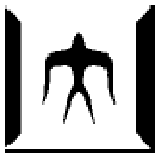
# An ultra-fast computing pipeline for metagenome analysis on TSUBAME 2.0

Yutaka Akiyama



Graduate School of Information Science and Engineering

Tokyo Institute of Technology

2011/12/14 GTC Asia (Beijing)

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# Agenda

- Background
  - Rapid improvement of DNA sequencing technologies
  - Metagenome analysis

- An automated pipeline system for metagenome analysis on TSUBAME 2.0
- GPU accelerated homology search tool  GHOSTM
- Large-scale performance evaluation on TSUBAME 2.0

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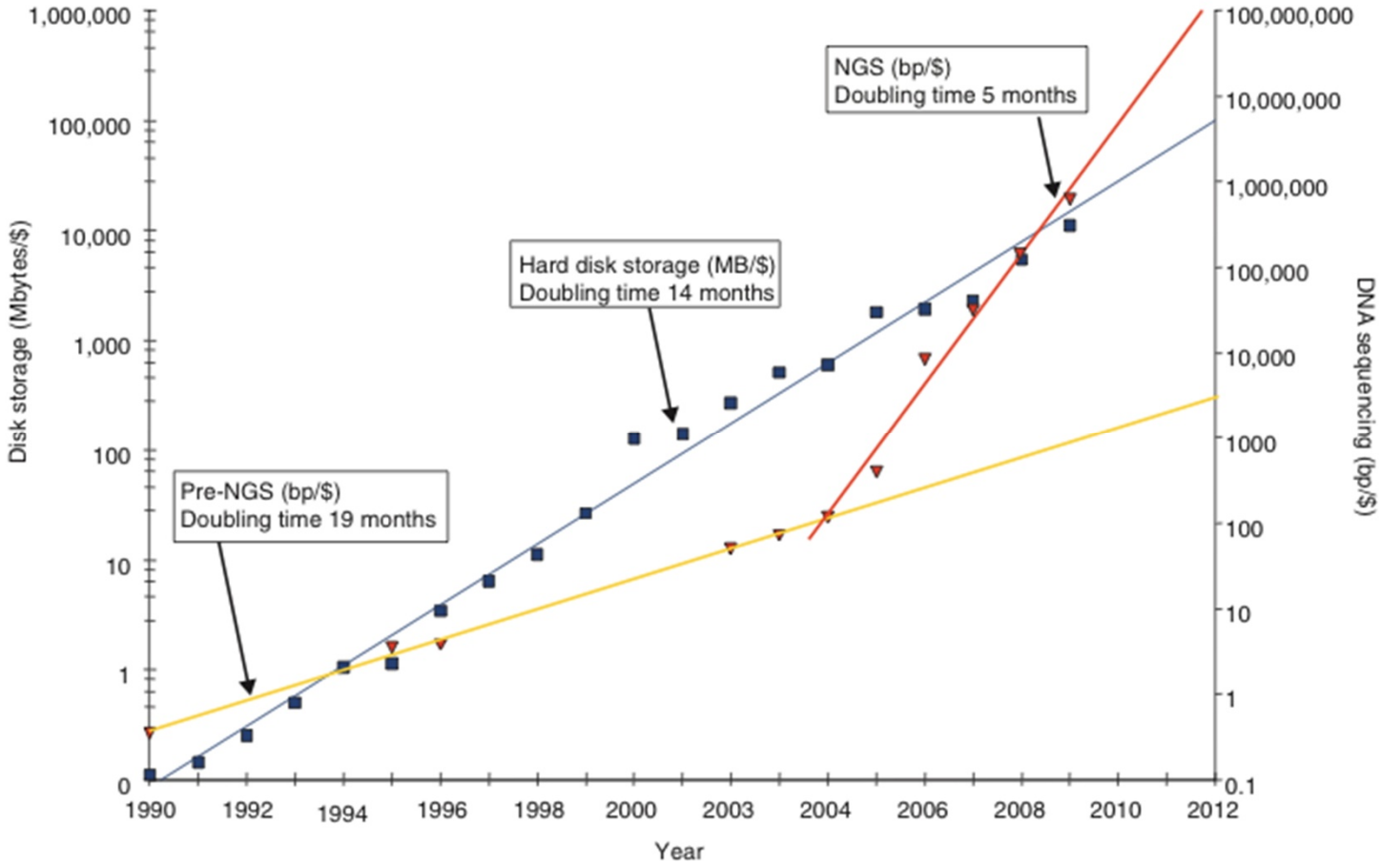
# Rapid improvement of DNA sequencing technology




Whole human genome (about 3 Gbp) now can be sequenced by about $1000.

Lincoln Stein, Genome Biology, vol. 11(5), 2010

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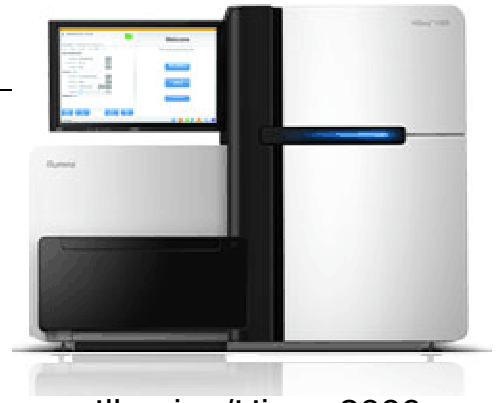
# Next-generation sequencer

- Next-generation sequencers (NGSs) can produce more than 100Gb genomic data on a single run

| | Pre-NGS (PRISM3730x) | NGS (Hiseq 2000) |
|---|---|---|
| Read length (bp) | 700 | 100 |
| Run time | 1 hour | 11 days |
| Data size (bp) | 67K | 600G |
| Throughput/day (bp) | 1.6M | 55G (55000M) |

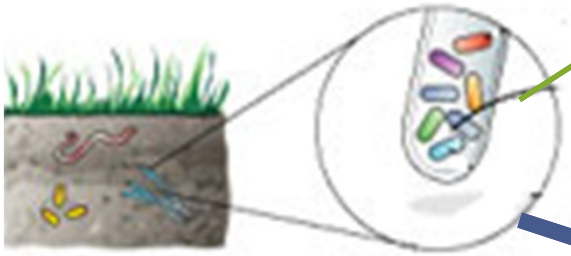


Illumina/Hiseq 2000

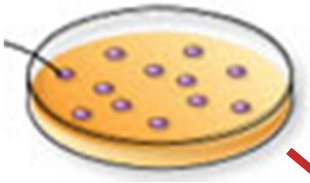
# Metagenome analysis

## General genome analysis

Reveals genomic data of a single organism



Environment
(including various organisms)



Select one organism and culture it

Sequence

Sequence directly

## Metagenome analysis

Directly analyze genetic materials of **all organisms** sampled from environment

- Identify genes and metabolic pathways of the environment
- Compare them to other environment

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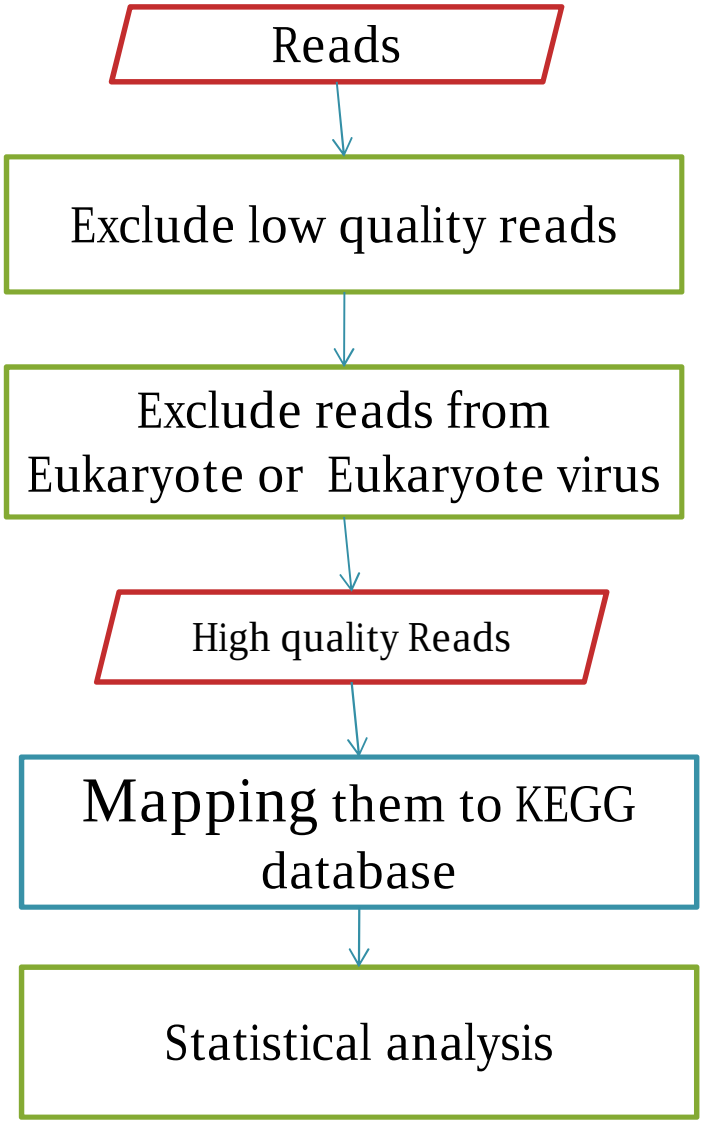
# A metagenome analysis pipeline for NGS reads




use only reads with Y flags and including bases better than B

Homology search for NCBI **nr** database

Homology search for **KEGG** genes.pep database

- Top hits & seq. id. > 0.7 & bit score > 40

(designed by Prof. Ken Kurokawa, Tokyo Tech.)

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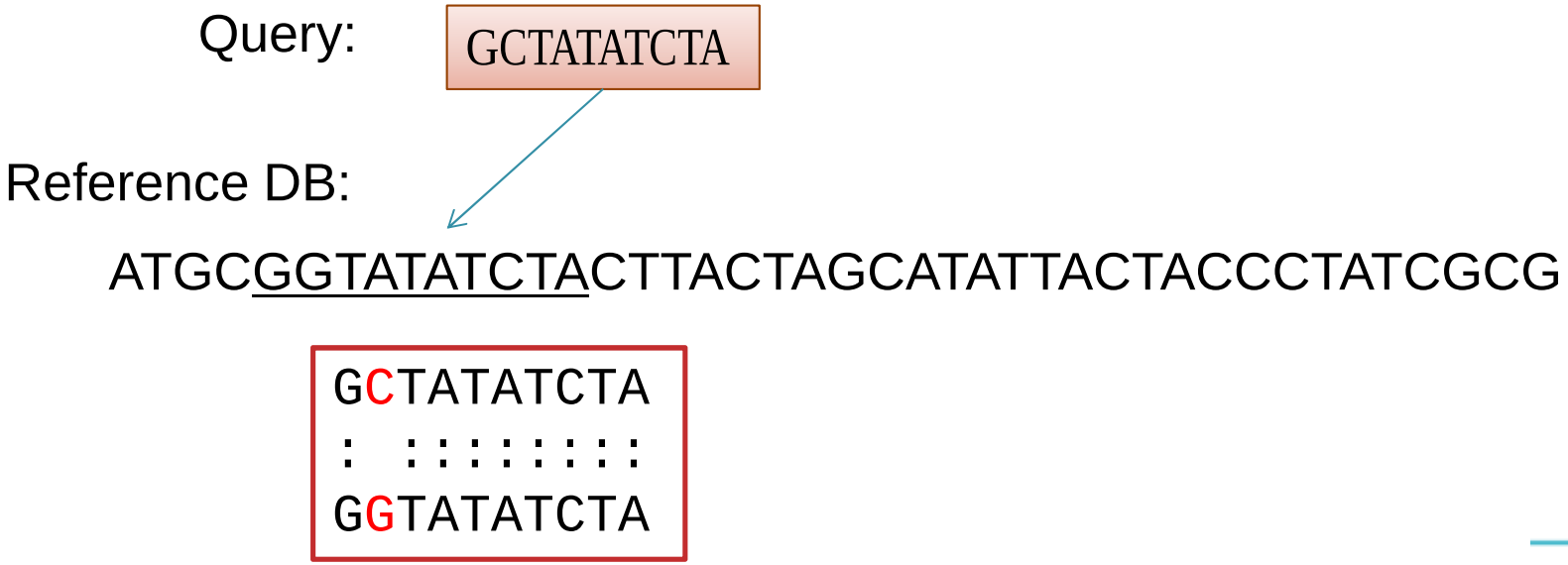
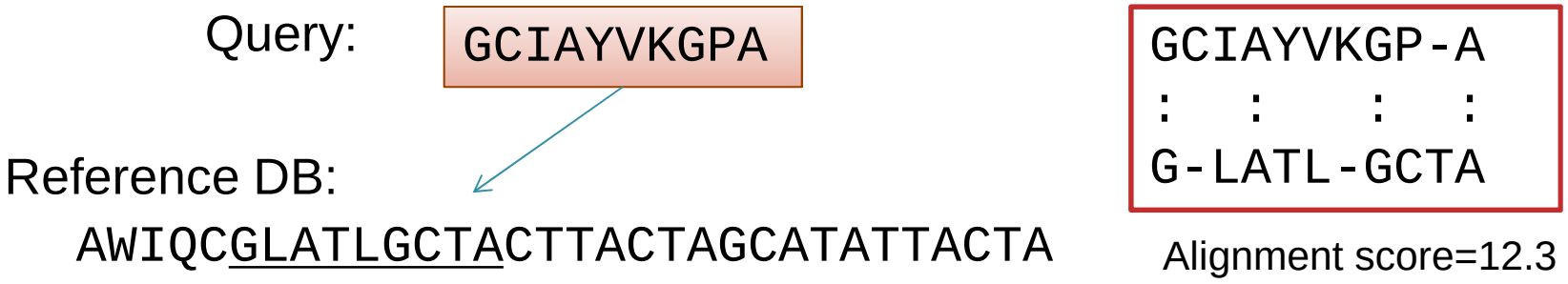
# Genome mapping

- Search same sequence for databases
  - Whole genome of the organism is already known
  - Search DNA sequence database (4 types, ATGC)
  - Only accept small (1, 2 or 3) errors
    - Sequencing errors
    - SNPs



# Metagenome mapping

- Search similar sequence for databases
  - Genomic data of same organism is unavailable
  - Sensitive homology searches are required
    - Have to search similar sequence for the sequences of homologues (similar species)
    - Search for amino acid sequence database (20 types)
    - Accept many mutations, insertion and deletion
    - Evaluate each match by using a score matrix



# Metagenomic analysis requires vast amount of computation

- BLASTX program (Altschul *et al.*, *JMB*, 1990) is generally used for metagenome mapping
  - Standard efficient sequence homology search software developed and maintained by NCBI
  - Requires large computational power

About 400 hours are required for an output of a single run of a NGS (20,000,000 reads) by using a small PC cluster (144 cores) (Prof. Ken Kurokawa)

Development of an automated metagenomic pipeline system on TSUBAME 2.0

# An automated pipeline system on TSUBAME 2.0

- Can utilize hundreds of computation nodes (thousands of CPU cores)
- Efficient DB copy
  - DB data are simultaneously copied from local disk (SSD) of a node to another in a binary-tree manner
- Web-interface (under development)

- Homology search tools;
  - BLASTX (Altschul *et al.*, *JMB*, 1990)
  - GHOSTM (Suzuki *et al.*, submitted.)

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# GHOSTM

- GPU-based HOmology Search Tool for Metagenomics

- Perform fast and sensitive homology search by using GPU computing technique
  - Implemented by NVIDIA's CUDA (required ver. 2.2 or higher)

- http://www.bi.cs.titech.ac.jp/ghostm/


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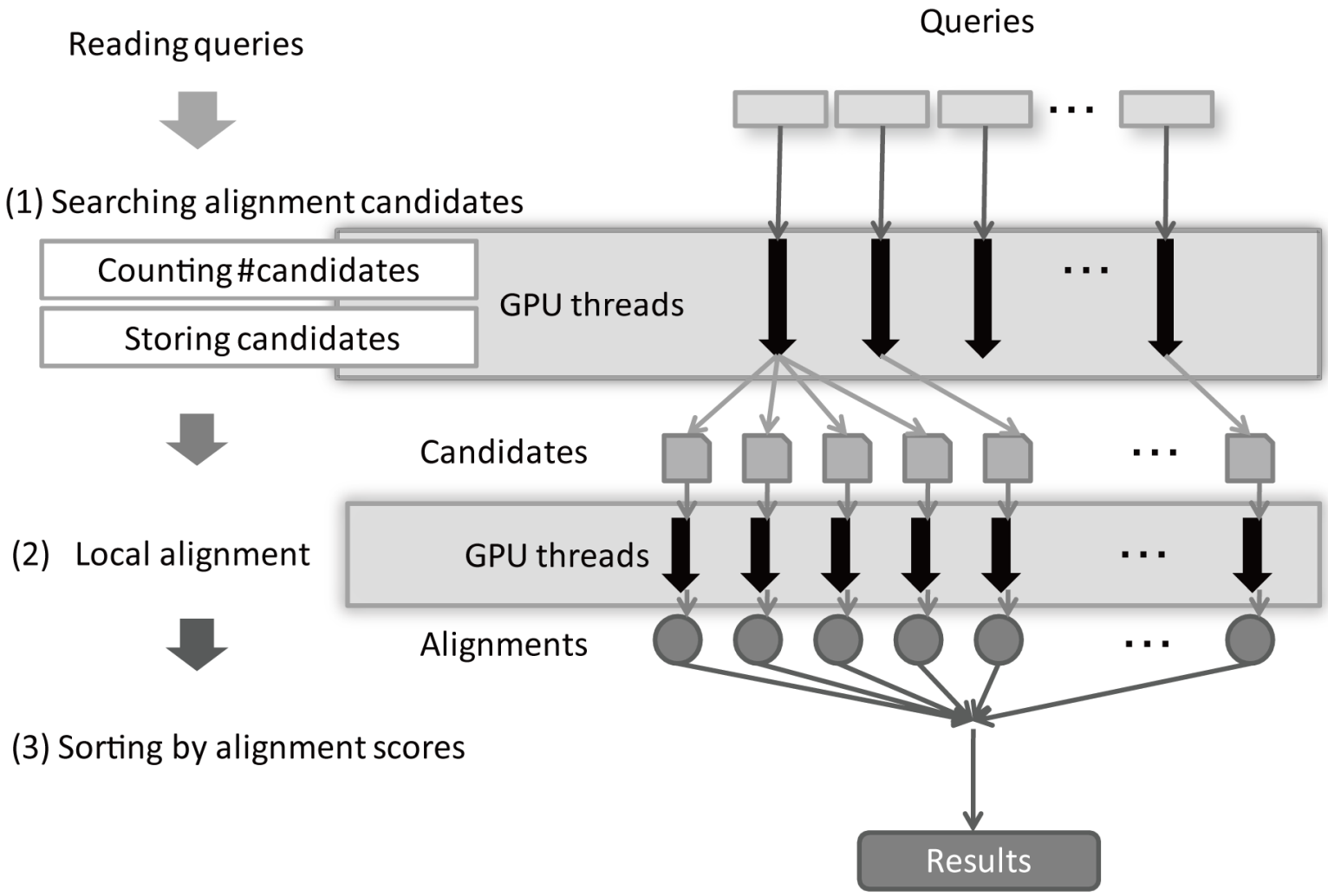
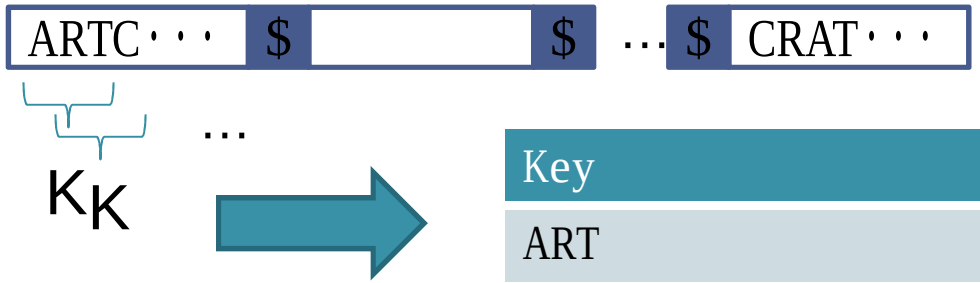
# GHOSTM: flowchart

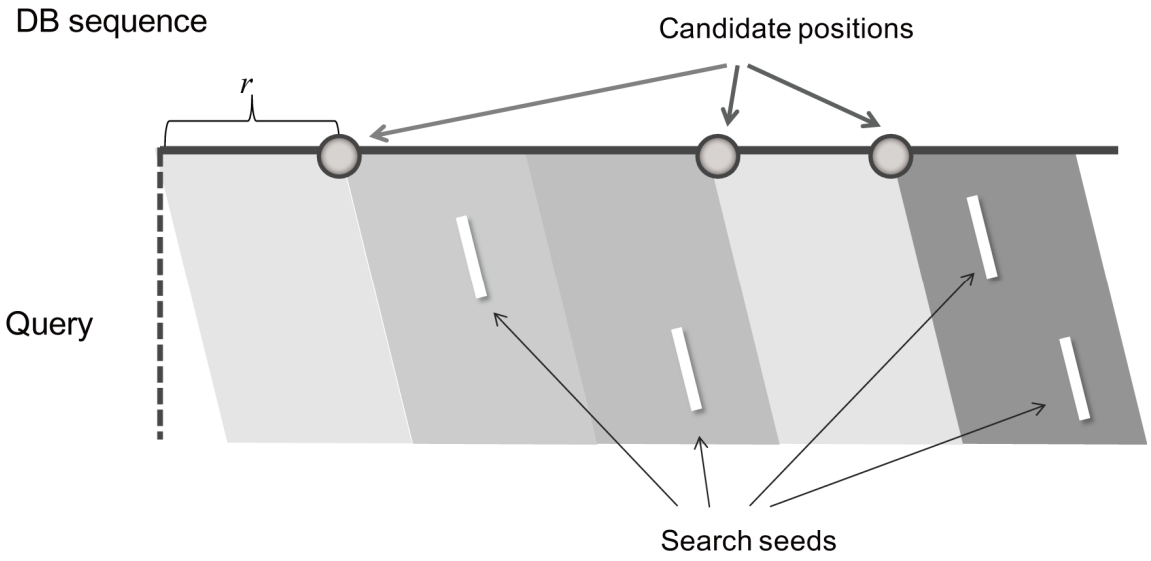


# GHOSTM: searching alignment candidates

- Search *k*-mer matches (seeds) between query and DB sequence

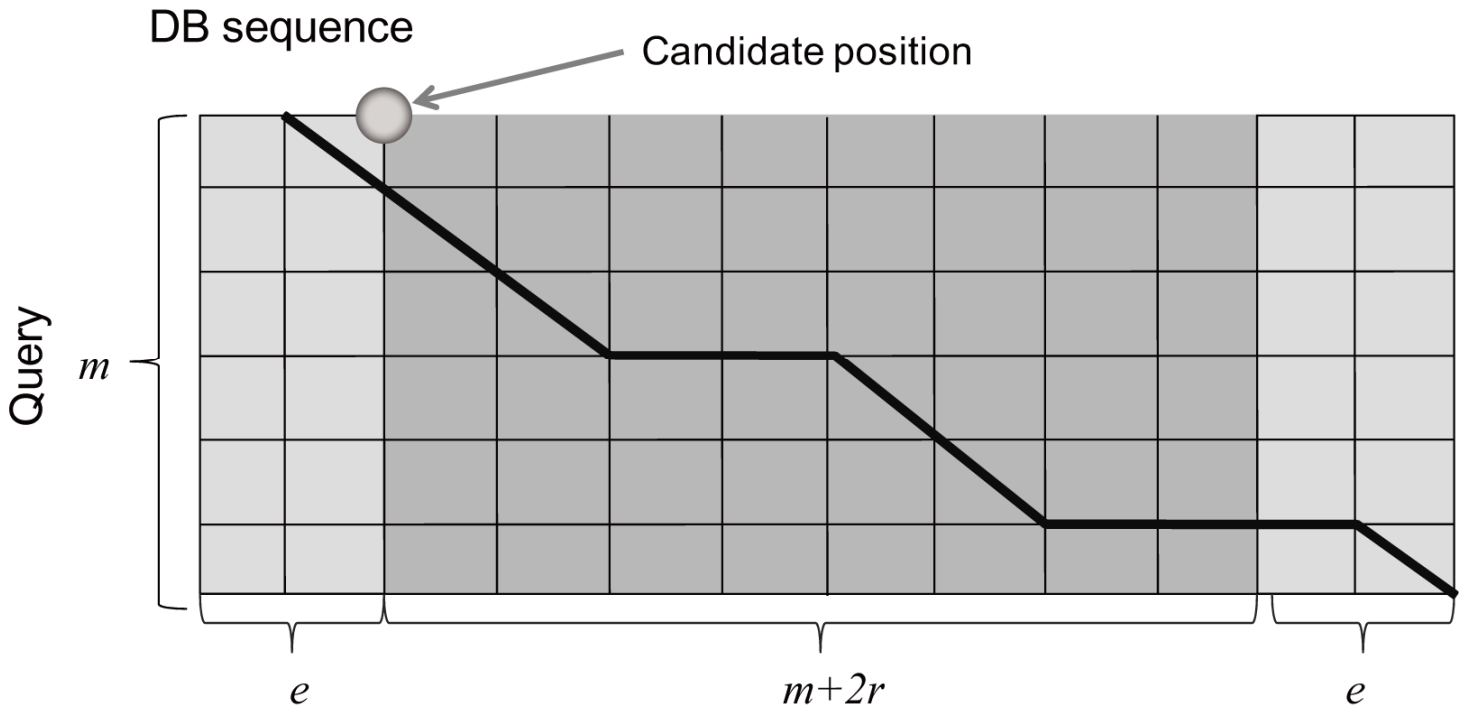



| Key | Positions |
|---|---|
| ART | 0, ・・・・・ |
| RTC | 1, ・・・・・ |

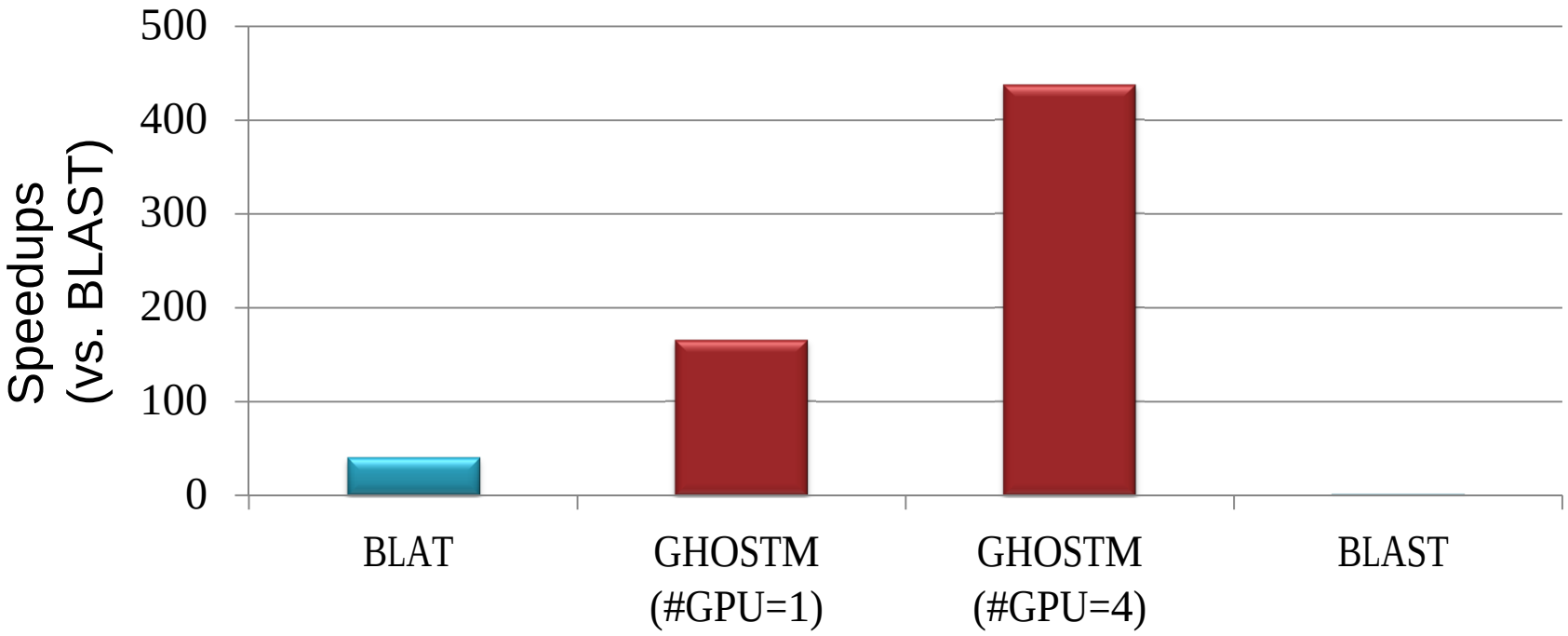


# GHOSTM: local alignment

- Calculate alignment score by dynamic programming (Smith-Waterman algorithm) for each alignment candidates



# GHOSTM: search speed




| Program | #GPUs | Time (s) | Speed up |
|---|---|---|---|
| GHOSTM (K = 4) | 1 | 2409 | 165.1 |
| GHOSTM (K = 4) | 4 | 909 | 437.6 |
| BLAT | | 9898 | 40.2 |
| BLAST | | 397798 | 1 |

* GPU: NVIDIA Tesla S1070 (on TSUBAME 1.2)

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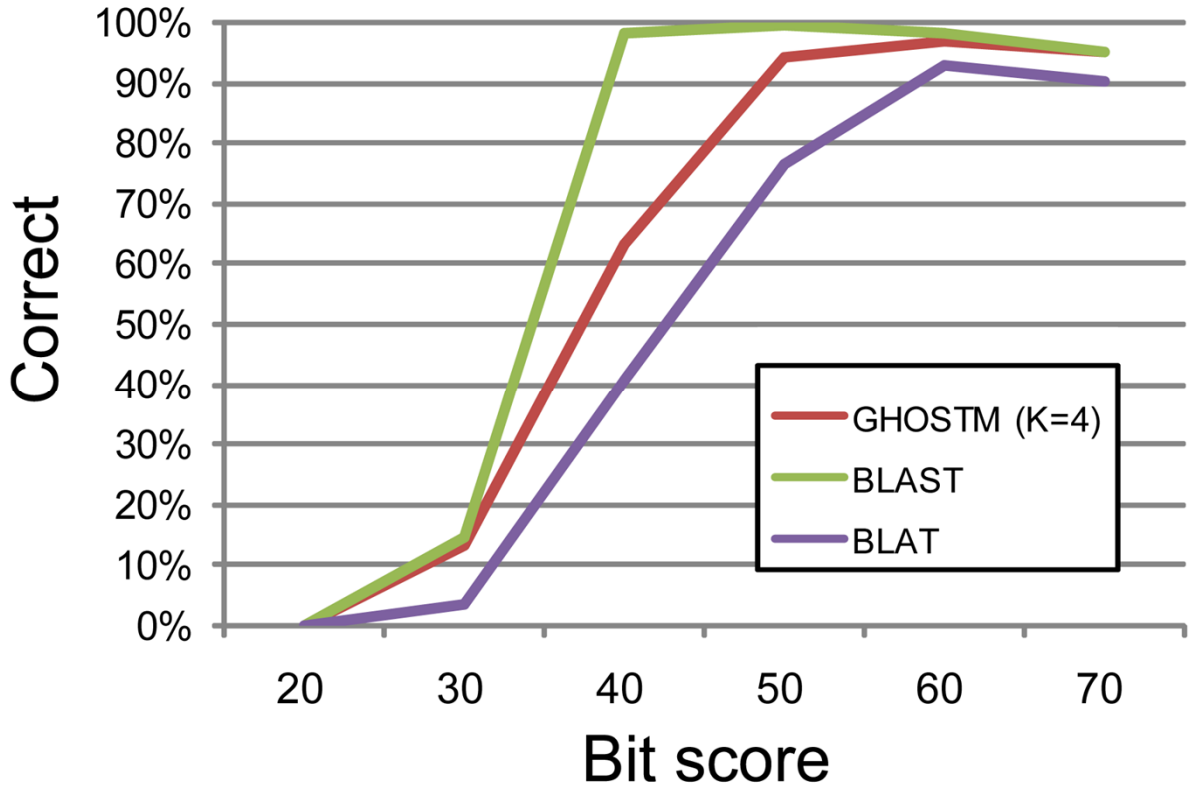
# GHOSTM: search accuracy

- Correct answer: Smith-waterman local alignment algorithm by using SSEARCH program



# Large-scale metagenome analysis on TSUBAME 2.0

- Metagenome analysis for organisms in soils
  - 2 conditions (polluted soil / control soil)
  - 7 time series data (0, 1, 2, 3, 6, 12, 20 weeks)
  - Sequenced by Illumina/Solexa

Each dataset contains;

Original metagenomic data:

about 20 million DNA reads (75 bp)

Size after excluding low-quality data:

about 7 million DNA reads

Homology search target DB:

NCBI nr amino-acid sequence DB (4.2GB)

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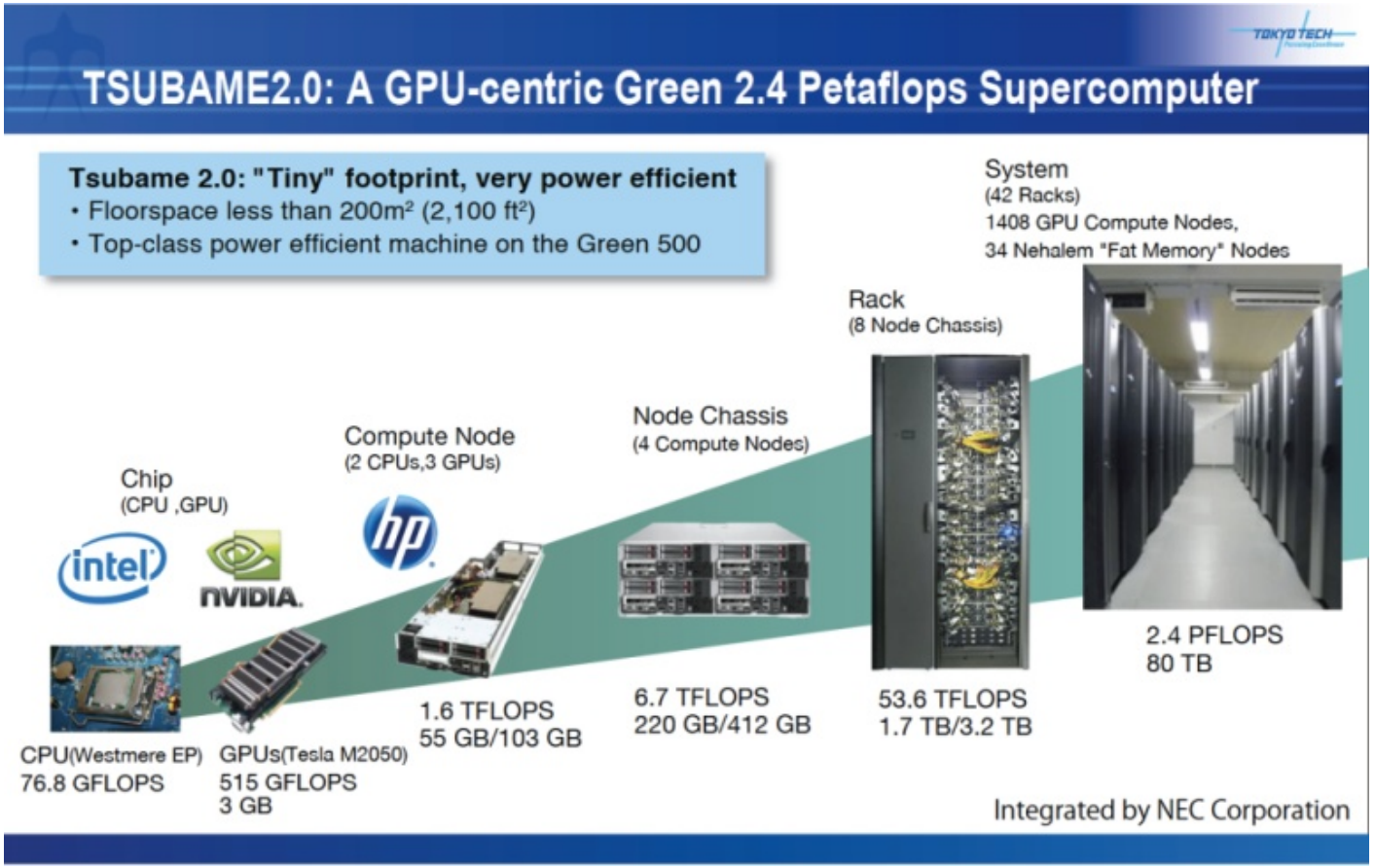
# Grand challenge on TSUBAME 2.0




CPU: >17,000 cores (12 cores x 1432 nodes)

GPU: > 4,000 GPUs (3 GPUs x 1432 nodes)

NVIDIA Tesla M2050

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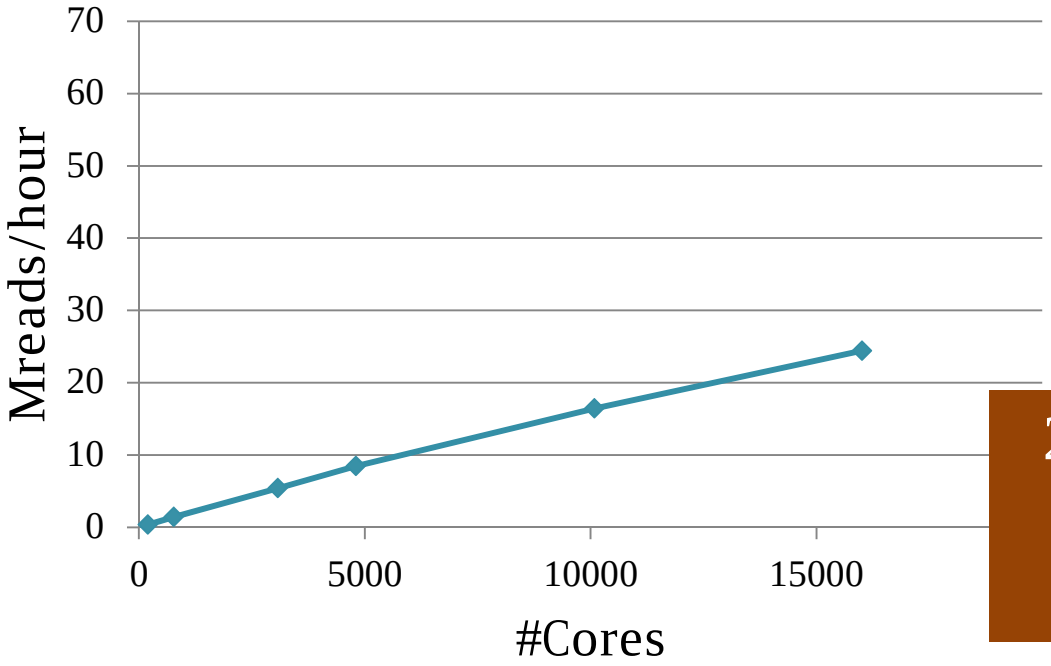
# Performance of the pipeline on TSUBAME 2.0

- BLASTX-based system

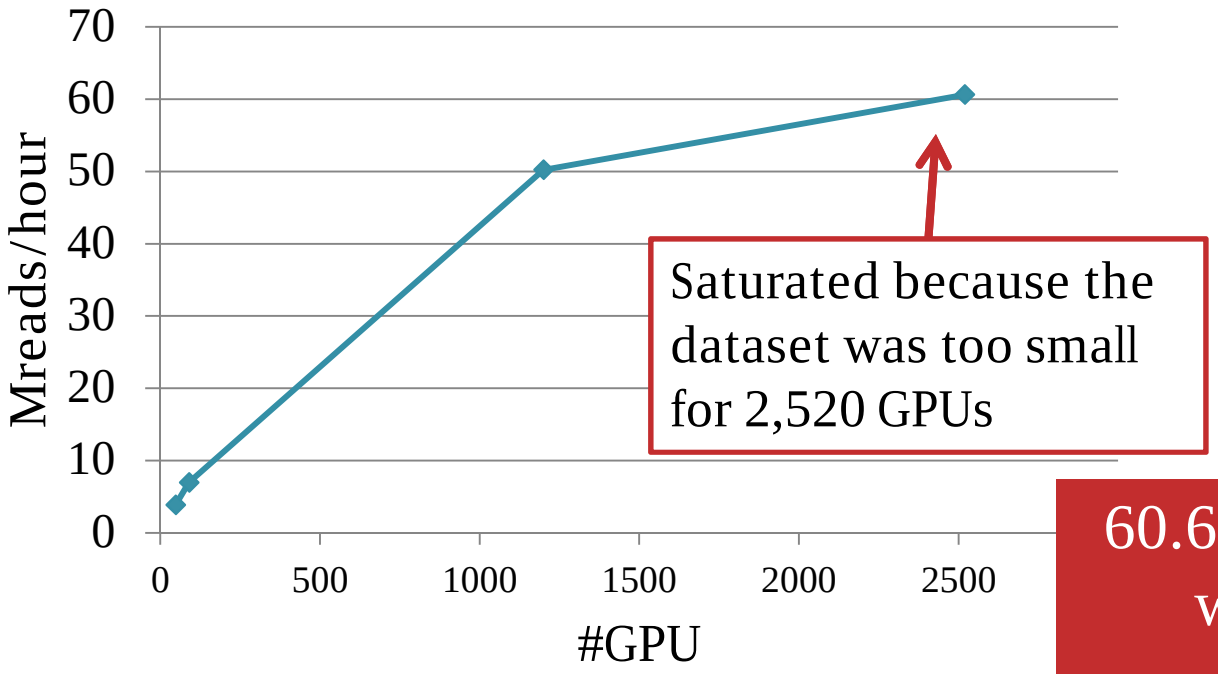



24.4 Million reads/hour
with 16,008 CPU cores
(1,334 nodes)

Achieve to analyze the output of a single run of a next-generation sequencer within 20 minutes.

# Performance of the pipeline on TSUBAME 2.0

- GHOSTM-based system





60.6 million reads/hour with 2,520 GPUs (840 nodes)

Achieve to analyze the output of a single run of a next-generation sequencer within 10 minutes.

# Conclusion

- We developed an automated pipeline system for metagenome analysis on TSUBAME 2.0
  - The system process about 24 million reads per an hour with 16,008 CPU cores and about 60 million reads per an hour with 2,520 GPUs
  - The system can process metagenome data obtained from a single run of a next generation sequencer within a hours
- We developed GPU-based fast homology search tool GHOSTM
  - About 165-times faster than BLAST (1GPU vs. 1CPU)
  - Has enough search sensitivity for metagenome analysis

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# Acknowledgement


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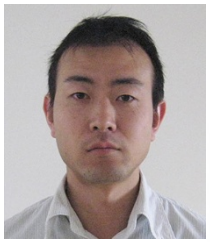


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