIM: SK Hynix AiM (PDF) (PPT)		
W7	21.04 Thu.	YouTube Premiere	M7: Programming PIM Architectures (PDF) (PPT)		
W8	28.04 Thu.	YouTube Premiere	M8: Benchmarking and Workload Suitability on PIM (PDF) (PPT)		
W9	05.05 Thu.	YouTube Premiere	M9: Real-world PIM: Samsung AxDIMM (PDF) (PPT)		
W10	12.05 Thu.	YouTube Premiere	M10: Real-world PIM: Alibaba HB-PNM (PDF) (PPT)		
W11	19.05 Thu.	YouTube Live	M11: SpMV on a Real PIM Architecture (PDF) (PPT)		
W12	26.05 Thu.	YouTube Live	M12: End-to-End Framework for Processing-using-Memory (PDF) (PPT)		
W13	02.06 Thu.	YouTube Live	M13: Bit-Serial SIMD Processing using DRAM (PDF) (PPT)		
W14	09.06 Thu.	YouTube Live	M14: Analyzing and Mitigating ML Inference Bottlenecks (PDF) (PPT)		
W15	15.06 Thu.	YouTube Live	M15: In-Memory HTAP Databases with HW/SW Co-design (PDF) (PPT)		
W16	23.06 Thu.	YouTube Live	M16: In-Storage Processing for Genome Analysis (PDF) (PPT)		
W17	18.07 Mon.	YouTube Premiere	M17: How to Enable the Adoption of PIM? (PDF) (PPT)		
W18	09.08 Tue.	YouTube Premiere	SS1: ISVLSI 2022 Special Session on PIM (PDF & PPT)		

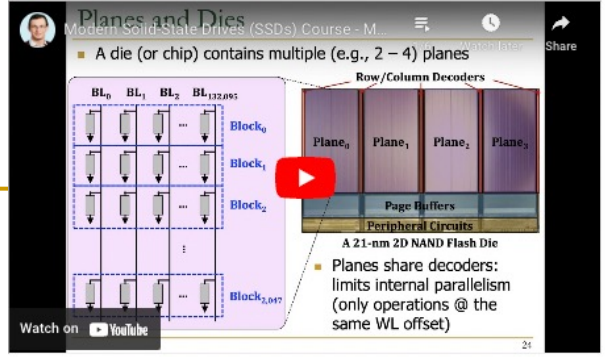
SSD Course (Spring 2023)

- **Spring 2023 Edition:**
  - https://safari.ethz.ch/projects_and_seminars/spring2023/doku.php?id=modern_ssds
- **Fall 2022 Edition:**
  - https://safari.ethz.ch/projects_and_seminars/fall2022/doku.php?id=modern_ssds

- **Youtube Livestream (Spring 2023):**
  - https://www.youtube.com/watch?v=4VTwOMmsnJY&list=PL5Q2soXY2Zi_8qOM5Icpp8hB2SHtm4z57&pp=iAQB
- **Youtube Livestream (Fall 2022):**
  - https://www.youtube.com/watch?v=hqLrd-Uj0aU&list=PL5Q2soXY2Zi9BJhenUq4JI5bwhAMpAp13&pp=iAQB

- Project course
  - Taken by Bachelor's/Master's students
  - SSD Basics and Advanced Topics
  - Hands-on research exploration
  - Many research readings

https://www.youtube.com/onurmutlulectures



Fall 2022 Meetings/Schedule

Week	Date	Livestream	Meeting	Learning Materials	Assignments
W1	06.10		M1: P&S Course Presentation PDF PPT	Required Recommended	
W2	12.10	YouTube Live	M2: Basics of NAND Flash-Based SSDs PDF PPT	Required Recommended	
W3	19.10	YouTube Live	M3: NAND Flash Read/Write Operations PDF PPT	Required Recommended	
W4	26.10	YouTube Live	M4: Processing inside NAND Flash PDF PPT	Required Recommended	
W5	02.11	YouTube Live	M5: Advanced NAND Flash Commands & Mapping PDF PPT	Required Recommended	
W6	09.11	YouTube Live	M6: Processing inside Storage PDF PPT	Required Recommended	
W7	23.11	YouTube Live	M7: Address Mapping & Garbage Collection PDF PPT	Required Recommended	
W8	30.11	YouTube Live	M8: Introduction to MQSim PDF PPT	Required Recommended	
W9	14.12	YouTube Live	M9: Fine-Grained Mapping and Multi-Plane Operation-Aware Block Management PDF PPT	Required Recommended	
W10	04.01.2023	YouTube Premiere	M10a: NAND Flash Basics PDF PPT	Required Recommended	
			M10b: Reducing Solid-State Drive Read Latency by Optimizing Read-Retry PDF PPT Paper	Required Recommended	
			M10c: Evanesco: Architectural Support for Efficient Data Sanitization in Modern Flash-Based Storage Systems PDF PPT Paper	Required Recommended	
			M10d: DeepSketch: A New Machine Learning-Based Reference Search Technique for Post-Deduplication Delta Compression PDF PPT Paper	Required Recommended	
W11	11.01	YouTube Live	M11: FLIN: Enabling Fairness and Enhancing Performance in Modern NVMe Solid State Drives PDF PPT	Required	
W12	25.01	YouTube Premiere	M12: Flash Memory and Solid-State Drives PDF PPT	Recommended	

Real PIM Tutorials [ISCA'23, ASPLOS'23, HPCA'23]

- June, March, Feb : Lectures + Hands-on labs + Invited talks

ISCA 2023 Real-World PIM Tutorial

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Table of Contents

- Real-world Processing-in-Memory Systems for Modern Workloads
  - Tutorial Description
  - Organizers
- Agenda (June 18, 2023)
  - Lectures (tentative)
  - Hands-on Labs (tentative)
  - Learning Materials

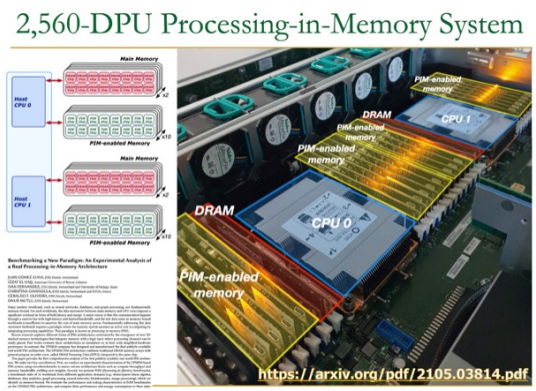
Real-world Processing-in-Memory Systems for Modern Workloads

Tutorial Description

Processing-in-Memory (PIM) is a computing paradigm that aims at overcoming the data movement bottleneck (i.e., the waste of execution cycles and energy resulting from the back-and-forth data movement between memory units and compute units) by making memory compute-capable.

Explored over several decades since the 1960s, PIM systems are becoming a reality with the advent of the first commercial products and prototypes.

A number of startups (e.g., UPMEM, Neuroblade) are already commercializing real PIM hardware, each with its own design approach and target applications. Several major vendors (e.g., Samsung, SK Hynix, Alibaba) have presented real PIM chip prototypes in the last two years. Most of these architectures have in common that they place compute units near the memory arrays. This type of PIM is called processing near memory (PNM).



PIM can provide large improvements in both performance and energy consumption for many modern applications, thereby enabling a commercially viable way of dealing with huge amounts of data that is bottlenecking our computing systems. Yet, it is critical to (1) study and understand the characteristics that make a workload suitable for a PIM architecture, (2) propose optimization strategies for PIM kernels, and (3) develop programming frameworks and tools that can lower the learning curve and ease the adoption of PIM.

This tutorial focuses on the latest advances in PIM technology, workload characterization for PIM, and programming and optimizing PIM kernels. We will (1) provide an introduction to PIM and taxonomy of PIM systems, (2) give an overview and a rigorous analysis of existing real-world PIM hardware, (3) conduct hand-on labs about important workloads (machine learning, sparse linear algebra, bioinformatics, etc.) using real PIM systems, and (4) shed light on how to improve future PIM systems for such workloads.

https://events.safari.ethz.ch/isca-pim-tutorial/

Real PIM Tutorial [ISCA 2023]

- June 18: Lectures + Hands-on labs + Invited talks

Tutorial Materials

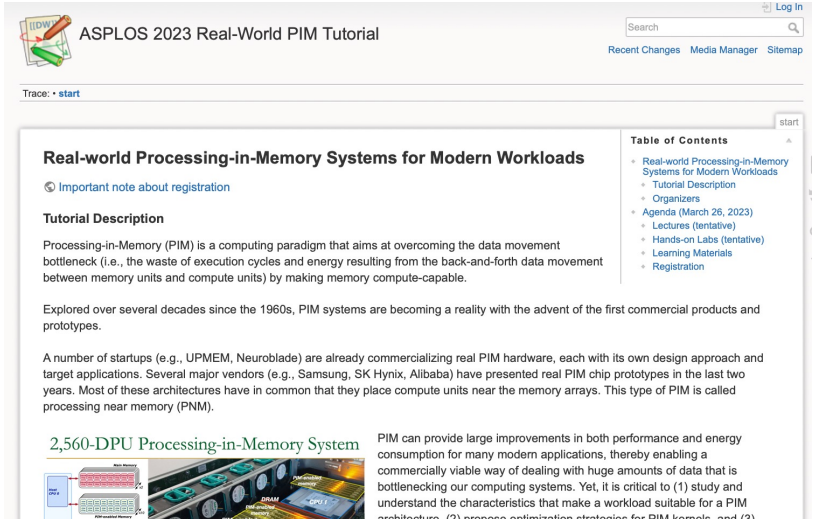
Time	Speaker	Title	Materials
8:55am-9:00am	Dr. Juan Gómez Luna	Welcome & Agenda	(PDF) (PPT)
9:00am-10:20am	Prof. Onur Mutlu	Memory-Centric Computing	(PDF) (PPT)
10:20am-11:00am	Dr. Juan Gómez Luna	Processing-Near-Memory: Real PNM Architectures / Programming General-purpose PIM	(PDF) (PPT)
11:20am-11:50am	Prof. Izzat El Hajj	High-throughput Sequence Alignment using Real Processing-in-Memory Systems	(PDF) (PPT)
11:50am-12:30pm	Dr. Christina Giannoula	SparseP: Towards Efficient Sparse Matrix Vector Multiplication for Real Processing-In-Memory Systems	(PDF) (PPT)
2:00pm-2:45pm	Dr. Sukhan Lee	Introducing Real-world HBM-PIM Powered System for Memory-bound Applications	(PDF) (PPT)
2:45pm-3:30pm	Dr. Juan Gómez Luna / Ataberk Olgun	Processing-Using-Memory: Exploiting the Analog Operational Properties of Memory Components / PUM Prototypes: PiDRAM	(PDF) (PPT) (PDF) (PPT)
4:00pm-4:40pm	Dr. Juan Gómez Luna	Accelerating Modern Workloads on a General-purpose PIM System	(PDF) (PPT)
4:40pm-5:20pm	Dr. Juan Gómez Luna	Adoption Issues: How to Enable PIM?	(PDF) (PPT)
5:20pm-5:30pm	Dr. Juan Gómez Luna	Hands-on Lab: Programming and Understanding a Real Processing-in-Memory Architecture	(Handout) (PDF) (PPT)

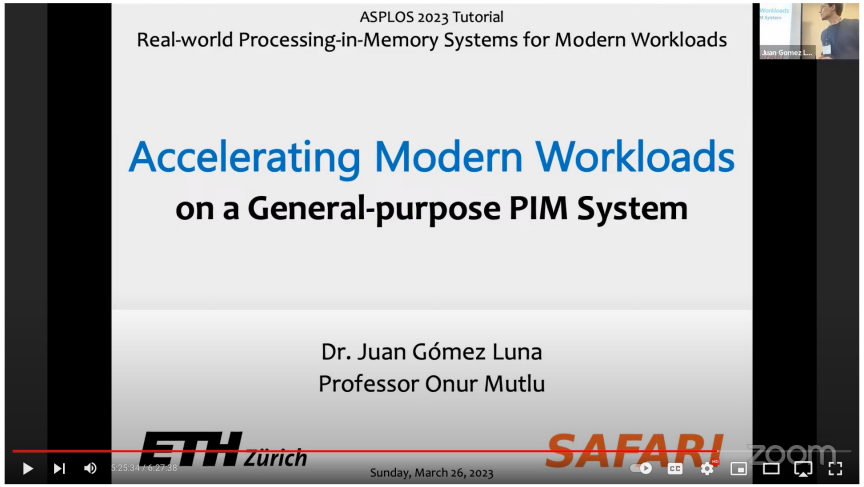
https://www.youtube.com/live/GIb5EgSrWk0

https://events.safari.ethz.ch/isca-pim-tutorial/

Real PIM Tutorial [ASPLOS 2023]

- March 26: Lectures + Hands-on labs + Invited talks





ASPLOS 2023 Tutorial: Real-world Processing-in-Memory Systems for Modern Workloads

Onur Mutlu Lectures
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views Streamed 7 days ago Livestream - Data-Centric Architectures: Fundamentally Improving Performance and Energy (Spring 2023)
LOS 2023 Tutorial: Real-world Processing-in-Memory Systems for Modern Workloads
://events.safari.ethz.ch/asplos-...

Tutorial Materials

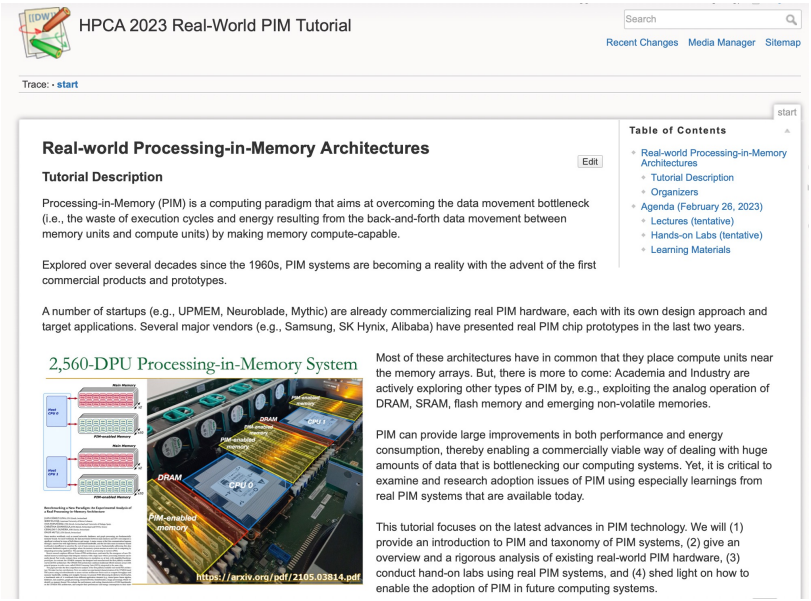
Time	Speaker	Title	Materials
9:00am-10:20am	Prof. Onur Mutlu	Memory-Centric Computing	(PDF) (PPT)
10:40am-12:00pm	Dr. Juan Gómez Luna	Processing-Near-Memory: Real PNM Architectures Programming General-purpose PIM	(PDF) (PPT)
1:40pm-2:20pm	Prof. Alexandra (Sasha) Fedorova (UBC)	Processing in Memory in the Wild	(PDF) (PPT)
2:20pm-3:20pm	Dr. Juan Gómez Luna & Ataberk Olgun	Processing-Using-Memory: Exploiting the Analog Operational Properties of Memory Components	(PDF) (PPT) (PDF) (PPT)
3:40pm-4:10pm	Dr. Juan Gómez Luna	Adoption issues: How to enable PIM? Accelerating Modern Workloads on a General-purpose PIM System	(PDF) (PPT) (PDF) (PPT)
4:10pm-4:50pm	Dr. Yongkee Kwon & Eddy (Chanwook) Park (SK Hynix)	System Architecture and Software Stack for GDDR6-AiM	(PDF) (PPT)
4:50pm-5:00pm	Dr. Juan Gómez Luna	Hands-on Lab: Programming and Understanding a Real Processing-in-Memory Architecture	(Handout) (PDF) (PPT)

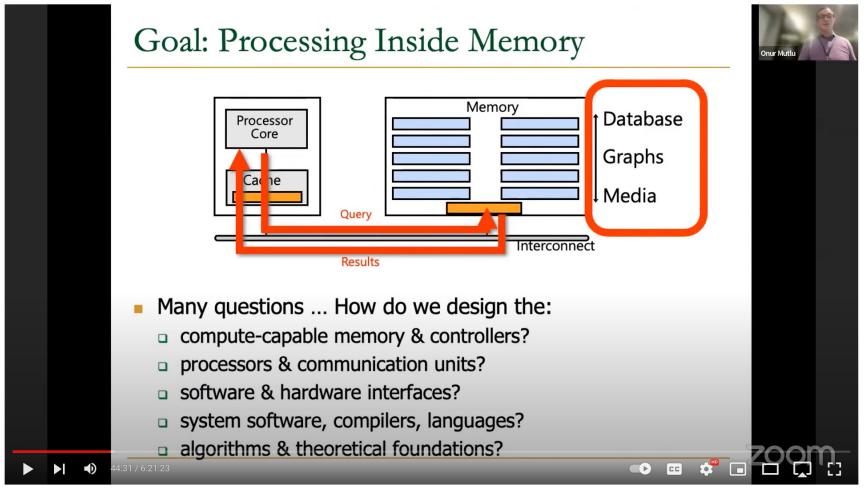
https://www.youtube.com/watch?v=oYCaLcT0Kmo

https://events.safari.ethz.ch/asplos-pim-tutorial/

Real PIM Tutorial [HPCA 2023]

- February 26: Lectures + Hands-on labs + Invited Talks





HPCA 2023 Tutorial: Real-World Processing-in-Memory Architectures

Onur Mutlu Lectures
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1.8K views Streamed 1 month ago Livestream - P&S Data-Centric Architectures: Fundamentally Improving Performance and Energy (Fall 2022)
HPCA 2023 Tutorial: Real-World Processing-in-Memory Architectures
https://events.safari.ethz.ch/real-pi...

Time	Speaker	Title	Materials
8:00am-8:40am	Prof. Onur Mutlu	Memory-Centric Computing	(PDF) (PPT)
8:40am-10:00am	Dr. Juan Gómez Luna	Processing-Near-Memory: Real PNM Architectures Programming General-purpose PIM	(PDF) (PPT)
10:20am-11:00am	Dr. Dimin Niu	A 3D Logic-to-DRAM Hybrid Bonding Process-Near-Memory Chip for Recommendation System	
11:00am-11:40am	Dr. Christina Giannoula	SparseP: Towards Efficient Sparse Matrix Vector Multiplication on Real Processing-In-Memory Architectures	(PDF) (PPT)
1:30pm-2:10pm	Dr. Juan Gómez Luna	Processing-Using-Memory: Exploiting the Analog Operational Properties of Memory Components	(PDF) (PPT)
2:10pm-2:50pm	Dr. Manuel Le Gallo	Deep Learning Inference Using Computational Phase-Change Memory	
2:50pm-3:30pm	Dr. Juan Gómez Luna	PIM Adoption Issues: How to Enable PIM Adoption?	(PDF) (PPT)
3:40pm-5:40pm	Dr. Juan Gómez Luna	Hands-on Lab: Programming and Understanding a Real Processing-in-Memory Architecture	(Handout) (PDF) (PPT)

https://www.youtube.com/watch?v=f5-nT1tbz5w

https://events.safari.ethz.ch/real-pim-tutorial/

Acknowledgments

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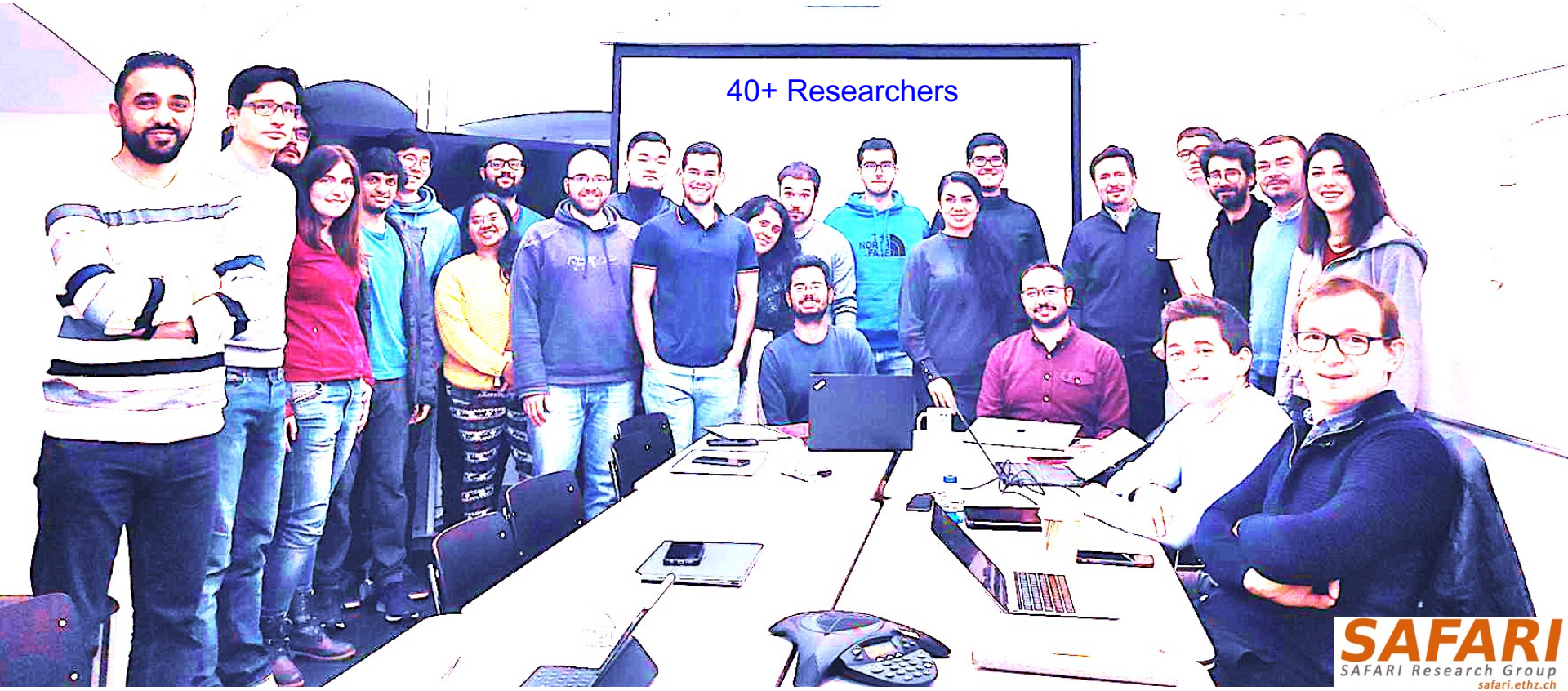
https://safari.ethz.ch

Onur Mutlu's SAFARI Research Group

Computer architecture, HW/SW, systems, bioinformatics, security, memory

https://safari.ethz.ch/safari-newsletter-january-2021/



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https://safari.ethz.ch

SAFARI Newsletter December 2021 Edition

- https://safari.ethz.ch/safari-newsletter-december-2021/

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SAFARI Newsletter June 2023 Edition

- https://safari.ethz.ch/safari-newsletter-june-2023/

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SAFARI Introduction & Research

Computer architecture, HW/SW, systems, bioinformatics, security, memory

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https://www.youtube.com/watch?v=mV2OuB2djEs

Referenced Papers, Talks, Artifacts

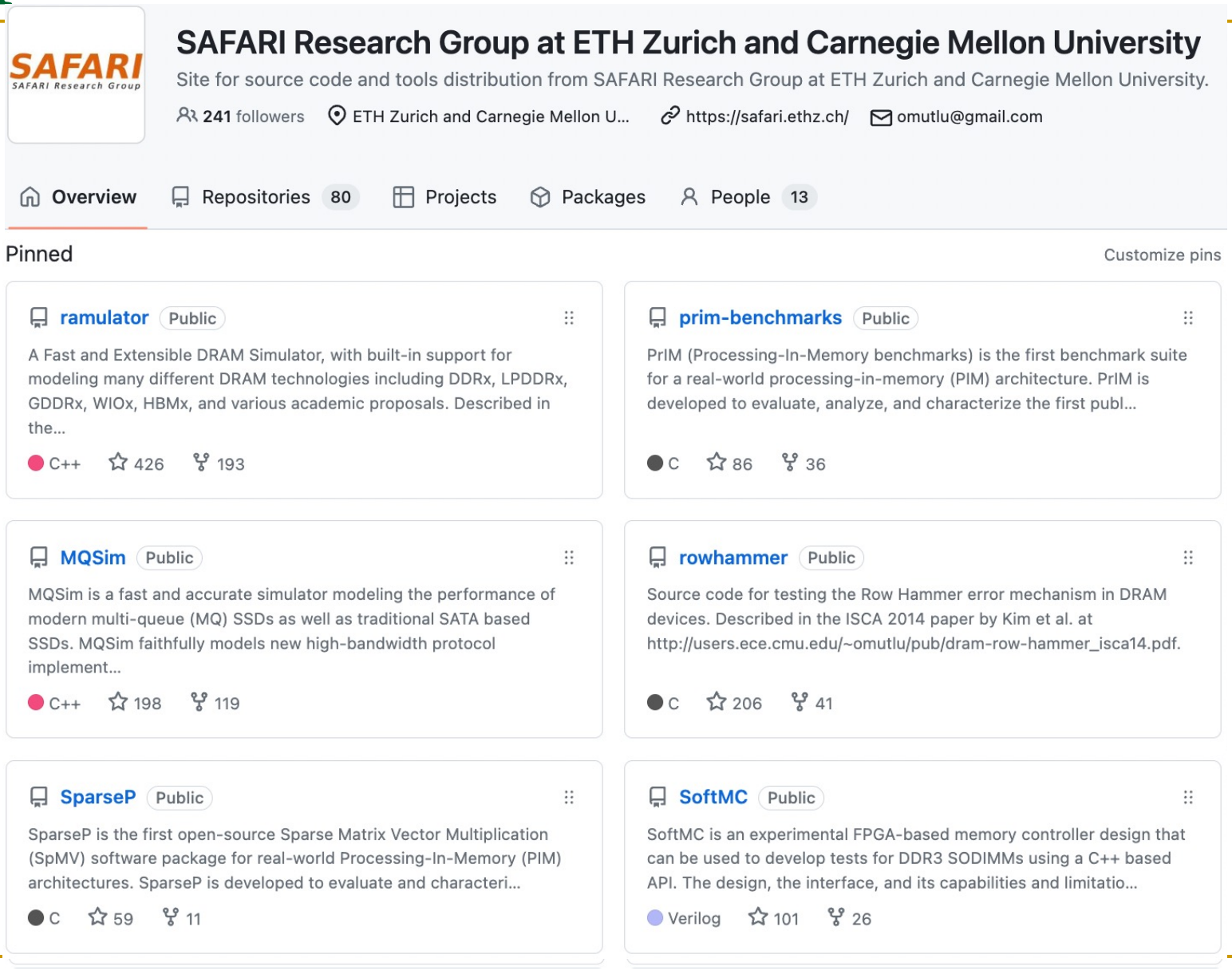
- All are available at

  https://people.inf.ethz.ch/omutlu/projects.htm

  https://www.youtube.com/onurmutlulectures

  https://github.com/CMU-SAFARI/

Open Source Tools: SAFARI GitHub



https://github.com/CMU-SAFARI/

Accelerating Genome Analysis
via Algorithm-Architecture Co-Design

Onur Mutlu
omutlu@gmail.com
https://people.inf.ethz.ch/omutlu

11 July 2023

DAC 2023 Special Session Talk

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60 DESIGN AUTOMATION CONFERENCE

FROM CHIPS TO SYSTEMS — LEARN TODAY, CREATE TOMORROW

Backup Slides for Further Info

Our First Step: Comprehensive Mapping

- + Guaranteed to find *all* mappings → sensitive
- + Can tolerate up to *e* errors

nature genetics

http://mrfast.sourceforge.net/

Personalized copy number and segmental duplication maps using next-generation sequencing

Can Alkan[1,2], Jeffrey M Kidd[1], Tomas Marques-Bonet[1,3], Gozde Aksay[1], Francesca Antonacci[1], Fereydoun Hormozdiari[4], Jacob O Kitzman[1], Carl Baker[1], Maika Malig[1], Onur Mutlu[5], S Cenk Sahinalp[4], Richard A Gibbs[6] & Evan E Eichler[1,2]

Alkan+, **"Personalized copy number and segmental duplication maps using next-generation sequencing"**, Nature Genetics 2009.

Resources & Acknowledgments

Special Research Sessions & Courses

- Special Session at ISVLSI 2022: 9 cutting-edge talks

https://www.youtube.com/watch?v=qeukNs5XI3g

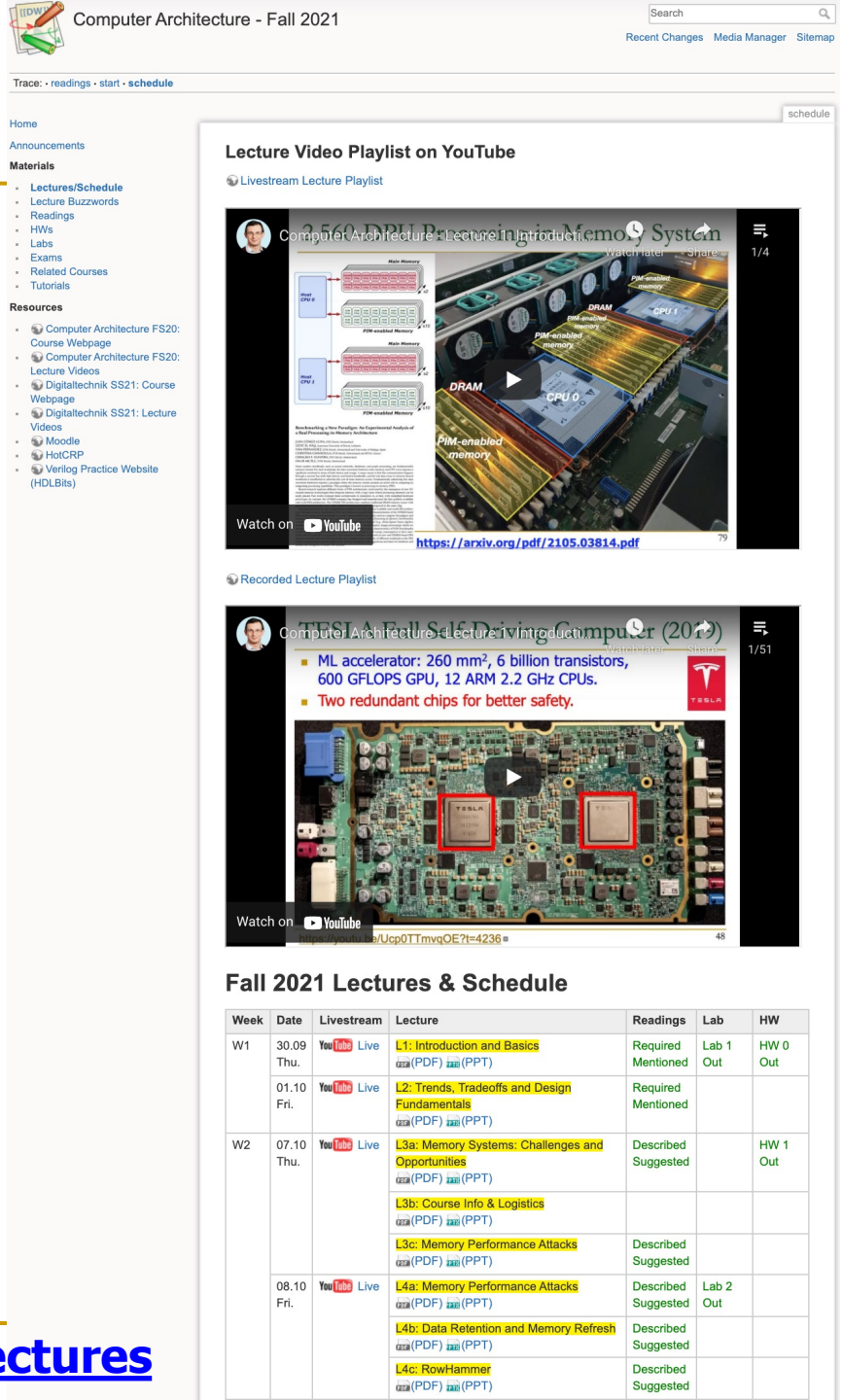
Detailed Lectures on Genome Analysis

- Computer Architecture, Fall 2020, Lecture 3a
  - **Introduction to Genome Sequence Analysis** (ETH Zürich, Fall 2020)
  - https://www.youtube.com/watch?v=CrRb32v7SJc&list=PL5Q2soXY2Zi9xidyIgBxUz7xRPS-wisBN&index=5
- Computer Architecture, Fall 2020, Lecture 8
  - **Intelligent Genome Analysis** (ETH Zürich, Fall 2020)
  - https://www.youtube.com/watch?v=ygmQpdDTL7o&list=PL5Q2soXY2Zi9xidyIgBxUz7xRPS-wisBN&index=14
- Computer Architecture, Fall 2020, Lecture 9a
  - **GenASM: Approx. String Matching Accelerator** (ETH Zürich, Fall 2020)
  - https://www.youtube.com/watch?v=XoLpzmN-Pas&list=PL5Q2soXY2Zi9xidyIgBxUz7xRPS-wisBN&index=15
- Accelerating Genomics Project Course, Fall 2020, Lecture 1
  - **Accelerating Genomics** (ETH Zürich, Fall 2020)
  - https://www.youtube.com/watch?v=rgjl8ZyLsAg&list=PL5Q2soXY2Zi9E2bBVAgCqLgwiDRQDTyId

Comp Arch (Fall'21)

- **Fall 2021 Edition:**
  - https://safari.ethz.ch/architecture/fall2021/doku.php?id=schedule
- **Fall 2020 Edition:**
  - https://safari.ethz.ch/architecture/fall2020/doku.php?id=schedule
- **Youtube Livestream (2021):**
  - https://www.youtube.com/watch?v=4yfkM_5EFgo&list=PL5Q2soXY2Zi-Mnk1PxjEIG32HAGILkTOF
- **Youtube Livestream (2020):**
  - https://www.youtube.com/watch?v=c3mPdZA-Fmc&list=PL5Q2soXY2Zi9xidyIgBxUz7xRPS-wisBN
- Master's level course
  - Taken by Bachelor's/Masters/PhD students
  - Cutting-edge research topics + fundamentals in Computer Architecture
  - 5 Simulator-based Lab Assignments
  - Potential research exploration
  - Many research readings

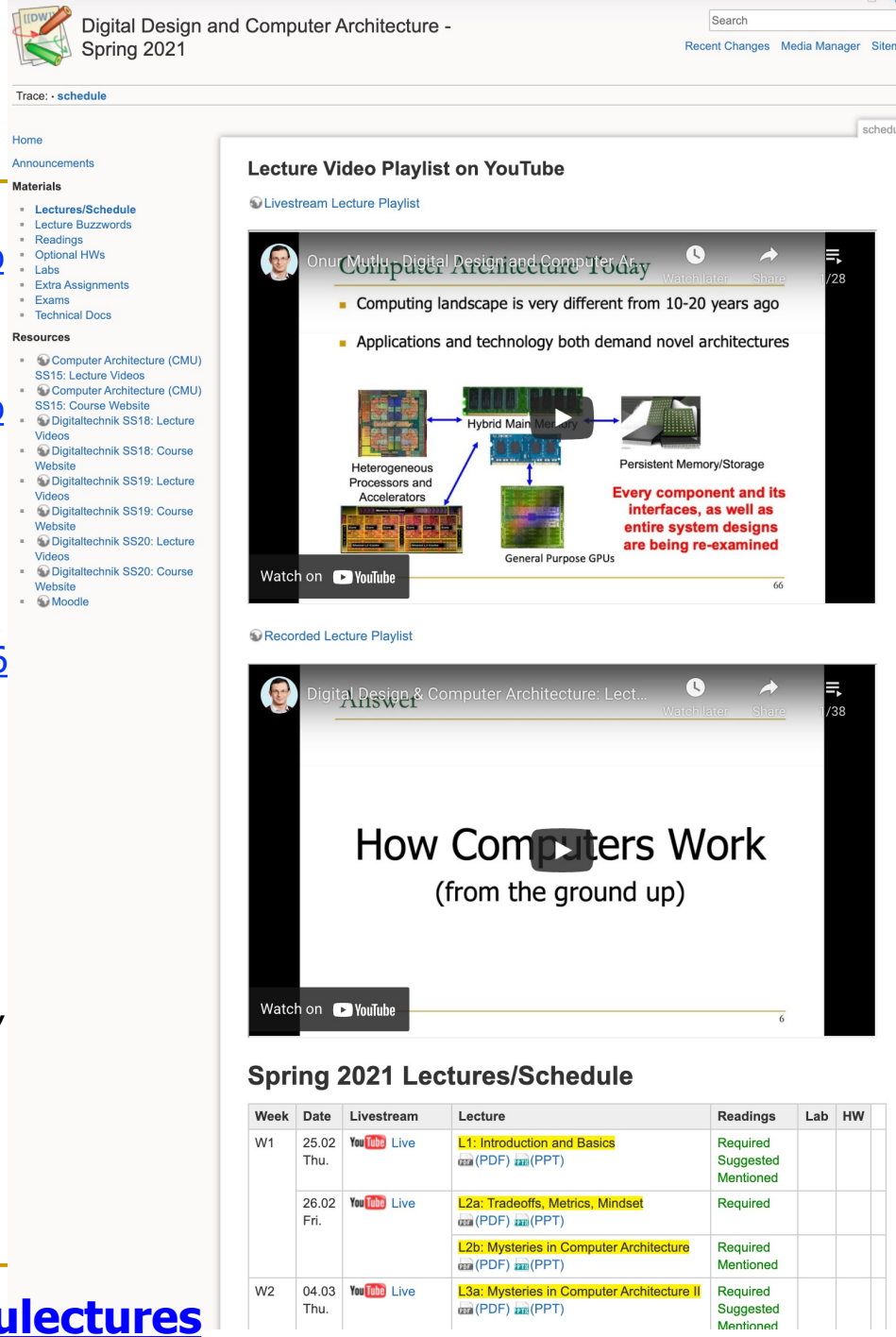
https://www.youtube.com/onurmutlulectures



DDCA (Spring 2022)

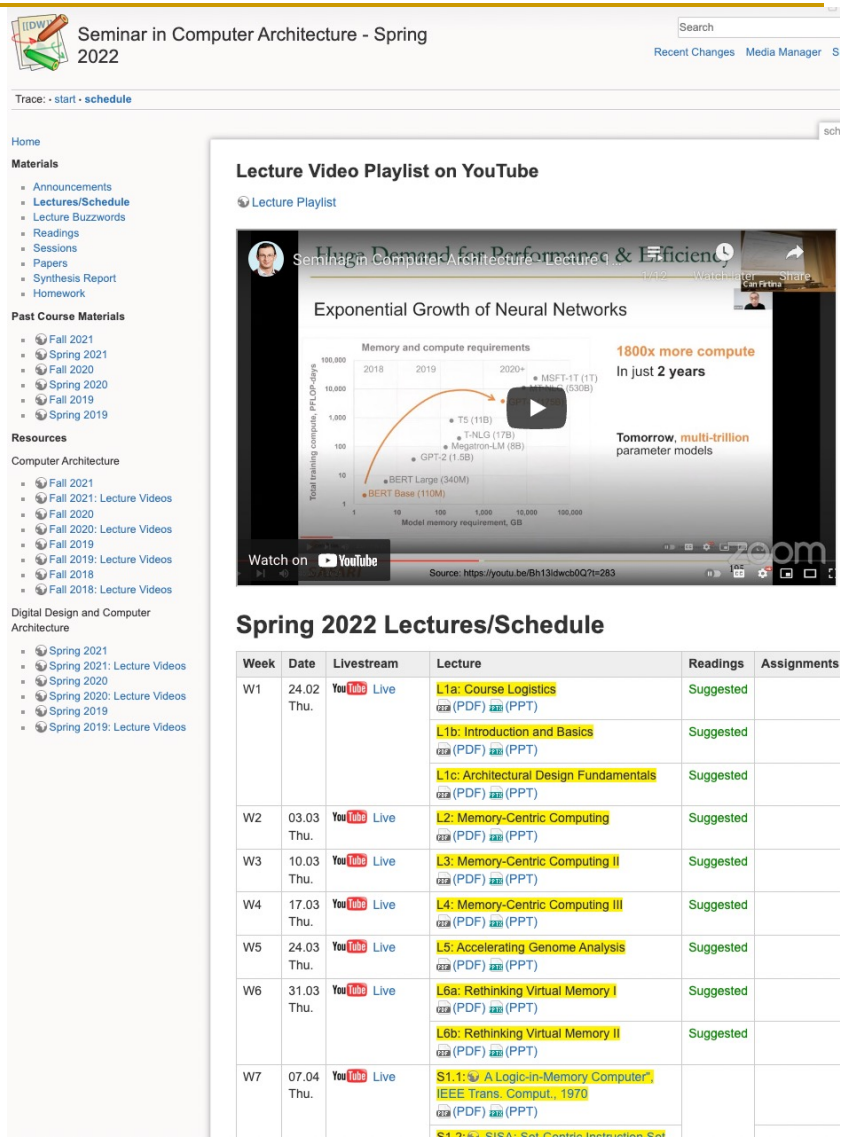
- **Spring 2022 Edition:**
  - https://safari.ethz.ch/digitaltechnik/spring2022/doku.php?id=schedule
- **Spring 2021 Edition:**
  - https://safari.ethz.ch/digitaltechnik/spring2021/doku.php?id=schedule
- **Youtube Livestream (Spring 2022):**
  - https://www.youtube.com/watch?v=cpXdE3HwvK0&list=PL5Q2soXY2Zi97Ya5DEUpMpO2bbAoaG7c6
- **Youtube Livestream (Spring 2021):**
  - https://www.youtube.com/watch?v=LbC0EZY8yw4&list=PL5Q2soXY2Zi_uej3aY39YB5pfW4SJ7LlN
- Bachelor's course
  - 2nd semester at ETH Zurich
  - Rigorous introduction into "How Computers Work"
  - Digital Design/Logic
  - Computer Architecture
  - 10 FPGA Lab Assignments

https://www.youtube.com/onurmutlulectures



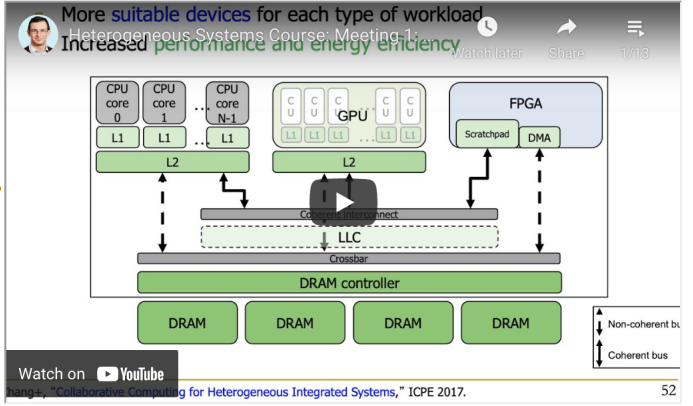
Seminar in Comp Arch (Spring & Fall)

- **Spring 2022 Edition:**
  - https://safari.ethz.ch/architecture_seminar/spring2022/doku.php?id=schedule
- **Fall 2021 Edition:**
  - https://safari.ethz.ch/architecture_seminar/fall2021/doku.php?id=schedule
- **Youtube Livestream (Spring 2022):**
  - https://www.youtube.com/watch?v=rS9UPk509AQ&list=PL5Q2soXY2Zi_hxizriwKmFHgcoe2Q8-m0
- **Youtube Livestream (Fall 2021):**
  - https://www.youtube.com/watch?v=4TcP297mdsI&list=PL5Q2soXY2Zi_7UBNmC9B8Yr5JSwTG9yH4
- Critical analysis course
  - Taken by Bachelor's/Masters/PhD students
  - Cutting-edge research topics + fundamentals in Computer Architecture
  - 20+ research papers, presentations, analyses



Hetero. Systems (Spring'22)

- **Spring 2022 Edition:**
  - https://safari.ethz.ch/projects_and_seminars/spring2022/doku.php?id=heterogeneous_systems
- **Youtube Livestream:**
  - https://www.youtube.com/watch?v=oFO5fTrgFIY&list=PL5Q2soXY2Zi9XrgXR38IM_FTjmY6h7Gzm
- Project course
  - Taken by Bachelor's/Master's students
  - GPU and Parallelism lectures
  - Hands-on research exploration
  - Many research readings

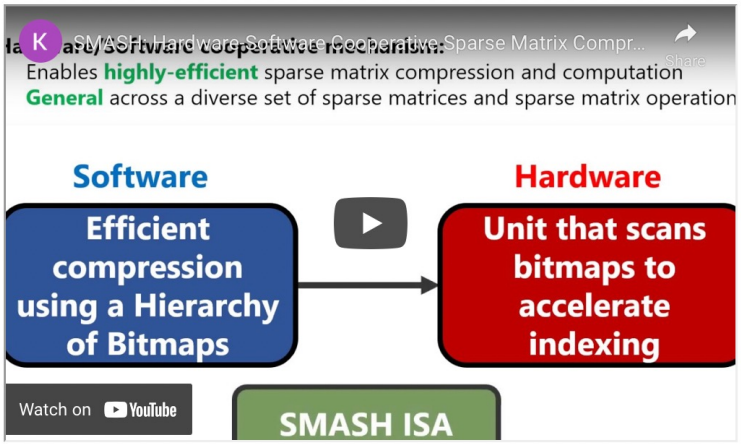


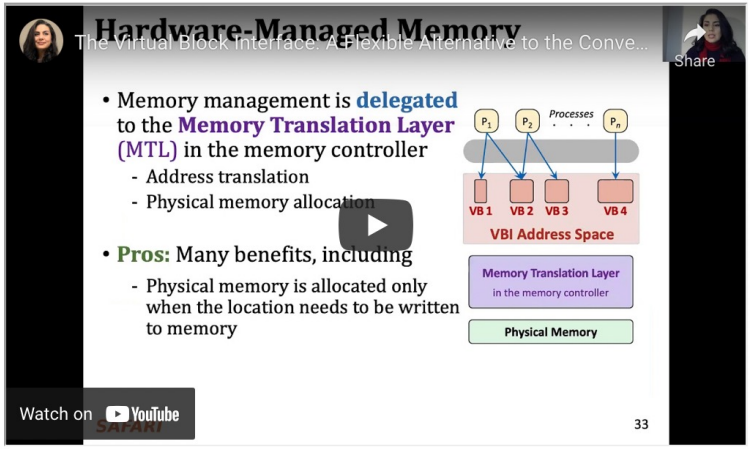
Spring 2022 Meetings/Schedule

Week	Date	Livestream	Meeting	Learning Materials	Assignments
W1	15.03 Tue.	Premiere	M1: P&S Course Presentation (PDF) (PPT)	Required Materials Recommended Materials	HW 0 Out
W2	22.03 Tue.	Premiere	M2: SIMD Processing and GPUs (PDF) (PPT)		
W3	29.03 Tue.	Premiere	M3: GPU Software Hierarchy (PDF) (PPT)		
W4	05.04 Tue.	Premiere	M4: GPU Memory Hierarchy (PDF) (PPT)		
W5	12.04 Tue.	Premiere	M5: GPU Performance Considerations (PDF) (PPT)		
W6	19.04 Tue.	Premiere	M6: Parallel Patterns: Reduction (PDF) (PPT)		
W7	26.04 Tue.	Premiere	M7: Parallel Patterns: Histogram (PDF) (PPT)		
W8	03.05 Tue.	Premiere	M8: Parallel Patterns: Convolution (PDF) (PPT)		
W9	10.05 Tue.	Premiere	M9: Parallel Patterns: Prefix Sum (Scan) (PDF) (PPT)		
W10	17.05 Tue.	Premiere	M10: Parallel Patterns: Sparse Matrices (PDF) (PPT)		
W11	24.05 Tue.	Premiere	M11: Parallel Patterns: Graph Search (PDF) (PPT)		
W12	01.06 Wed.	Premiere	M12: Parallel Patterns: Merge Sort (PDF) (PPT)		
W13	07.06 Tue.	Premiere	M13: Dynamic Parallelism (PDF) (PPT)		
W14	15.06 Wed.	Premiere	M14: Collaborative Computing (PDF) (PPT)		
W15	24.06 Fri.	Premiere	M15: GPU Acceleration of Genome Sequence Alignment (PDF) (PPT)		
W16	14.07 Thu.	Premiere	M16: Accelerating Agent-based Simulations (PDF) (ODP)		

HW/SW Co-Design (Spring 2022)

- **Spring 2022 Edition:**
  - https://safari.ethz.ch/projects_and_seminars/spring2022/doku.php?id=hw_sw_codesign
- **Youtube Livestream:**
  - https://youtube.com/playlist?list=PL5Q2soXY2Zi8nH7un3ghD2nutKWWDk-NK
- Project course
  - Taken by Bachelor's/Master's students
  - HW/SW co-design lectures
  - Hands-on research exploration
  - Many research readings





Edit

2022 Meetings/Schedule (Tentative)

Week	Date	Livestream	Meeting	Materials	Assignments
W0	16.03	YouTube Live	Intro to HW/SW Co-Design (PPTX) (PDF)	Required	HW 0 Out
W1	23.03		Project selection	Required	
W2	30.03	YouTube Live	Virtual Memory (I) (PPTX) (PDF)		
W3	13.04	YouTube Live	Virtual Memory (II) (PPTX) (PDF)		

Some Other Recent Papers

Finding Approximate Seed Matches

- Can Firtina, Jisung Park, Mohammed Alser, Jeremie S. Kim, Damla Senol Cali, Taha Shahroodi, Nika Mansouri-Ghiasi, Gagandeep Singh, Konstantinos Kanellopoulos, Can Alkan, and Onur Mutlu,
  "BLEND: A Fast, Memory-Efficient, and Accurate Mechanism to Find Fuzzy Seed Matches"
  Preprint in *arXiv*, 2021.
  [arXiv preprint]
  [BLEND Source Code and Data]

BLEND: A Fast, Memory-Efficient, and Accurate Mechanism to Find Fuzzy Seed Matches

Can Firtina[1] Jisung Park[1] Mohammed Alser[1] Jeremie S. Kim[1] Damla Senol Cali[2]
Taha Shahroodi[3] Nika Mansouri-Ghiasi[1] Gagandeep Singh[1] Konstantinos Kanellopoulos[1]
Can Alkan[4] Onur Mutlu[1]
[1]*ETH Zurich* [2]*Bionano Genomics* [3]*TU Delft* [4]*Bilkent University*

Hardware Acceleration for pHMMs

- Can Firtina, Kamlesh Pillai, Gurpreet S. Kalsi, Bharathwaj Suresh, Damla Senol Cali, Jeremie S. Kim, Taha Shahroodi, Meryem Banu Cavlak, Joel Lindegger, Mohammed Alser, Juan Gómez-Luna, Sreenivas Subramoney, and Onur Mutlu, "ApHMM: A Profile Hidden Markov Model Acceleration Framework for Genome Analysis"
  Preprint in *arXiv*, 2022.
  [Source Code]

ApHMM: A Profile Hidden Markov Model Acceleration Framework for Genome Analysis

Can Firtina[1] Kamlesh Pillai[2] Gurpreet S. Kalsi[2] Bharathwaj Suresh[2] Damla Senol Cali[3]
Jeremie S. Kim[1] Taha Shahroodi[4] Meryem Banu Cavlak[1] Joel Lindegger[1] Mohammed Alser[1]
Juan Gómez Luna[1] Sreenivas Subramoney[2] Onur Mutlu[1]
[1]*ETH Zurich* [2]*Intel Labs* [3]*Bionano Genomics* [4]*TU Delft*

Remapping Reads Between References

- Jeremie S. Kim, Can Firtina, Meryem Banu Cavlak, Damla Senol Cali, Nastaran Hajinazar, Mohammed Alser, Can Alkan, and Onur Mutlu,
  "AirLift: A Fast and Comprehensive Technique for Remapping Alignments between Reference Genomes"
  Preprint in arXiv and bioRxiv, 2021.
  [bioRxiv preprint]
  [arXiv preprint]
  [AirLift Source Code and Data]

METHOD

AirLift: A Fast and Comprehensive Technique for Remapping Alignments between Reference Genomes

Jeremie S. Kim[1†], Can Firtina[1†], Meryem Banu Cavlak[2], Damla Senol Cali[3], Nastaran Hajinazar[1,4], Mohammed Alser[1], Can Alkan[2] and Onur Mutlu[1,2,3*]

Mapping Constant Regions Between References

- Jeremie S. Kim, Can Firtina, Meryem Banu Cavlak, Damla Senol Cali, Can Alkan, and Onur Mutlu,
  "FastRemap: A Tool for Quickly Remapping Reads between Genome Assemblies"
  Bioinformatics, btac554.
  [FastRemap Source Code]

FastRemap: A Tool for Quickly Remapping Reads between Genome Assemblies

Jeremie S. Kim[1] Can Firtina[1] Meryem Banu Cavlak[1] Damla Senol Cali[2,3]
Can Alkan[4] Onur Mutlu[1,2,4]

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COVIDHunter

Mohammed Alser, Jeremie S. Kim, Nour Almadhoun Alserr, Stefan W. Tell, Onur Mutlu
"COVIDHunter: COVID-19 Pandemic Wave Prediction and Mitigation via Seasonality Aware Modeling"
Frontiers in Public Health 2022
[Source Code]

frontiers | Frontiers in Public Health

ORIGINAL RESEARCH
published: 17 June 2022
doi: 10.3389/fpubh.2022.877621

COVIDHunter: COVID-19 Pandemic Wave Prediction and Mitigation via Seasonality Aware Modeling

Mohammed Alser, Jeremie S. Kim, Nour Almadhoun Alserr, Stefan W. Tell and Onur Mutlu*

Department of Information Technology and Electrical Engineering (D-ITET), ETH Zurich, Zurich, Switzerland

Packaging Omics Methods

Mohammed Alser, Sharon Waymost, Ram Ayyala, Brendan Lawlor, Richard J. Abdill, Neha Rajkumar, Nathan LaPierre, Jaqueline Brito, Andre M. Ribeiro-dos-Santos, Can Firtina, Nour Almadhoun, Varuni Sarwal, Eleazar Eskin, Qiyang Hu, Derek Strong, Byoung-Do (BD)Kim, Malak S. Abedalthagafi, Onur Mutlu, Serghei Mangul
"Packaging, containerization, and virtualization of computational omics methods: Advances, challenges, and opportunities"
arrXiv 2022

Packaging, containerization, and virtualization of computational omics methods: Advances, challenges, and opportunities

Mohammed Alser[1], Sharon Waymost[2], Ram Ayyala[3,4], Brendan Lawlor[5], Richard J. Abdill[6], Neha Rajkumar[7], Nathan LaPierre[2], Jaqueline Brito[4], André M. Ribeiro-dos-Santos[8], Can Firtina[1], Nour Almadhoun[1], Varuni Sarwal[2], Eleazar Eskin[2,9,10], Qiyang Hu[11], Derek Strong[12], Byoung-Do (BD) Kim[12], Malak S. Abedalthagafi[13,14,15*], Onur Mutlu[1,*], Serghei Mangul[4,*]

Demeter (HD Food Microbiome Profiling)

Taha Shahroodi, Mahdi Zahedi, Can Firtina, Mohammed Alser, Stephan Wong, Onur Mutlu, Said Hamdioui
"Demeter: A Fast and Energy-Efficient Food Profiler using Hyperdimensional Computing in Memory"
IEEE Access, 2022

Demeter: A Fast and Energy-Efficient Food Profiler Using Hyperdimensional Computing in Memory

TAHA SHAHROODI[1], MAHDI ZAHEDI[1], CAN FIRTINA[2], MOHAMMED ALSER[2], STEPHAN WONG[1], (Senior Member, IEEE), ONUR MUTLU[2], (Fellow, IEEE), AND SAID HAMDIOUI[1], (Senior Member, IEEE)
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End of Backup Slides