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EXCELENCIA SEVERO OCHOA

BIMSA: Accelerating Long Sequence Alignment Using Processing-In-Memory

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1. Introduction and Motivation
2. Background
3. PIM-enabled BiWFA Implementation
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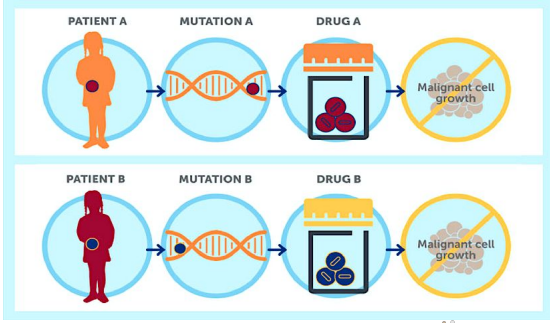
1.1 Genomic Sequencing and Sequence Alignment

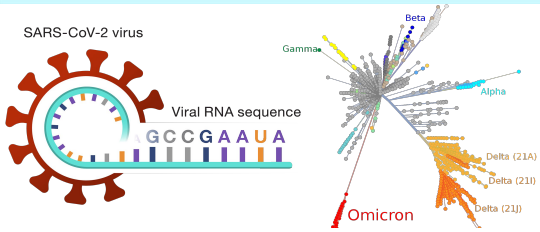
Sequencing an organism's genome enables:

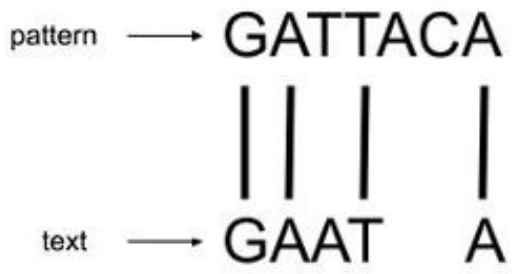
- **Personalized medicine/therapies**.
- **Tracing a real-time virus outbreak**.
- **Editing an organism genome**.



Genomic Sequencing requires Sequence Alignment which compares DNA/RNA sequences to obtain:

- **Path of operations** to transform one sequence into another (aka CIGAR).
- **Distance/error/score** (sum of the operation weights).





1.2 Sequence Alignment Algorithms

Classical sequence alignment algorithms are based on **Dynamic Programming** (DP) (e.g., Needleman-Wunsch, Smith-Waterman) which compute the full matrix (n×m).

- **Complexity O(n×m)** in memory and time.

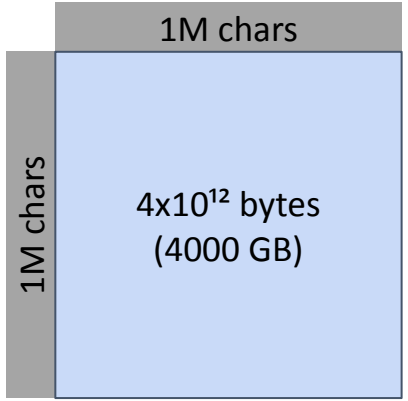
Wavefront Algorithm (WFA): computes the cells in increasing score **(s)**, avoiding suboptimal cells.

- **Complexity O(n×s)** in compute and **O(s^2)** in memory.

Bidirectional Wavefront Algorithm (BiWFA): computes **WFA** in both ends of the matrix.

- **Complexity O(n×s)** in compute and **O(s)** in memory.

All algorithms are a **memory bound** problem.



		G	A	A	T	A
	0	1	2	3	4	5
G	1	0	1	2	3	4
A	2	1	0	1	2	3
T	3	2	1	1	1	2
T	4	3	2	2	1	2
A	5	4	3	2	2	1
C	6	5	4	3	3	2
A	7	6	5	4	4	3

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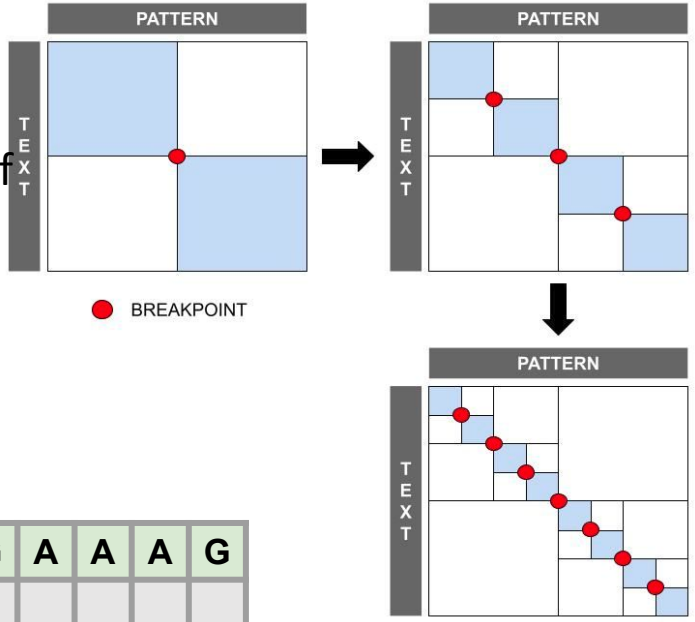
2.1 BiWFA Key Concept

1. Compute independent **WFA from both ends**.
2. Find where the two WFA collide/meet (breakpoint of the alignment).
3. **Recursively divide and conquer the problem.**

Breakpoint gives **distance**, offset and operation of the optimal path ⟶ All breakpoints = **Operation path**.

BiWFA needs **4 increasing arrays** (wavefronts) **O(s)**.

WFA stores intermediate wavefronts **O(s^2)**.



s=1	s=2
	4
2	5
	3

		T	G	G	A	A	A	G
	T	0	1	2				
	C	1	1					
	T	2		2				
	A				2			
	G							
	C							
	G							

FORWARD WAVEFRONT

		T	G	G	A	A	A	G
	T							
	C							
	T							
	A				2		2	
	G					2		2
	C						1	1
	G					2	1	0

REVERSE WAVEFRONT

s=2	s=1
5	
5	2
3	

2.2 Processing-In-Memory (PIM) Paradigm

Processing-In-Memory (PIM) is a paradigm that aims to alleviate memory bound problems.

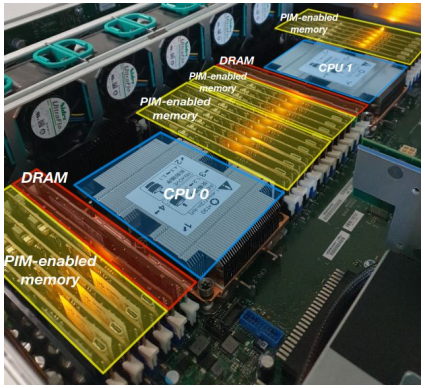
Key idea: place compute units close to data.

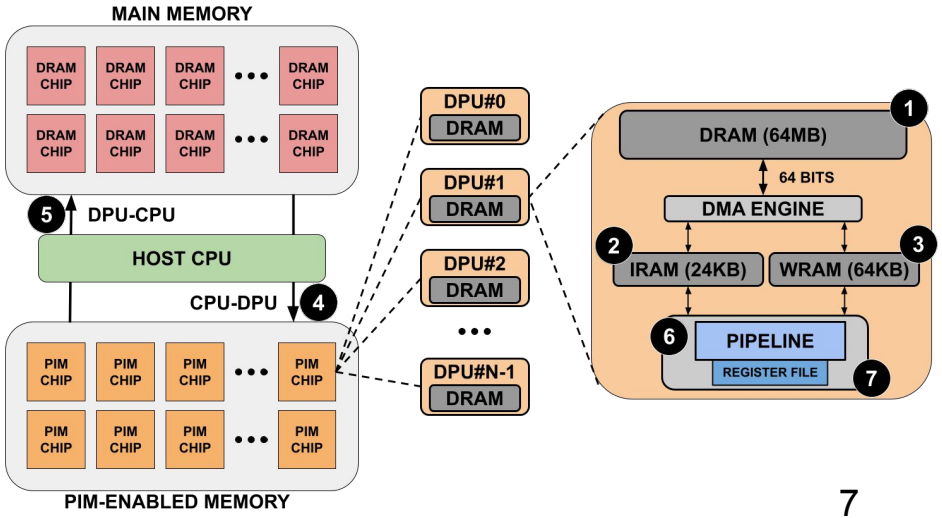
This enables:

- Exploiting **higher bandwidth** and **lower latency**.
- **Reducing energy** consumption.

We use the **UPMEM** PIM architecture.

1. Up to 2500 compute units (DPUs).
2. Up to 24 hardware threads.
3. 64MB DRAM memory (MRAM).
4. 64KB scratchpad memory (WRAM).
5. General purpose processor.





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3.1 BIMSA: BiWFA PIM-based Implementation

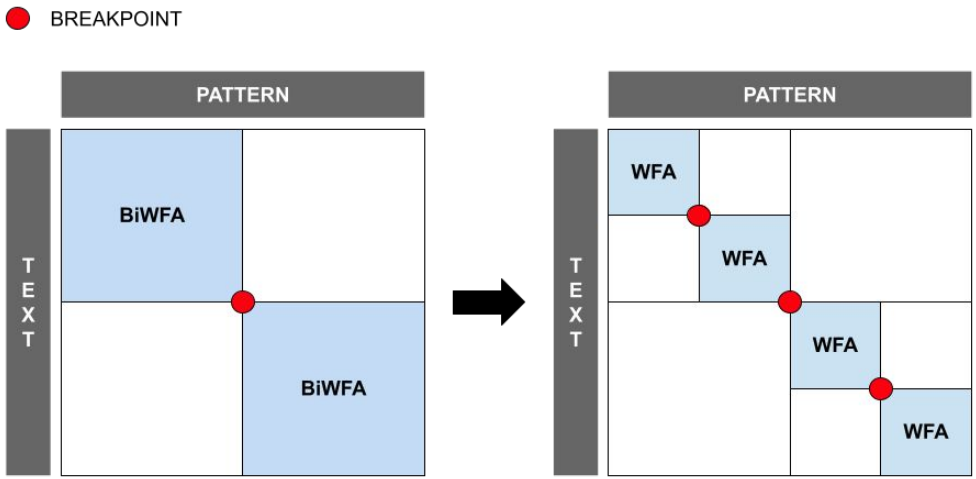
Challenge: Full-recursive BiWFA presents many corner cases.

Key idea: Execute BiWFA until the slices have a suitable size for WFA.

Leverage: BiWFA property → breakpoint gives distance.

For each thread (coarse-grain parallelism):

1. Compute BiWFA and find a **breakpoint**.
2. Slice sequences in half.
3. Compute BiWFA in both slices.
4. Iterate until distance equals a **threshold**.
5. Use WFA for the small slices **(base case)**.
6. Obtaining **partial CIGARs** from the base cases.
7. **Join partial CIGARs**.



3.2 BIMSA Optimizations: Base Case in Scratchpad

BiWFA steps use **4 scratchpad blocks independently** and **access DRAM** when the block is used.

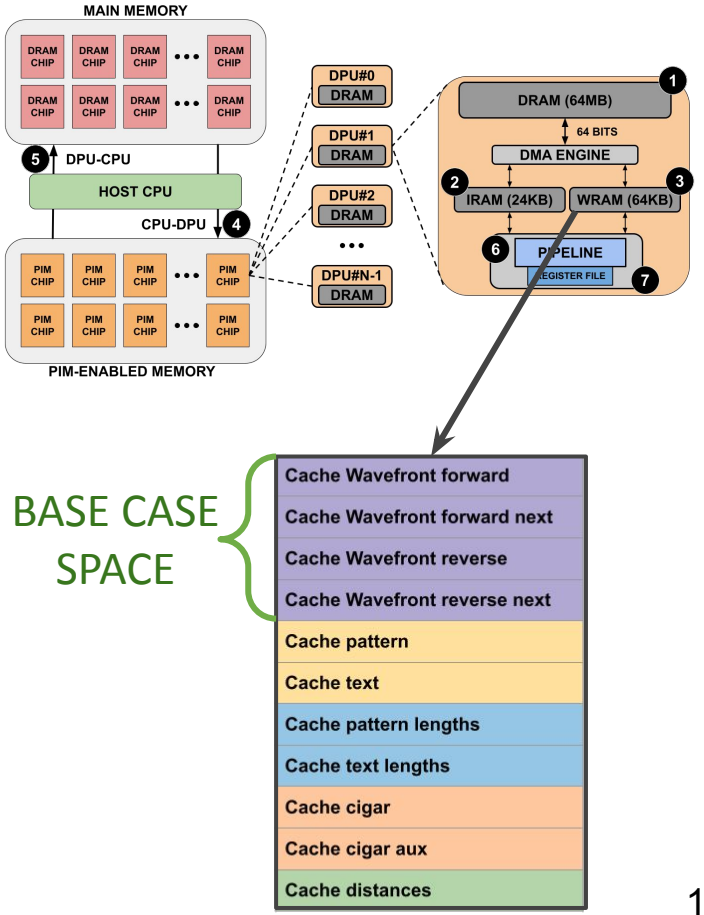
These 4 blocks are not needed for the base case.

- **Merge the 4 blocks** and use them for the base case.

WFA memory space is defined by distance.

- Use the **4 blocks size** as base case **threshold**.

We eliminate completely any DRAM access.

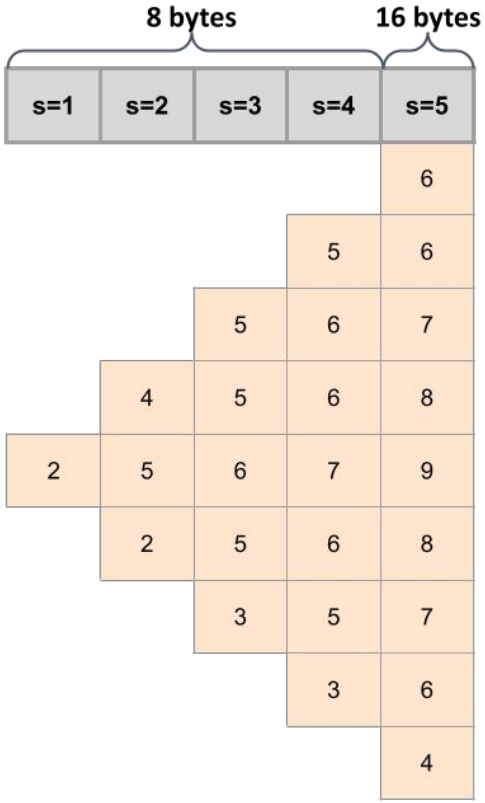


3.2 BIMSA Optimizations: Adaptive Transfers

BiWFA uses **increasing data structures** that reset its size after each breakpoint.

However, **we know** exactly the **amount of data to transfer** in each iteration.

- UPMEM allows to **indicate the transfer size** in each DRAM/scratchpad transfer.
- We define the scratchpad data structures to the maximum size we expect to transfer (2048 max).
- **Start from 8 byte** transfers and **increase x2** upon surpassing the current transfer size.
- **Reset to 8 bytes** after each breakpoint.
- With this mechanism we read minimum useless data.

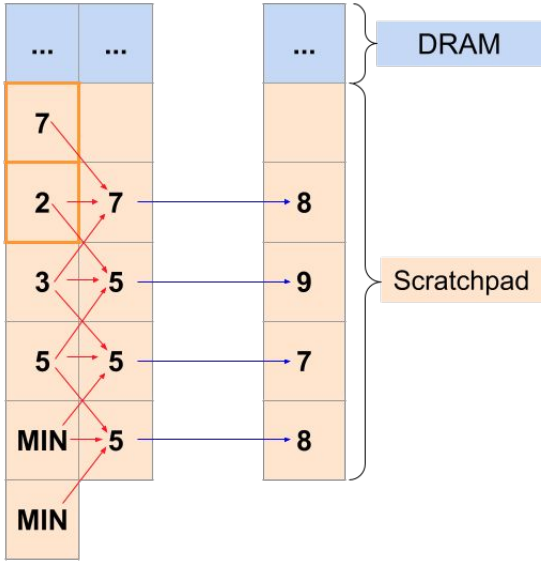


3.2 BIMSA Optimizations: BiWFA Steps Fusion

The original BiWFA makes use of vectorization ⟶ UPMEM does not support vectorization.

BiWFA uses **two main** computation **steps**. Applying them in large wavefronts require several memory transfers.

- UPMEM allows to explicitly **manage scratchpad** memory **blocks**.
- **Apply both steps on a scratchpad block.**
- Two elements are read twice per block.
- We reduce up to 40% the MRAM accesses.



3.2 BIMSA Optimizations: CPU Recovery

BIMSA is based on coarse-grain parallelism:

- No DPU intercommunication.
- High cost tasklet communication.

Datasets from real sequencers (e.g., Nanopore, PacBio) produce heterogeneous alignment times between tasklets and DPUs.

Solution (**BIMSA-Hybrid**):

- Alignment batching and different dpu_sets.
- Add distance/score limit to alignments O(ns) & finish larger alignments on CPU.

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4.1 Experimental Setup

- Datasets
  - 9 simulated datasets (different sequence lengths and different error rates).
  - 4 real sequencer datasets (Illumina x2, Nanopore, PacBio).
- Applications
  - **CPU:** Official BiWFA implementation (WFA2lib).
  - **PIM:** state-of-the-art AIM implementations, WFA and NW (AIM-WFA, AIM-NW).
  - **BIMSA (Ours):** PIM - BiWFA implementation (UPMEM-v1B).
  - **BIMSA Next generation** projection (UPMEM-v1A) ⟶ Based on scalability results.
- Machines
  - **CPU**: Intel Xeon Silver 4215 2.50 GHz, 2 sockets of 8 cores each; 16 hardware threads.
  - **UPMEM-node**: 2556 DPUs 350 MHz, 24 threads.

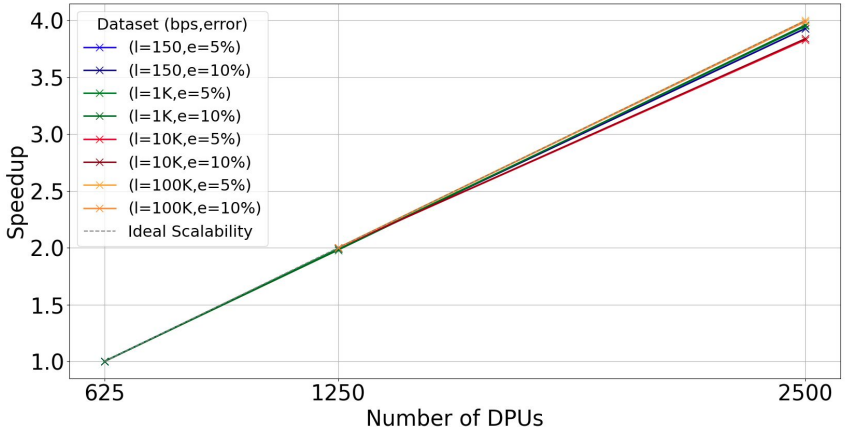
4.2 BIMSA Scalability (DPUs & Threads)

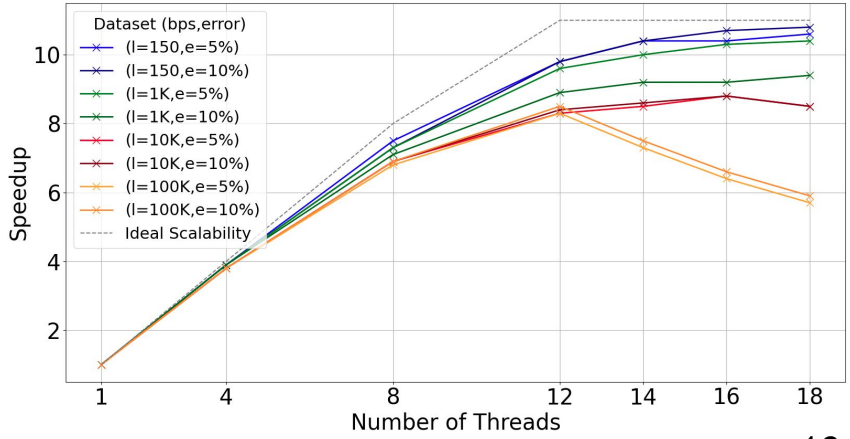
Optimal DPU scaling as long as the number of sequences is enough to feed all DPUs.

- **DPUs** are **not limited** by memory **bandwidth** like CPU (each DPU has its own memory bank).

11 threads are enough to obtain peak performance from the DPUs.

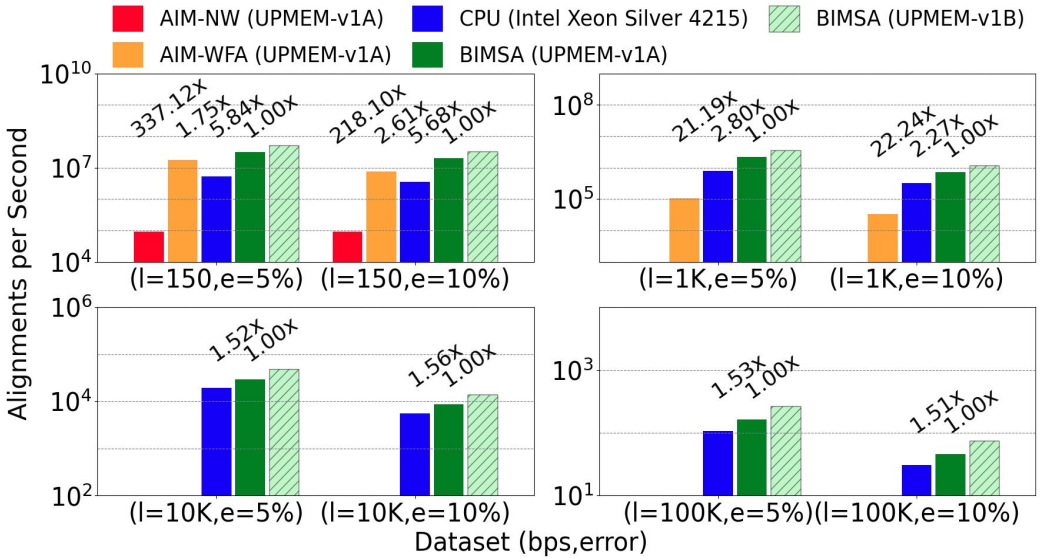
- Each thread can issue an instruction every **11 cycles** on the DPU pipeline.
- **Saturating** at **11 threads** means the **pipeline is** fully utilized.
- We start **saturating** at **8 threads** which indicates some **MRAM** access **saturation**.





4.3 PIM Performance Scaling in respect to CPU

- **AIM-NW** (DP-based on PIM) is outperformed by all the other implementations.
- **AIM-WFA** (WFA-based on PIM) is **unable to execute** long sequences and is outperformed by **BIMSA**.
- **BIMSA** (Ours) outperforms all other implementations and shows the **best scalability** for all datasets.
  Up to **22.23x** speedup against **AIM-WFA** and **5.84x** times against **WFA2lib.**
- **BIMSA projected** is almost able to double the performance in all cases.



4.4 PIM Performance for Heterogeneous Datasets

- **BIMSA** is **outperformed by CPU** in PacBIO and Nanopore **due to alignment heterogeneity**.
- **BIMSA-Hybrid outperforms CPU** by utilizing CPU recovery on the larger alignments.

Application	Illumina.150	Illumina.250	PacBio.CSS	Nanopore
AIM-NW	53.5	149.5	N/A	N/A
AIM-WFA	1.2	2.2	N/A	N/A
WFA2lib	0.8	1.2	9.2	206.1
BIMSA	0.6	1.1	182.4	314.5
BIMSA-Hybrid	0.6	1.1	7.6	105.6

New Feature: WRAM parallelism.

- Currently: Execute all batch alignments and stop to send to the CPU the larger alignments.
- Upcoming: Send large alignments to the CPU while computing the next alignment.

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5.1 Take Away Messages

- **Genomic sequencing** is a **fundamental** tool **in** modern **biology and healthcare**, which uses **sequence alignment,** a **memory bound** problem.

- **PIM** places computation closer to data, aiming the acceleration of **memory bound** problems such as **sequence alignment**.

- We present **BIMSA**, a PIM-aware optimized implementation of BiWFA for UPMEM. BIMSA achieves up to **22.23x** speedup against **AIM-WFA** and **5.84x** times against **WFA2lib**.

- **PIM** technology, while being immature, demonstrates promising results to accelerate memory-bound problems. We expect **significant improvements in the near future**.

Thanks for your attention!

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