CS-BWAMEM: A Fast and Scalable Read Aligner at the Cloud Scale for Whole Genome Sequencing

Center for Domain Specific Computing

Yu-Ting Chen[1], Jason Cong[1], Jie Lei[1], Sen Li[1], Myron Peto[2], Paul Spellman[2], Peng Wei[1], and Peipei Zhou[1]

[1] Computer Science Department, UCLA, USA
[2] Dept. of Molecular and Medical Genetics, Oregon Health State University, USA

Contact: ytchen@cs.ucla.edu

Available at: https://github.com/ytchen0323/cloud-scale-bwamem

Motivation: Build a Fast and Scalable Read Aligner for WGS Data

- Target: whole-genome sequencing
  - A huge amount of data (500M ~ 1B reads for 30x coverage)
    - Pair-end sequencing
  - Goal: improve the speed of whole-genome sequencing
- Limitation of the state-of-the-art aligners
  - BWA-MEM takes about 10 hours to align WGS data
    - Multi-threaded parallelization in a single server
    - The speed is limited by the single-node computation power and I/O bandwidth when data size is huge
- Proposed tool: Cloud-Scale BWAMEM
  - Leverage the BWA-MEM algorithm
  - Exploit the enormous parallelism by using cloud infrastructures
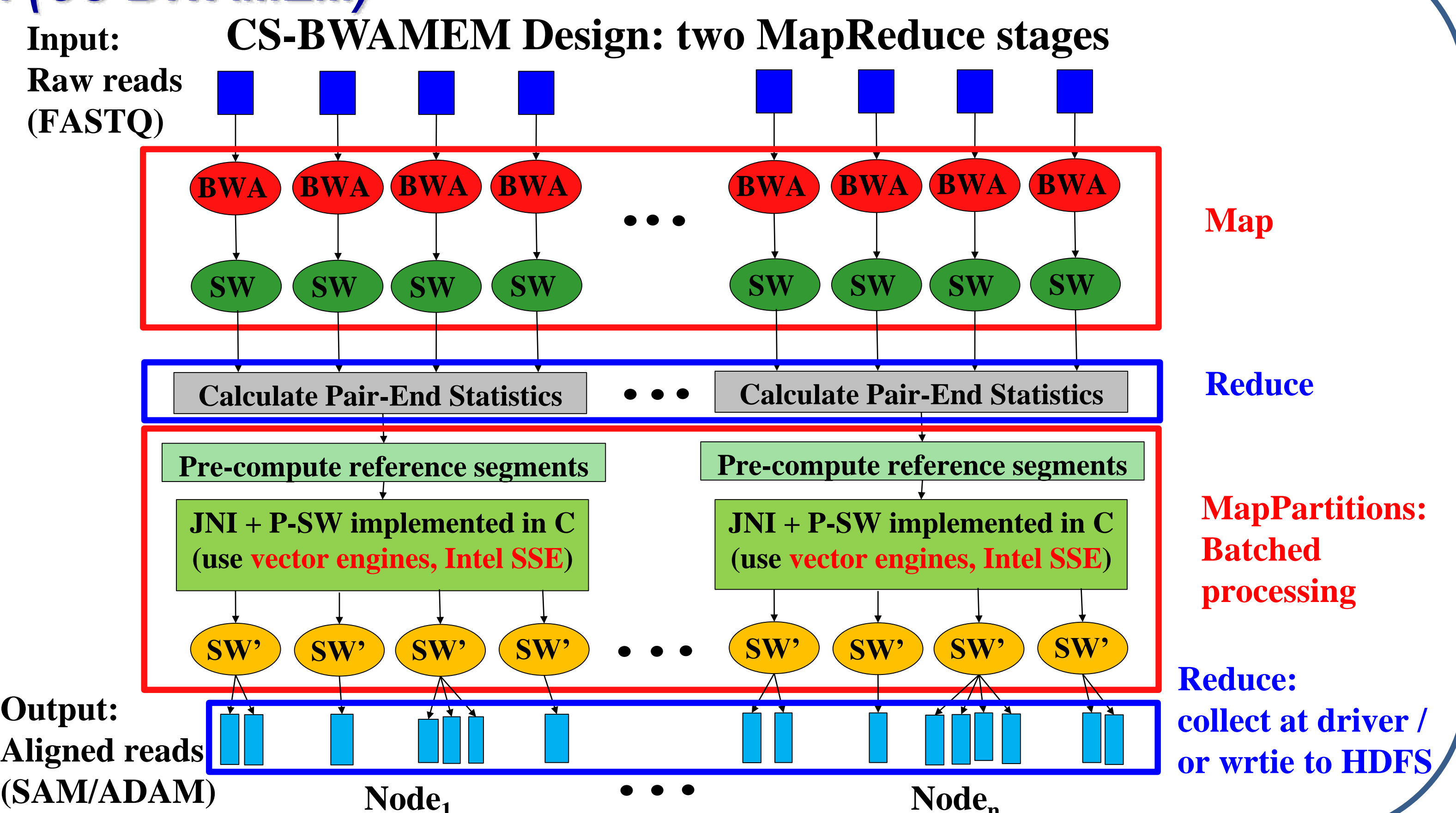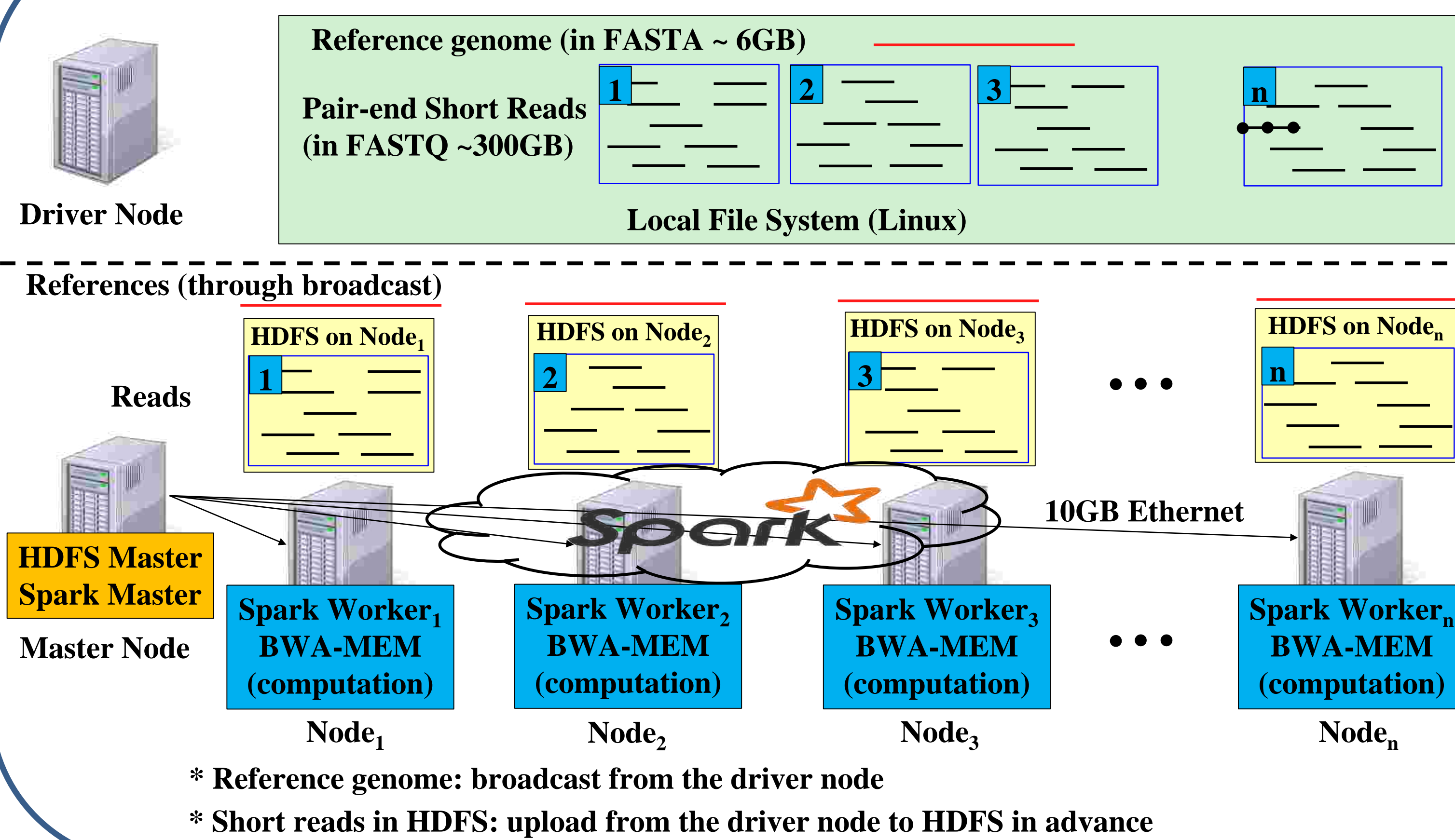
Tool Highlight

- Provide **scalable** speedup for read alignment
  - Users can choose an adequate number of nodes in their cluster based on their alignment performance target
- Speed of aligning a whole-genome sample
  - **< 80 minutes: whole-genome data (30x coverage; ~300GB)**
    - 25-node cluster with 300 cores
  - BWA-MEM: 9.5 hours
- Features
  - Support both pair-end and single-end alignment
  - Achieve similar quality to BWA-MEM
  - Input: FASTQ files
  - Output: SAM (single-node) or ADAM (cluster) format

Methods

- Use **MapReduce** programming model in a **cluster**
  - Most commonly used for big data analytics
  - Good for large-scale deployment – handle enormous parallelism of input reads
- Computation infrastructure: **Spark**
  - In-memory MapReduce system
  - Cache intermediate data in memory for future steps
    - Avoid unnecessary slow disk I/O accesses
- Storage infrastructure: **Hadoop distributed file system (HDFS)**
  - HDFS brings scalable I/O bandwidth since the disk I/O are linearly proportional to the size of a cluster
  - Store the FASTQ input in a distributed fashion
 - Spark can get data from HDFS before processing

Cloud-Scale BWAMEM (CS-BWAMEM)

* Reference genome: broadcast from the driver node
* Short reads in HDFS: upload from the driver node to HDFS in advance

CS-BWAMEM Design: two MapReduce stages

Performance

- Input: whole-genome data sample (30x coverage; about 300GB FASTA files)
- **7x speedup over BWA-MEM**
  - Can align whole-genome data **within 80 minutes**
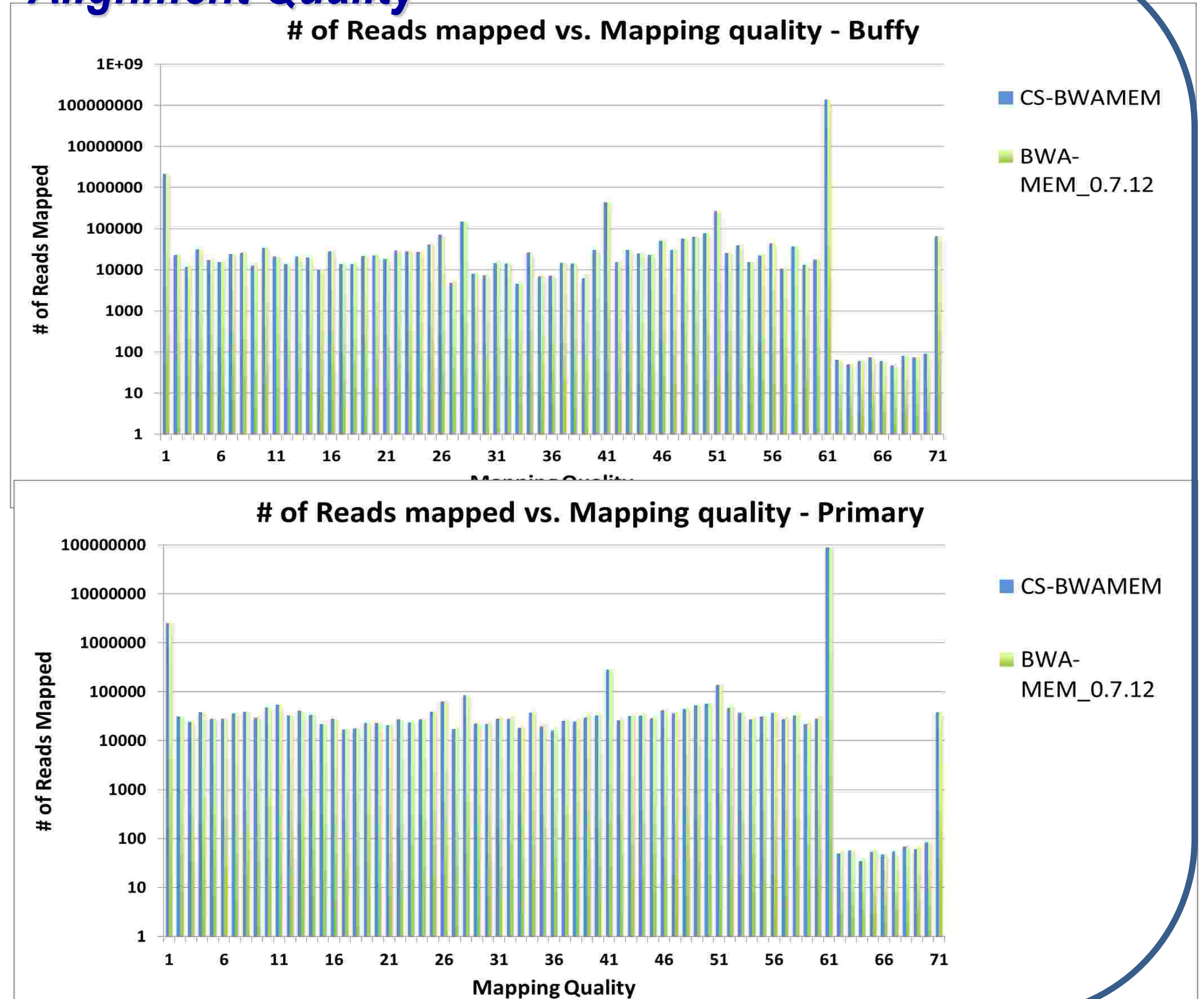 - User can adjust the cluster size based on their performance demand

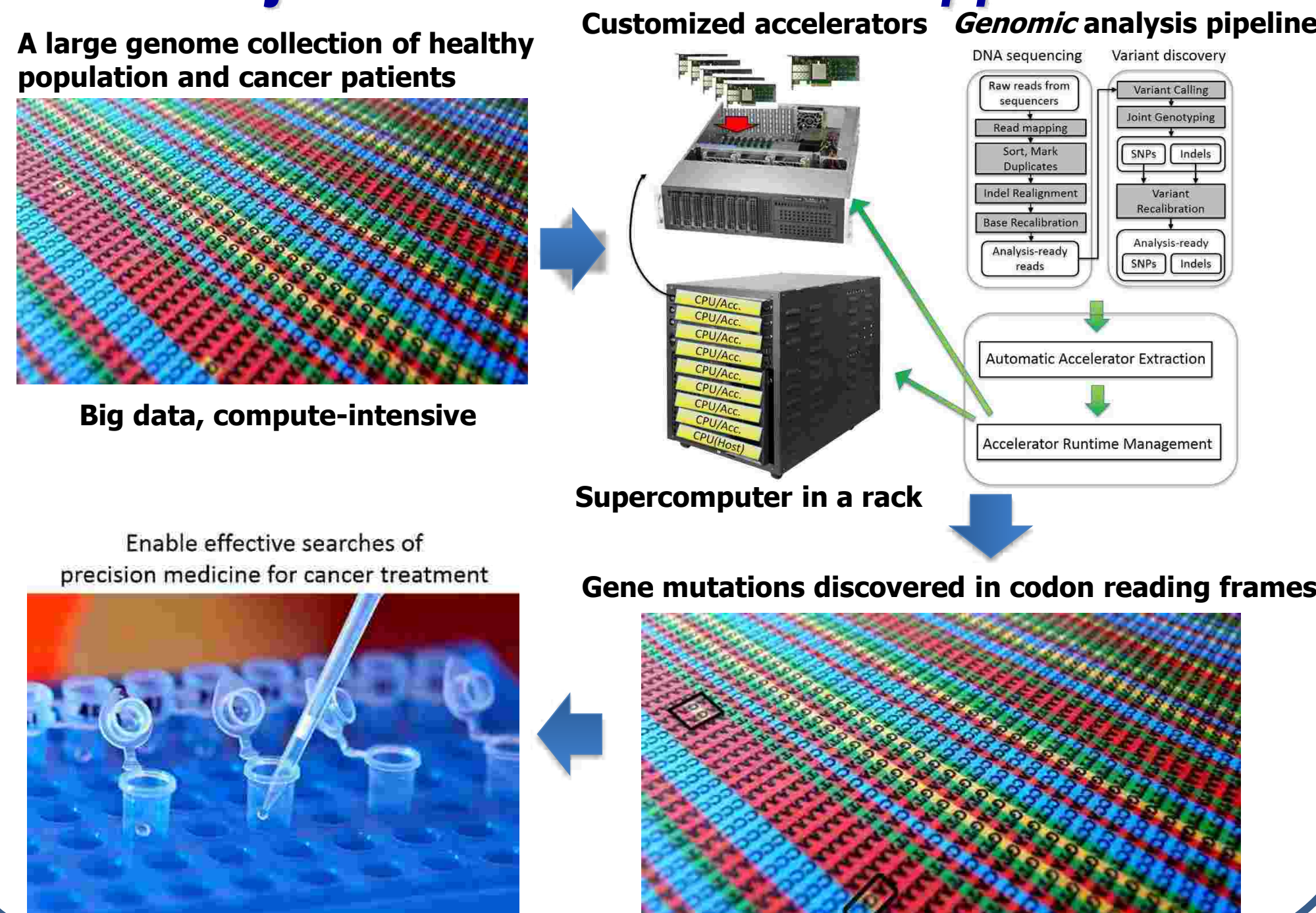BWA-MEM vs. CS-BWAMEM
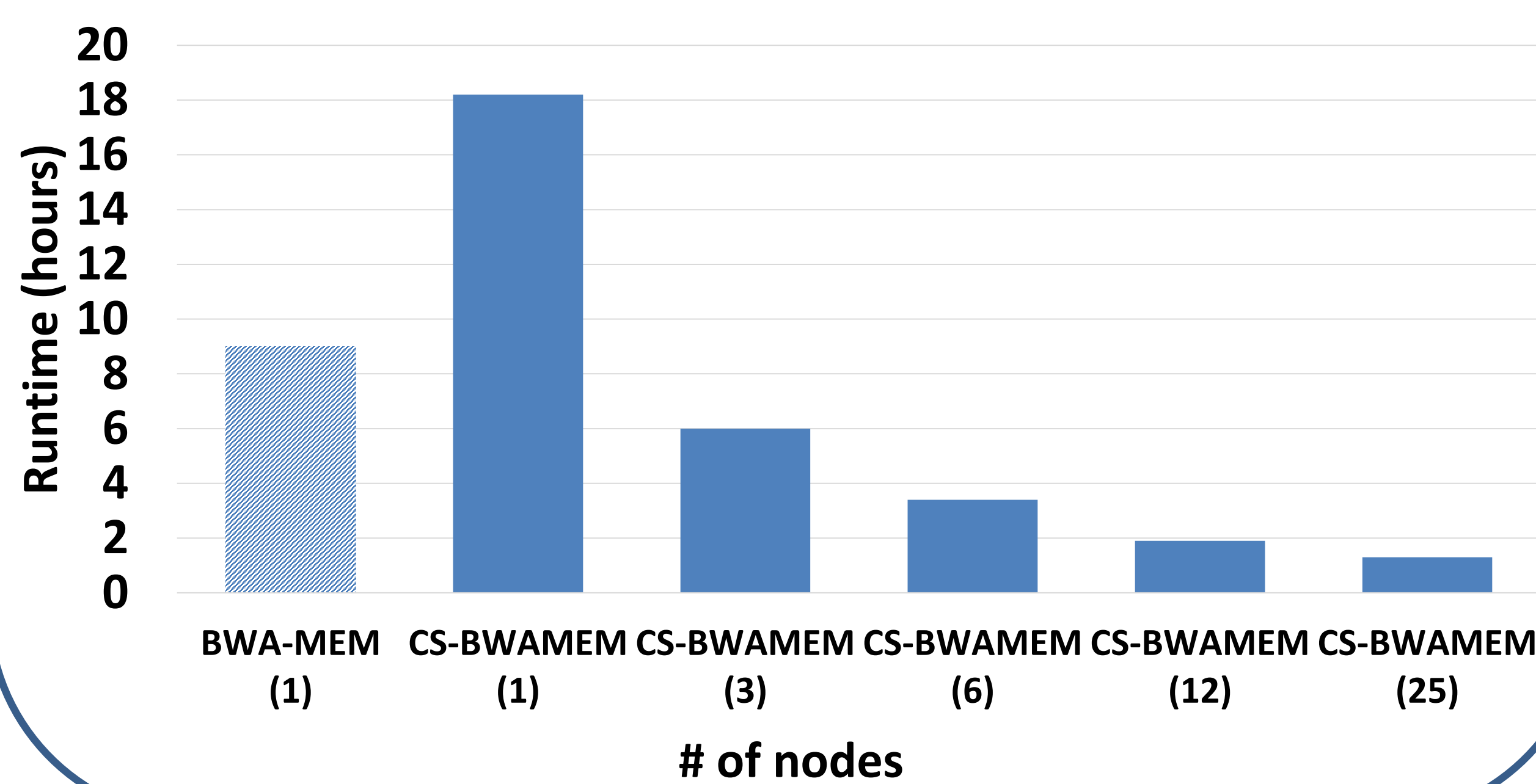
Alignment Quality

- Comparison with BWA-MEM
  - Flow: CS-BWAMEM / BWA-MEM -> sort -> markduplicate -> indelrealignment -> baserecalibration
- Detailed analysis on two cancer exome samples
  - Buffy sample and primary tumor sample
- **Almost same mapping quality to BWA-MEM**
- The numbers of mapped reads:
  - CS-BWAMEM vs. BWA-MEM
  - Buffy sample: 99.59% vs. 99.59%
  - Primary sample: 99.28% vs. 99.28%
- Difference on total reads
  - CS-BWAMEM vs. BWA-MEM
  - Buffy sample: 0.006%
  - Primary sample: 0.04%

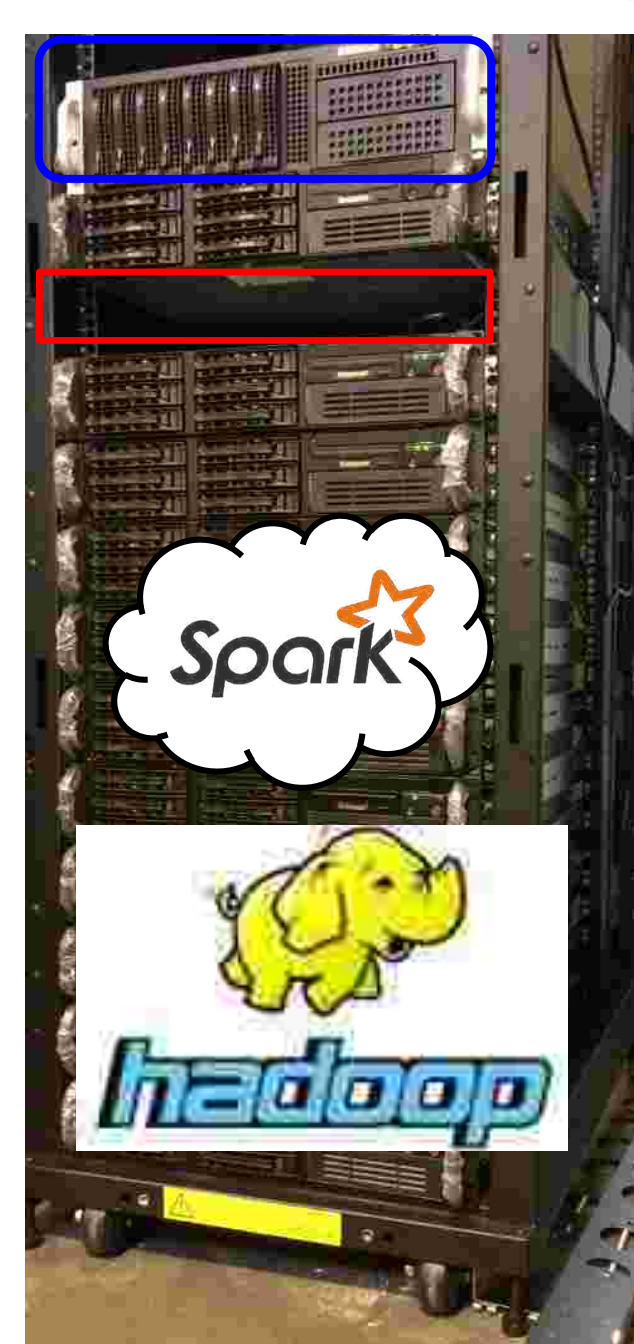# of Reads mapped vs. Mapping quality - Buffy

# of Reads mapped vs. Mapping quality - Primary

Our Project & Cancer Genome Applications

A large genome collection of healthy population and cancer patients

Big data, compute-intensive

Customized accelerators. *Genomic* analysis pipeline

Supercomputer in a rack

Gene mutations discovered in codon reading frames

Enable effective searches of precision medicine for cancer treatment

Cluster Deployment

One master / driver node

10GbE switch

25 worker nodes

- **Server node setting**
  - Intel Xeon server
  - Two E5-2620 v3 CPUs
  - 64GB DDR3/4 RAM
  - 10GBE NIC
- **Software infrastructure**
  - Spark 1.3.1 (v0.9 – v1.3.0 tested)
  - Hadoop 2.5.2 (v2.4.1 tested)
- **Hardware acceleration**
  - On-going project
  - PCIe-based FPGA board
  - Ex: Smith-Waterman / Burrows-Wheeler transform kernels

Collaborations

- Test our aligner on the data from our collaborators
- Oregon Health State University (OHSU)
  - Spellman Lab
    - Application: cancer genomics and precision medicine
- UCLA
  - Coppola Lab
    - Application: neuroscience
      - Neurodegenerative conditions, including Alzheimer's Disease (AD), Frontotemporal Dementia (FTD), and Progressive Supranuclear Palsy
  - Fan Lab
- University of Michigan, Ann Arbor
  - University of Michigan comprehensive cancer center (UMCCC)
    - Application:
      - Motility based cell selection for understanding cancer metastasis