Cloud-scale Sequence Analysis

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March 18, 2013

NY Genome Center / AWS

Outline

1. The need for cloud computing

2. Cloud-scale applications

3. Challenges and opportunities

Big Data in Bioinformatics

<Insert Moore's Law Graph Here>

Huge need for:

trimming/qc,

aligning,

variant detection,

de novo assembly,

expression quantification,

peak finding

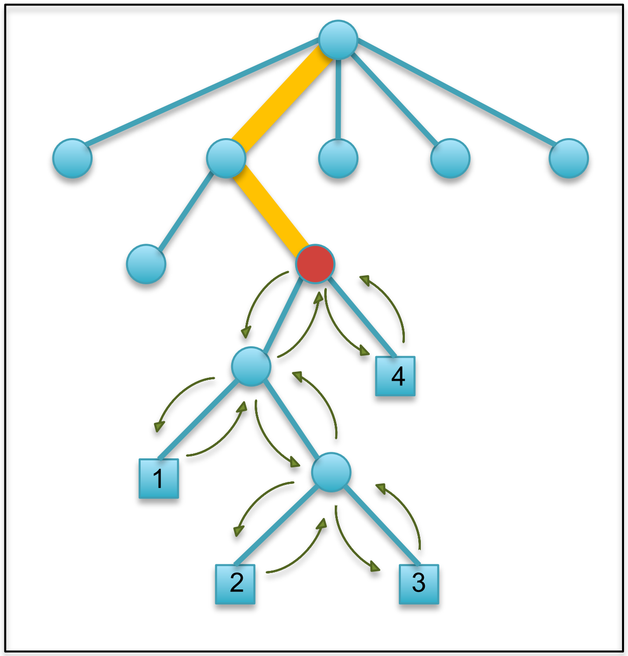
clustering

…

MUMmerGPU

http://mummergpu.sourceforge.net

- Index reference using a suffix tree
  - Each suffix represented by path from root
  - Reorder tree along space filling curve
- Map many reads simultaneously on GPU
  - Find matches by walking the tree
  - Find coordinates with depth first search
- Performance on nVidia GTX 8800
  - Match kernel was ~10x faster than CPU
  - Search kernel was ~4x faster than CPU
  - End-to-end runtime ~4x faster than CPU



- Cores are only part of the solution.
- Need storage, fast IO
- Locality is king

High-throughput sequence alignment using Graphics Processing Units.
Schatz, MC, Trapnell, C, Delcher, AL, Varshney, A. (2007) BMC Bioinformatics 8:474.

Web-Scale Information Processing

Jimmy Lin
The iSchool
University of Maryland

Monday, January 28, 2008

Material adapted from slides by Christophe Bisciglia, Aaron Kimball, & Sierra Michels-Slettvet, Google Distributed Computing Seminar, 2007 (licensed under Creation Commons Attribution 3.0 License)

Hadoop MapReduce

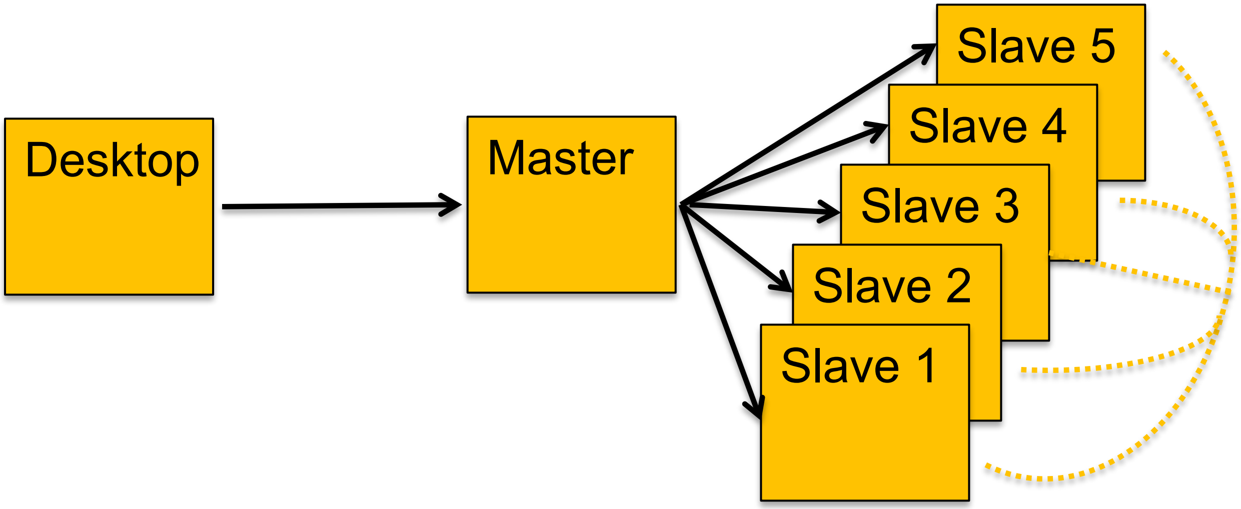
http://hadoop.apache.org

- MapReduce is Google's framework for large data computations
  - Data and computations are spread over thousands of computers
    - Indexing the Internet, PageRank, Machine Learning, etc… (Dean and Ghemawat, 2004)
    - 946PB processed in May 2010 (Jeff Dean at Stanford, 11.10.2010)
  - Hadoop is the leading open source implementation
    - Developed and used by Yahoo, Facebook, Twitter, Amazon, etc
    - GATK is an alternative implementation specifically for NGS

- Benefits
  - Scalable, Efficient, Reliable
  - Easy to Program
  - Runs on commodity computers

- Challenges
  - Redesigning / Retooling applications
    - Not Condor, Not MPI
    - Everything in MapReduce

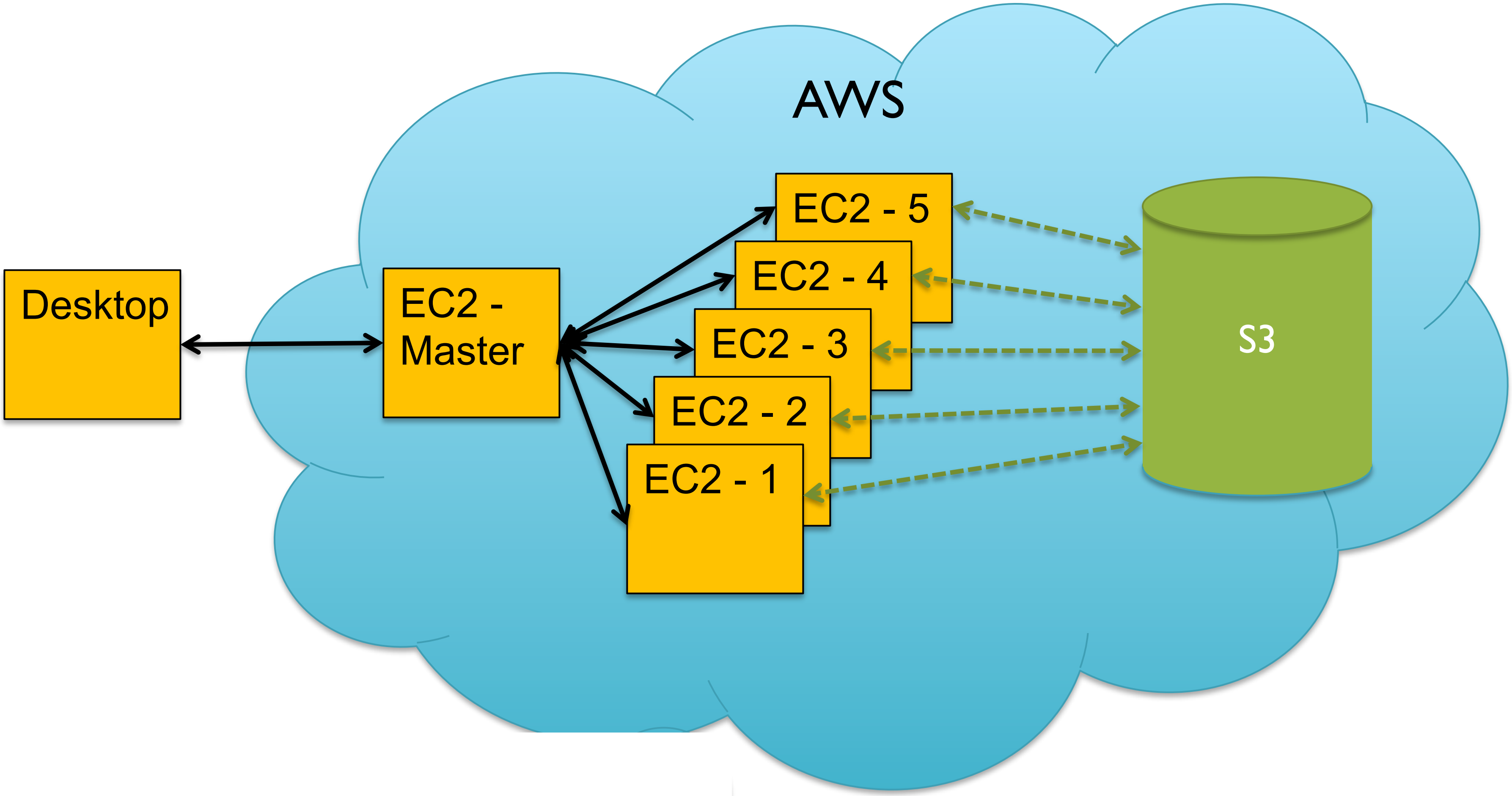
System Architecture



- Hadoop Distributed File System (HDFS)
  - Data files partitioned into large chunks (64MB), replicated on multiple nodes
  - Computation moves to the data, rack-aware scheduling

- Hadoop MapReduce system won the 2009 GreySort Challenge
  - Sorted 100 TB in 173 min (578 GB/min) using 3452 nodes and 4x3452 disks

Hadoop on AWS



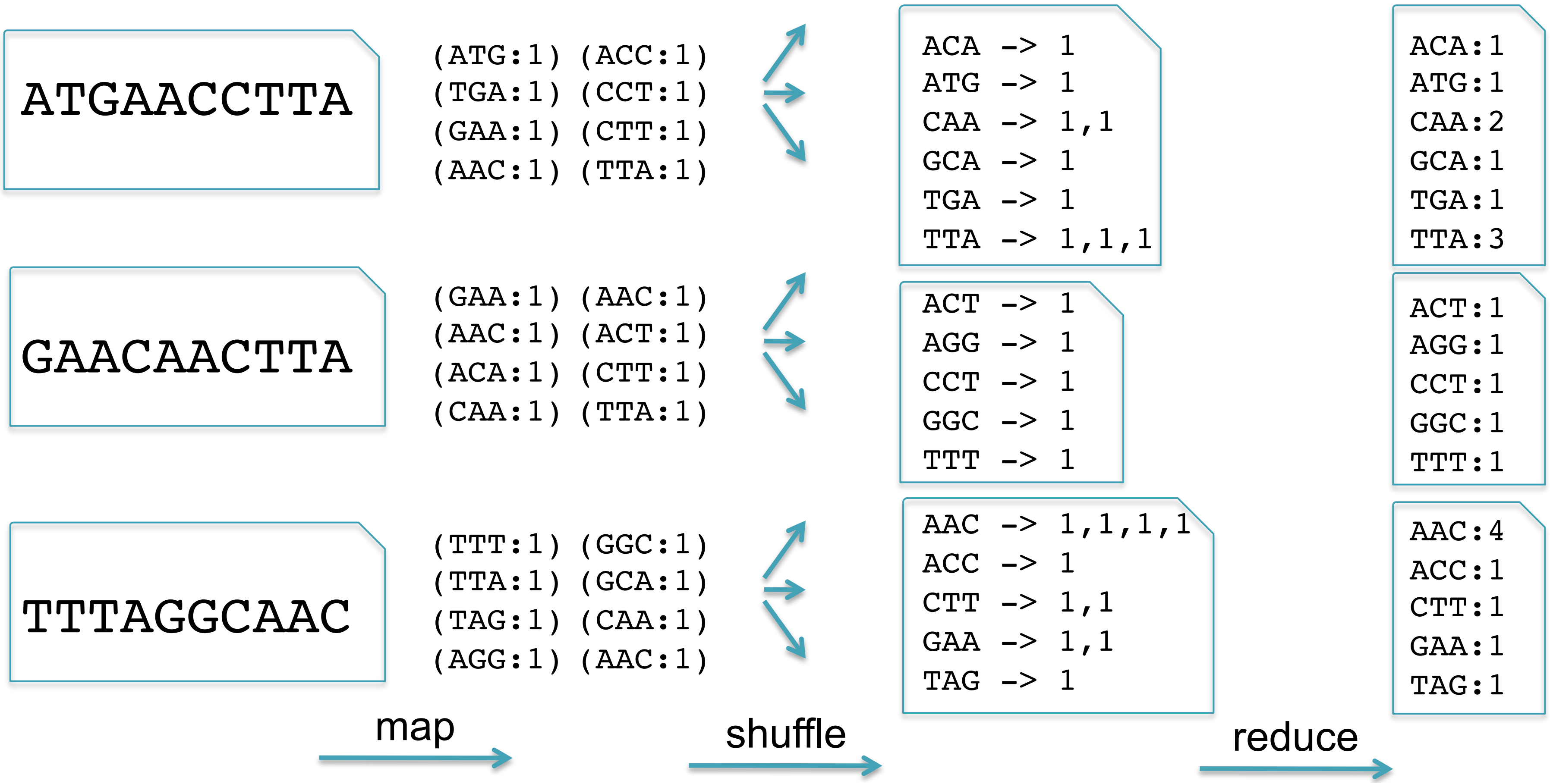
If you don't have 1000s of machines, rent them from Amazon

- After machines spool up, ssh to master as if it was a local machine.
- Use S3 for persistent data storage, with very fast interconnect to EC2.

K-mer Counting

- Application developers focus on 2 (+1 internal) functions
  - Map: input ➔ key:value pairs
  - Shuffle: Group together pairs with same key
  - Reduce: key, value-lists ➔ output

Map, Shuffle & Reduce
All Run in Parallel



```
ATGAACCTTA

(ATG:1) (ACC:1)
(TGA:1) (CCT:1)
(GAA:1) (CTT:1)
(AAC:1) (TTA:1)
```

```
GAACAACTTA

(GAA:1) (AAC:1)
(AAC:1) (ACT:1)
(ACA:1) (CTT:1)
(CAA:1) (TTA:1)
```

```
TTTAGGCAAC

(TTT:1) (GGC:1)
(TTA:1) (GCA:1)
(TAG:1) (CAA:1)
(AGG:1) (AAC:1)
```

```
ACA -> 1
ATG -> 1
CAA -> 1,1
GCA -> 1
TGA -> 1
TTA -> 1,1,1
```

```
ACT -> 1
AGG -> 1
CCT -> 1
GGC -> 1
TTT -> 1
```

```
AAC -> 1,1,1,1
ACC -> 1
CTT -> 1,1
GAA -> 1,1
TAG -> 1
```

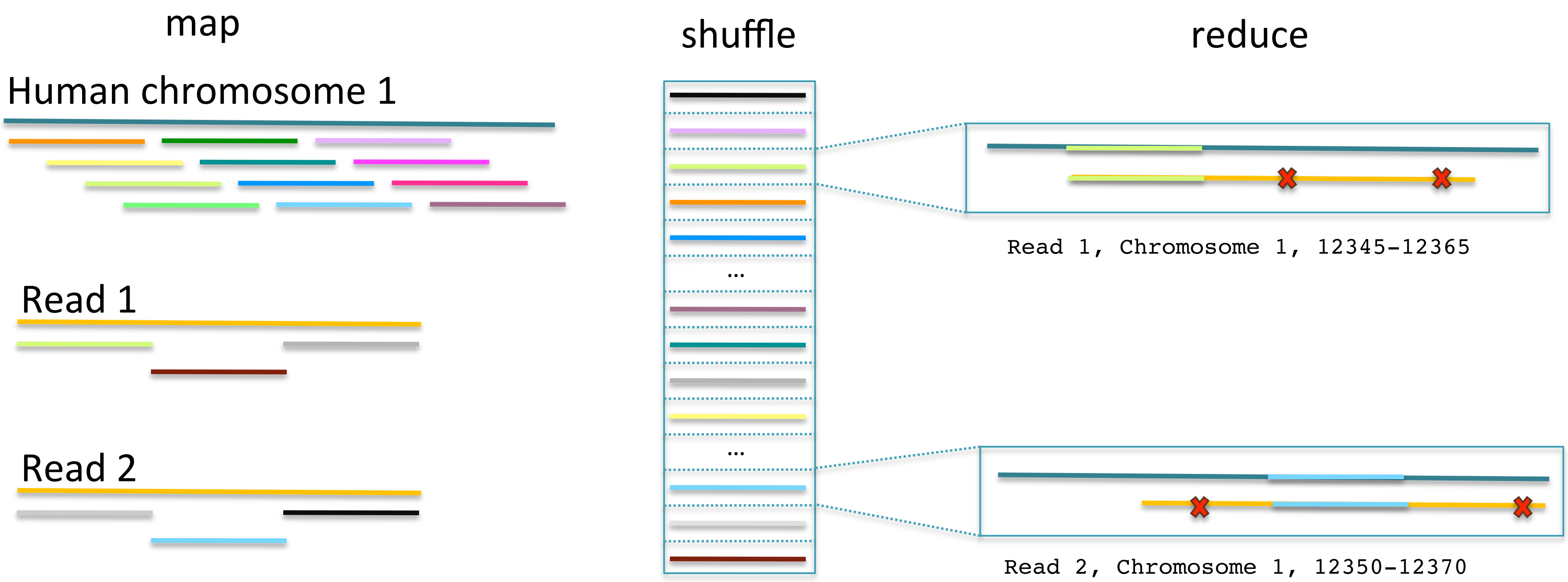
```
ACA:1
ATG:1
CAA:2
GCA:1
TGA:1
TTA:3
```

```
ACT:1
AGG:1
CCT:1
GGC:1
TTT:1
```

```
AAC:4
ACC:1
CTT:1
GAA:1
TAG:1
```

CloudBurst

1. Map: Catalog K-mers
   - Emit k-mers in the genome and reads
2. Shuffle: Collect Seeds
   - Conceptually build a hash table of k-mers and their occurrences
3. Reduce: End-to-end alignment
   - If read aligns end-to-end with ≤ k errors, record the alignment



map

shuffle

reduce

Human chromosome 1

Read 1

Read 2

…

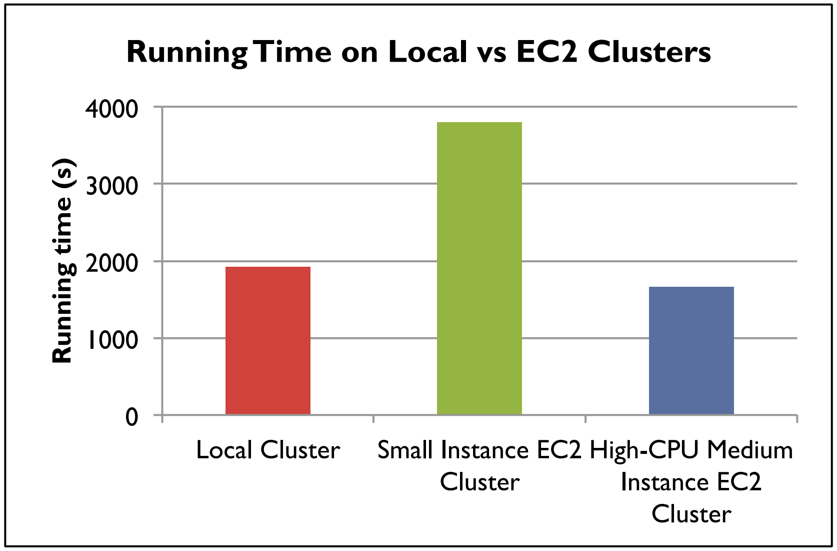
…

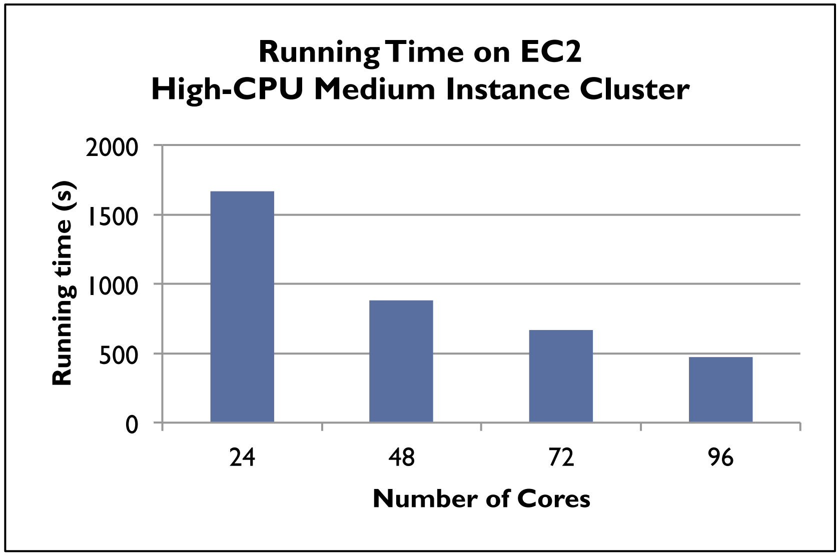
```
Read 1, Chromosome 1, 12345-12365
```

```
Read 2, Chromosome 1, 12350-12370
```

CloudBurst: Highly Sensitive Read Mapping with MapReduce.
Schatz, MC (2009) *Bioinformatics*. 25:1363-1369

AWS EC2 Performance



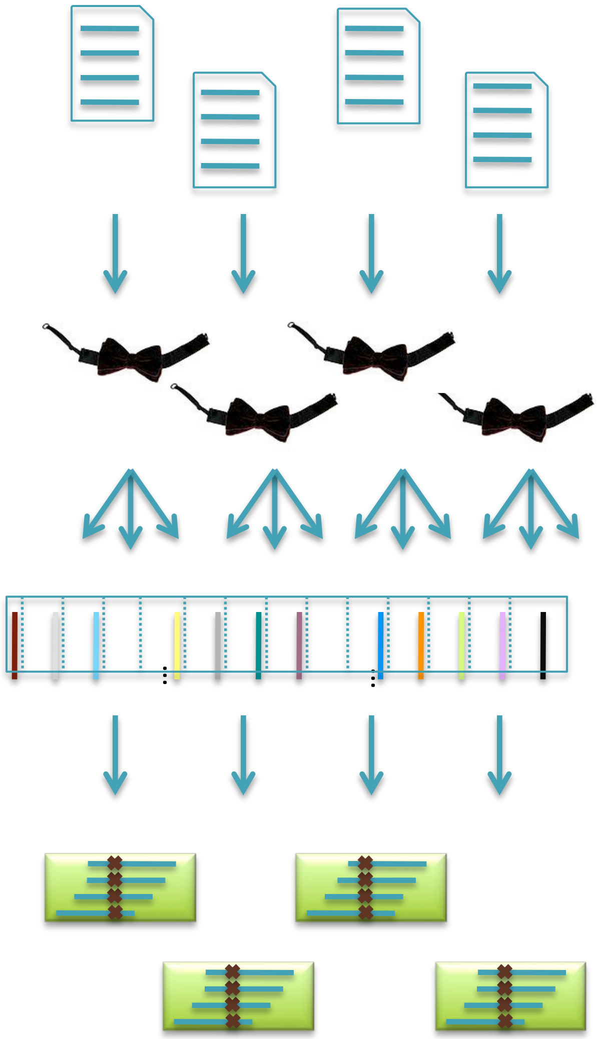


- CloudBurst running times for mapping 7M reads to human chromosome 22 with at most 4 mismatches on the local and EC 2 clusters.
  - The 24-core Amazon High-CPU Medium Instance EC2 cluster is faster than the 24-core Small Instance EC2 cluster, and the 24-core local dedicated cluster.
  - The 96-core cluster on AWS was 100x faster than serial RMAP.

- Cloud can be very effective for genomics
- When computing at scale, space is time
- Implementing from scratch is expensive

Crossbow

http://bowtie-bio.sourceforge.net/crossbow



- Align billions of reads and find SNPs
  - Reuse software components: Hadoop Streaming
- Map: Bowtie (Langmead *et al.*, 2009)
  - Find best alignment for each read
  - Emit (chromosome region, alignment)
- Shuffle: Hadoop
  - Group and sort alignments by region
- Reduce: SOAPsnp (Li *et al.*, 2009)
  - Scan alignments for divergent columns
  - Accounts for sequencing error, known SNPs

Searching for SNPs with Cloud Computing.
Langmead B, Schatz MC, Lin J, Pop M, Salzberg SL (2009) *Genome Biology.* **10**:R134

Performance in Amazon EC2

	Asian Individual Genome		
Data Loading	3.3 B reads	106.5 GB	$10.65
Data Transfer	1h :15m	40 cores	$3.40
Setup	0h : 15m	320 cores	$13.94
Alignment	1h : 30m	320 cores	$41.82
Variant Calling	1h : 00m	320 cores	$27.88
End-to-end	4h : 00m		$97.69

Discovered 3.7M SNPs in one human genome for ~$100 in an afternoon.
Accuracy validated at >99%

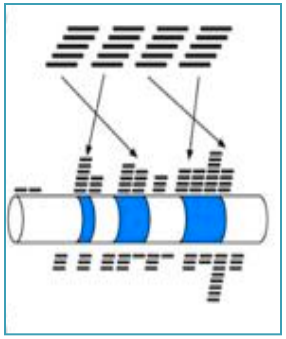
- Very compelling example of cloud computing in genomics
- Transfer takes time, but totally depends on institution
- Need more applications!

Hadoop for NGS Analysis

Myrna

Cloud-scale differential gene expression for RNA-seq

Expression of 1.1 billion RNA-Seq reads in ~2 hours for ~$66



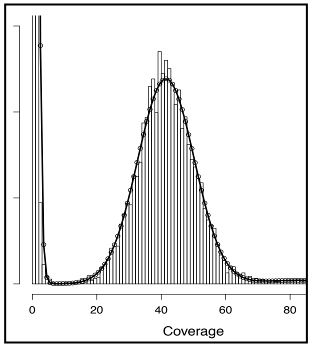
(Langmead, Hansen, Leek, 2010)

http://bowtie-bio.sf.net/myrna/

Quake

Quality-aware error correction of short reads

Correct 97.9% of errors with 99.9% accuracy



(Kelley, Schatz, Salzberg, 2010)

http://www.cbcb.umd.edu/software/quake/

Contrail

Assembly of Large Genomes Using Cloud Computing

Quickly assemble the human genome with hundreds of commodity cores

(Schatz, 2010)

http://contrail-bio.sf.net/

Genome Indexing

Rapid Parallel Construction of Genome Index

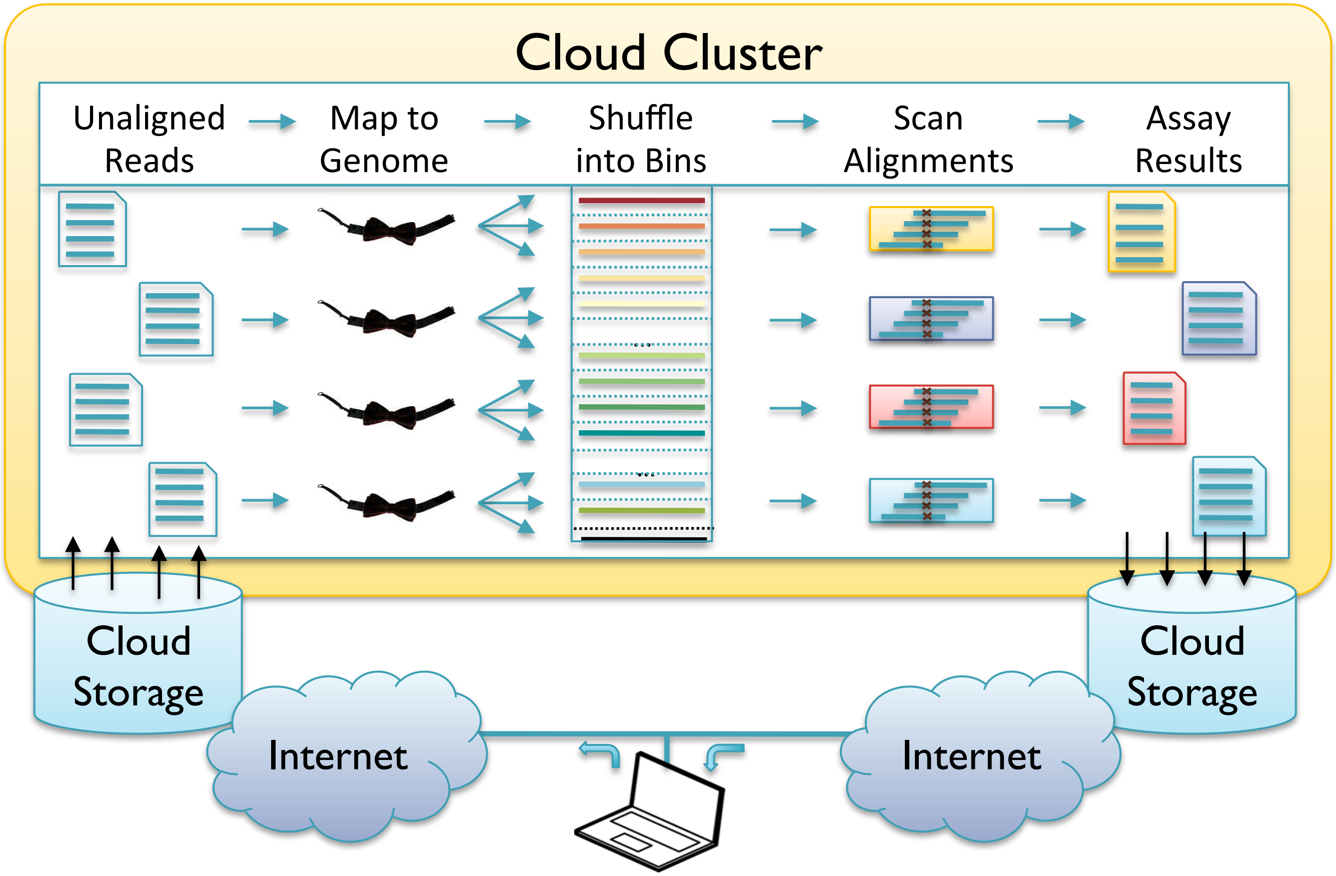
Construct the BWT of the human genome in 9 minutes

$GATTACA
A$GATTAC
ACA$GATT
ATTACA$G
CA$GATTA
GATTACA$
TACA$GAT
TTACA$GA

(Menon, Bhat, Schatz, 2011)

http://code.google.com/p/genome-indexing/

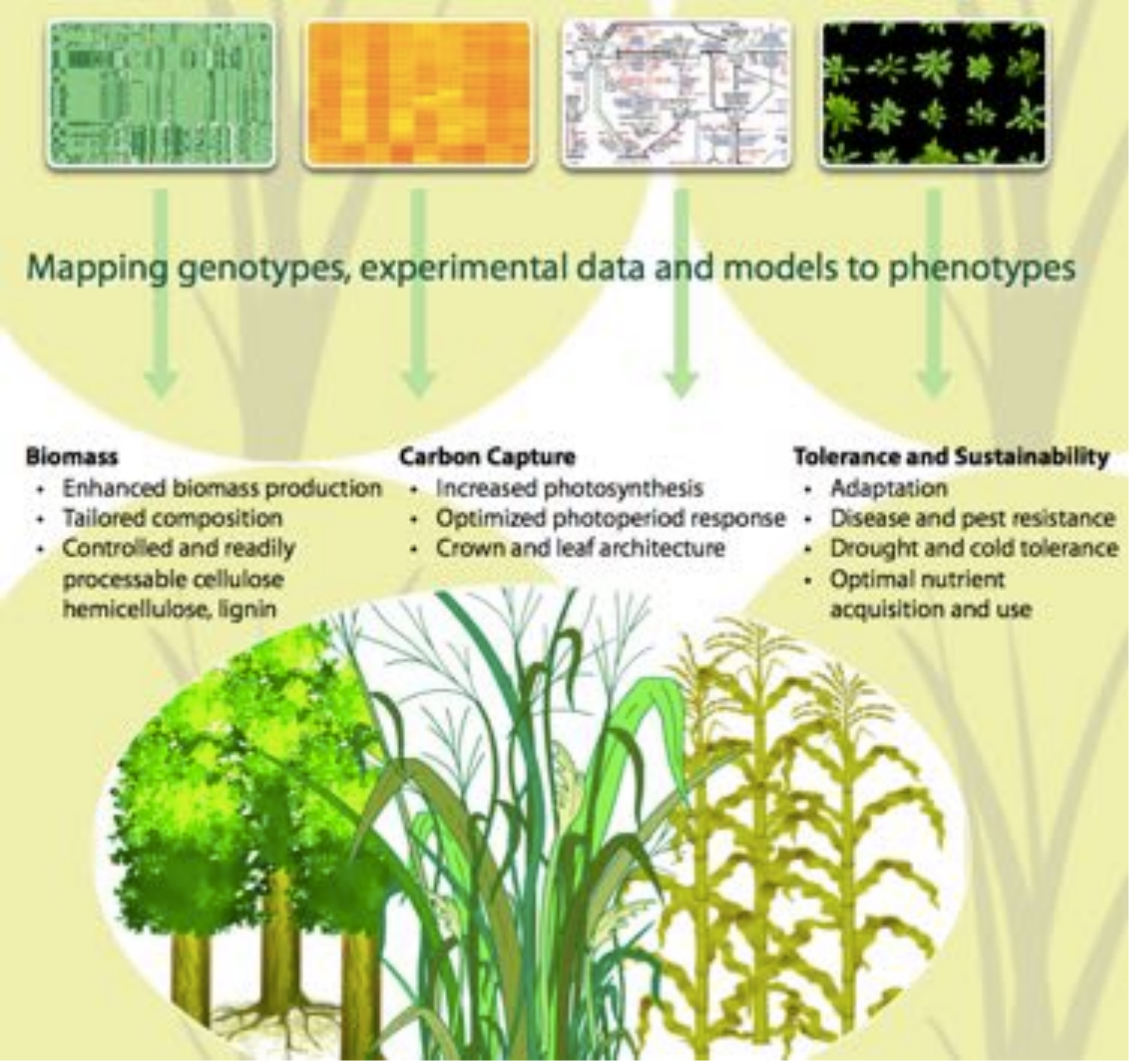
Map-Shuffle-Scan for Genomics



- Genomics+Cloud is very effective
- Need more applications, users, and a scientific goal

Cloud Computing and the DNA Data Race.
Schatz, MC, Langmead B, Salzberg SL (2010) *Nature Biotechnology.* **28**:691-693

Systems Biology Knowledgebase



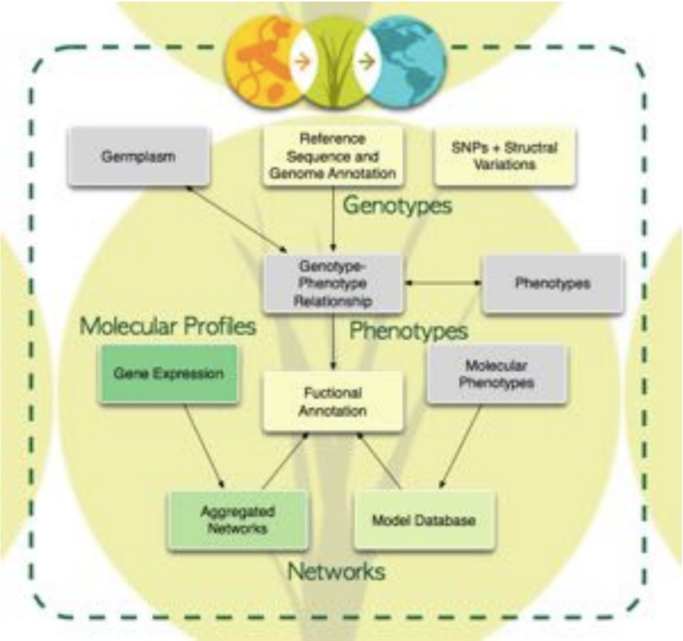
Mapping genotypes, experimental data and models to phenotypes

Biomass
- Enhanced biomass production
- Tailored composition
- Controlled and readily processable cellulose hemicellulose, lignin

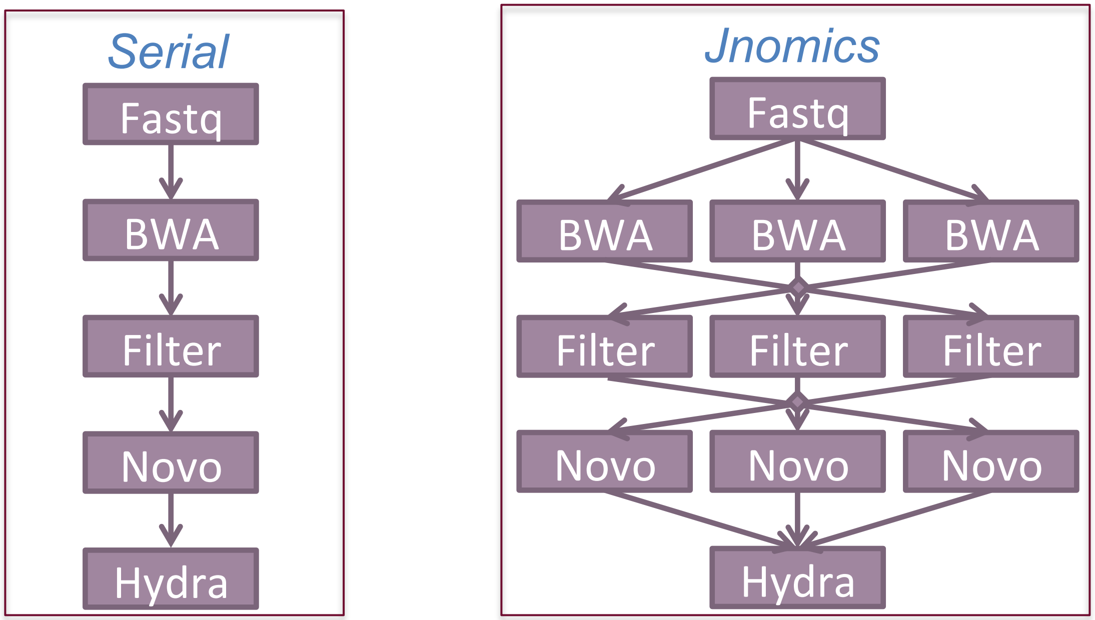
Carbon Capture
- Increased photosynthesis
- Optimized photoperiod response
- Crown and leaf architecture

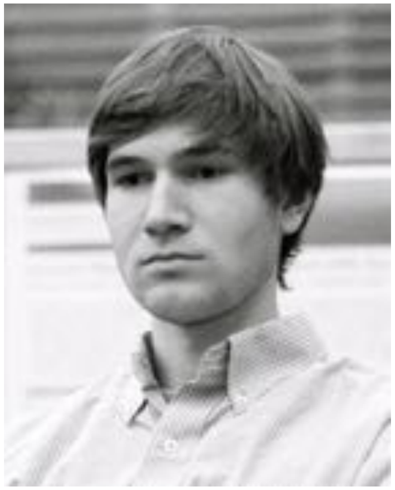
Tolerance and Sustainability
- Adaptation
- Disease and pest resistance
- Drought and cold tolerance
- Optimal nutrient acquisition and use

Model development
Hypothesis testing
Knowledge Synthesis



Jnomics: Cloud-scale genomics





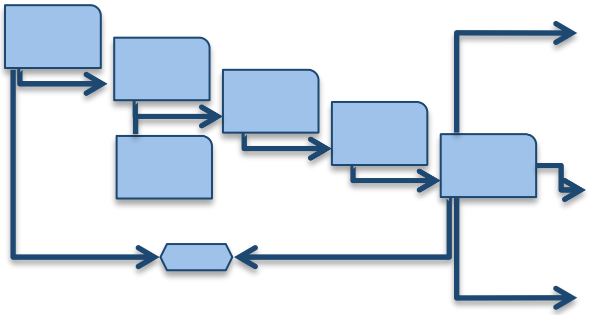
- Rapid parallel execution of data-intensive analysis
  - FASTX, BWA, Bowtie2, Novoalign, SAMTools, Hydra
  - Sorting, merging, filtering, selection, clustering, correlating
  - Supports BAM, SAM, BED, fastq

Answering the demands of digital genomics
Titmus, MA, Gurtowski, J, Schatz, MC (2012) *Concurrency & Computation*

Jnomics API 1.0

Genotyping API

- **Bowtie**: Launch alignment task with Bowtie
- **BWA**: Launch alignment task with BWA
- **SNPCalling**: Launch SNPcalling task with SAMTools
- **SortAlignments**: Launch task to sort by chromosome



Job API

- **ClusterStatus**: return basic status of cluster (jobs running, nodes available, etc)
- **JobStatus**: Given a JobID, returns current status
- **ListJobs**: List JobID running with a given username
- **KillJob**: Kills a given JobID

Data API

- **List**: List files in a directory
- **Fetch**: Fetch files from HDFS
- **Put**: Put files into HDFS
- **RM**: Delete files on HDFS
- **FetchBAM**: On-the-fly conversion to BAM
- **PutFastq**: Put reads into HDFS with conversion

Notes:

- All calls are authenticated with KBase username/password

Maize Population Analysis

Align & call SNPs from 131 maize samples
1TB fastq / 408Gbp input data

	Serial	KBase cloud (small)	KBase Cloud (large)
Config	1 core (1 node)	210 cores (15 nodes)	854 cores (61 nodes)
Bowtie2	1311 hr*	19.5 hr	5 hr
Sort	58 hr*	N/A	N/A
Samtools	58 hr*	3.5 hr	1.5 hr
End-to-End Speedup	1427 hr* 1x	23 hr 62x	6.5 hr 219x

*estimated time

Summary

Staying afloat in the data deluge means computing in parallel

- Hadoop + Cloud computing is an attractive platform for large scale sequence analysis, computation, and collaboration

Diversity is the biggest barrier to adoption

1. Diversity of applications
   - Long tail distribution of critical to experimental
2. Diversity of requirements
   - Storage, Network, IO, cache, RAM, cores
3. Diversity of data
   - Datatypes, scale, formats, available bandwidth
4. Diversity of users
   - Super-scripters to point-and-click users

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Levy Lab
Lippman Lab
Lyon Lab
Martienssen Lab
McCombie Lab
Ware Lab
Wigler Lab

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Cole Trapnell

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Thank You!

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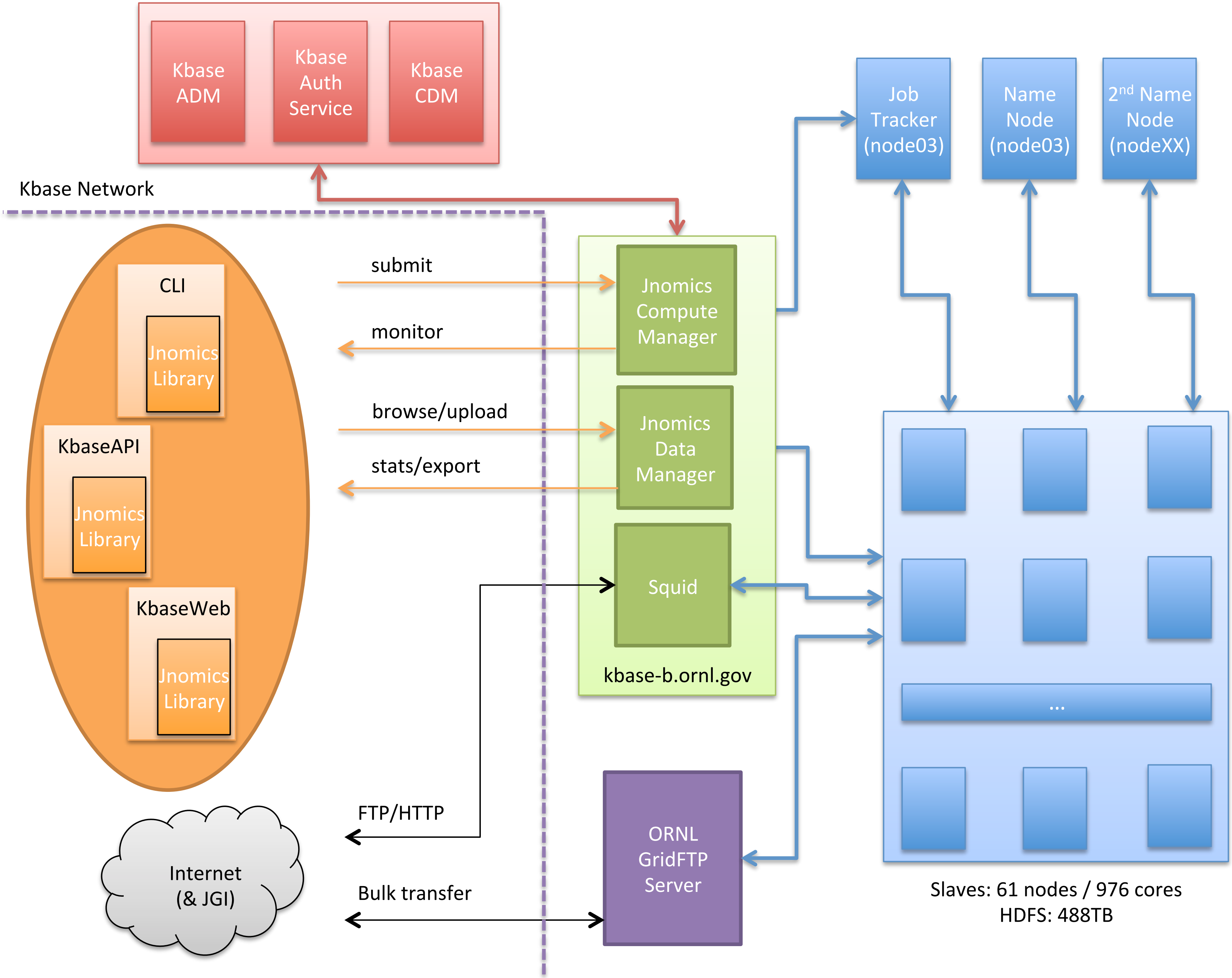
Kbase ADM
Kbase Auth Service
Kbase CDM
Kbase Network
CLI
Jnomics Library
KbaseAPI
Jnomics Library
KbaseWeb
Jnomics Library
submit
monitor
browse/upload
stats/export
Jnomics Compute Manager
Jnomics Data Manager
Squid
kbase-b.ornl.gov
Job Tracker (node03)
Name Node (node03)
2nd Name Node (nodeXX)
...
Slaves: 61 nodes / 976 cores
HDFS: 488TB
FTP/HTTP
Bulk transfer
Internet (& JGI)
ORNL GridFTP Server