Analyzing 100's of TB of Genomic Data with ADAM and Toil

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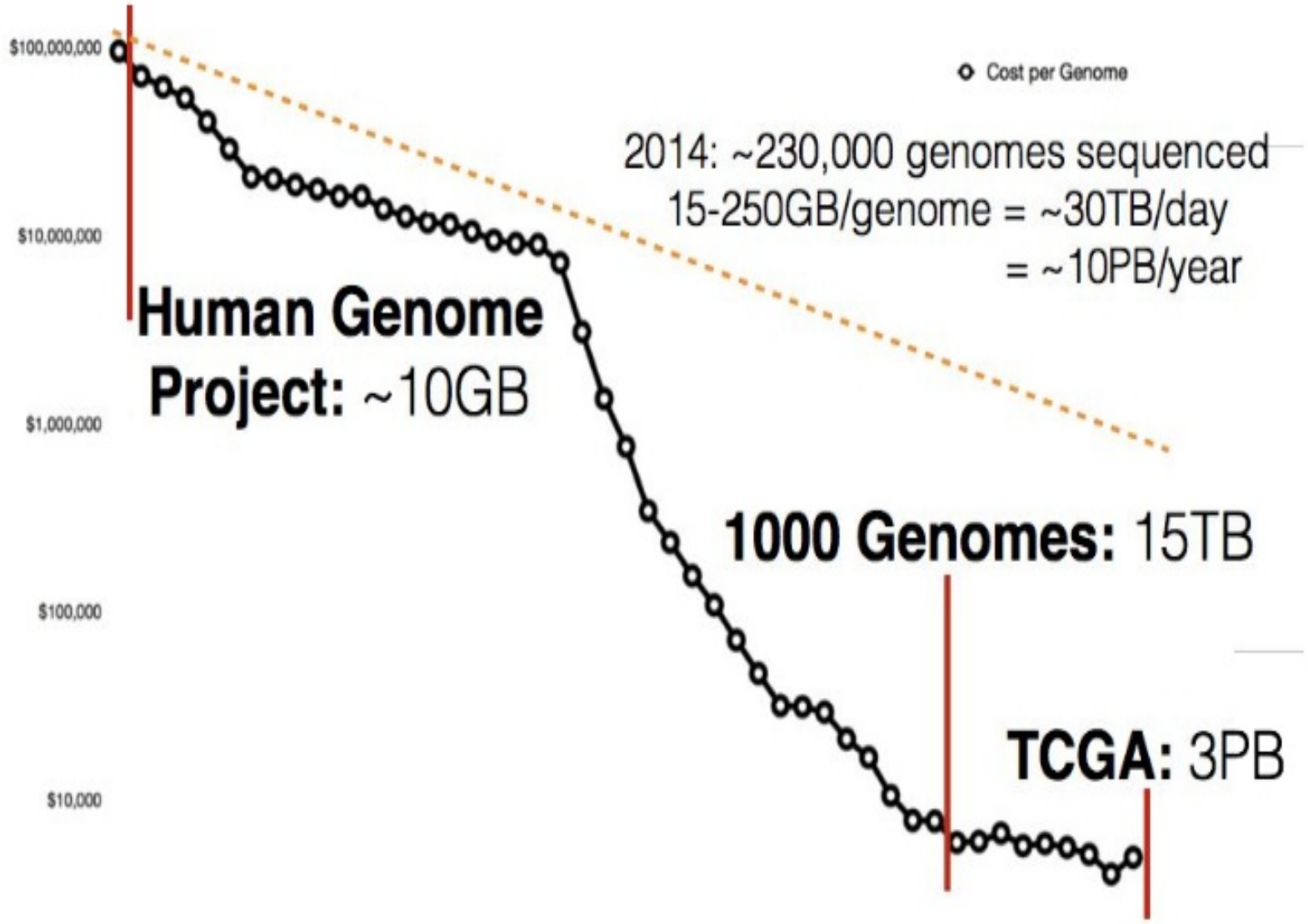
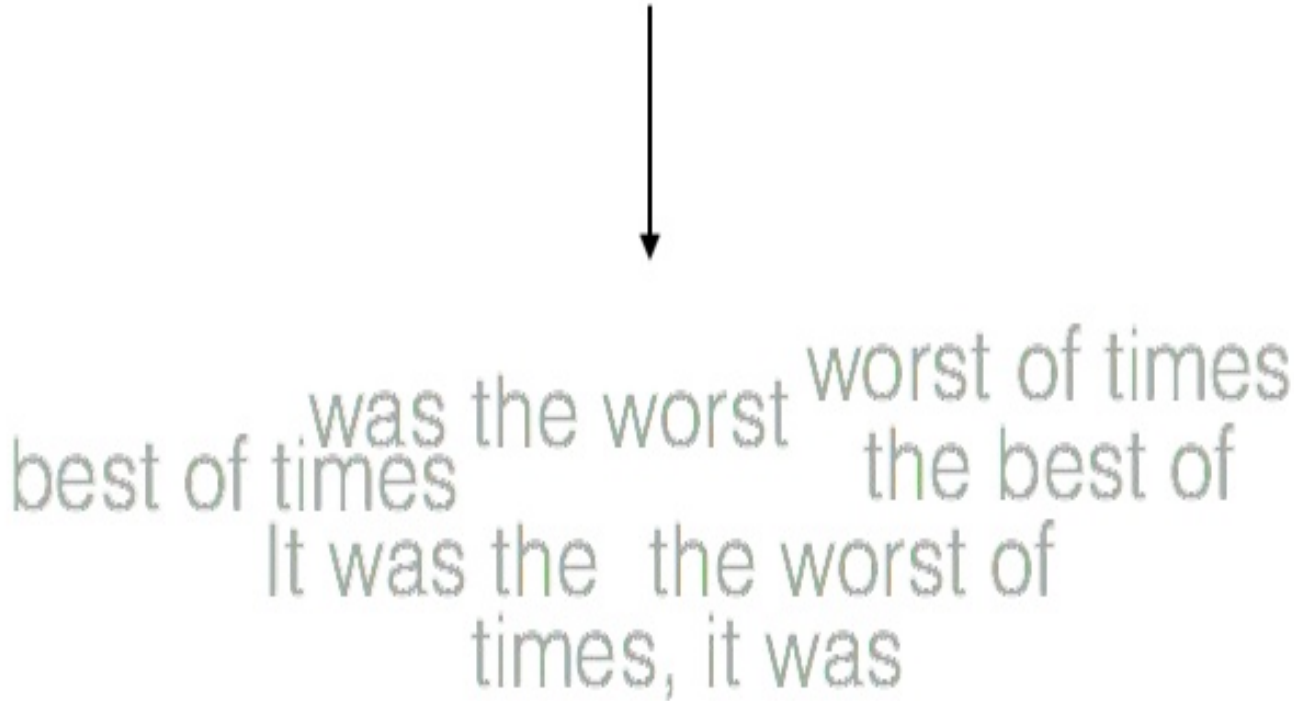
6/8/2016

Compulsory Moore's Law Slide



The Sequencing Abstraction

It was the best of times, it was the worst of times…



- Sequencing is a Poisson substring sampling process
- For $1,000, we can sequence a 30x copy of your genome, but what is the

The Alignment Process

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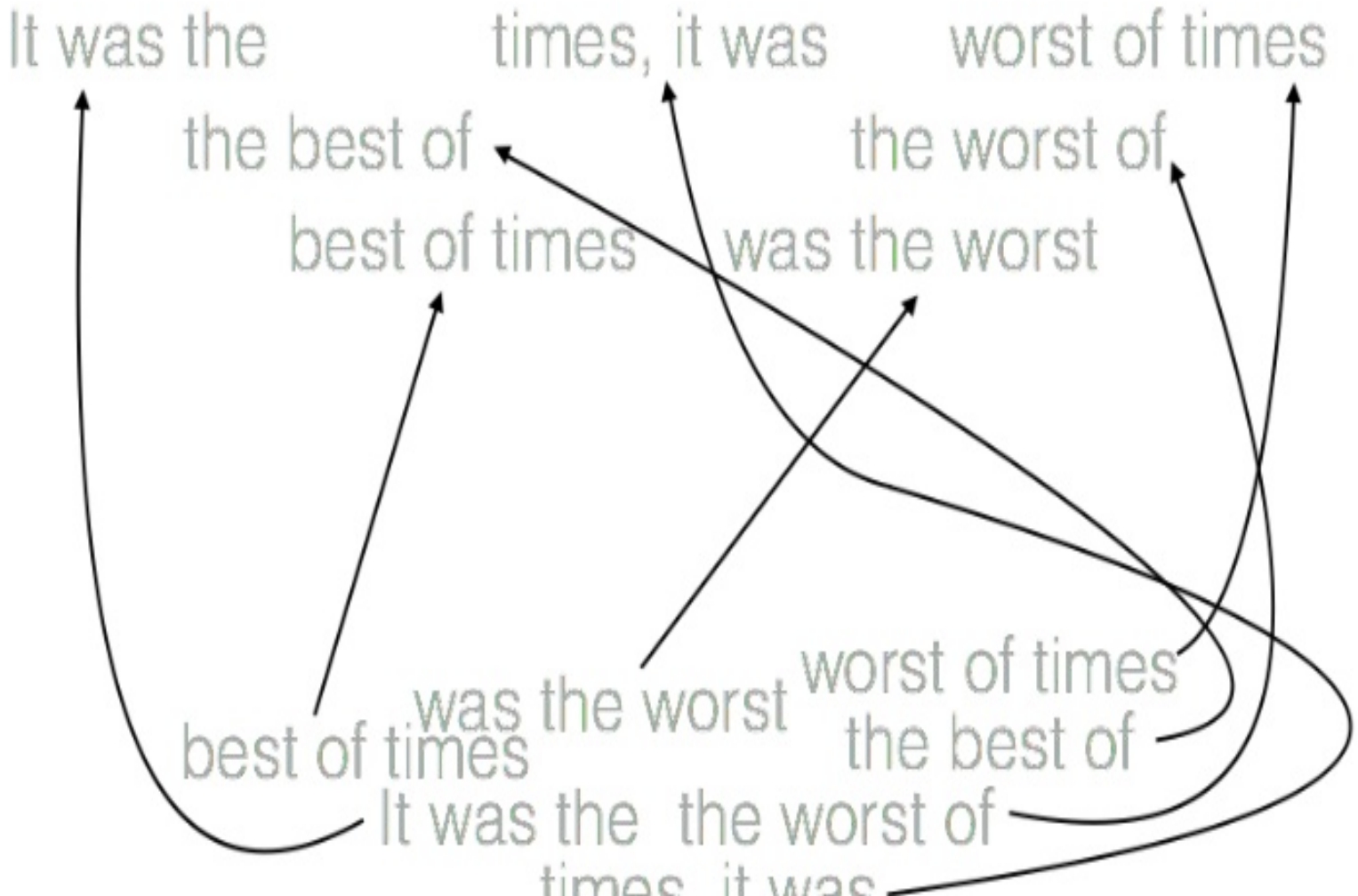
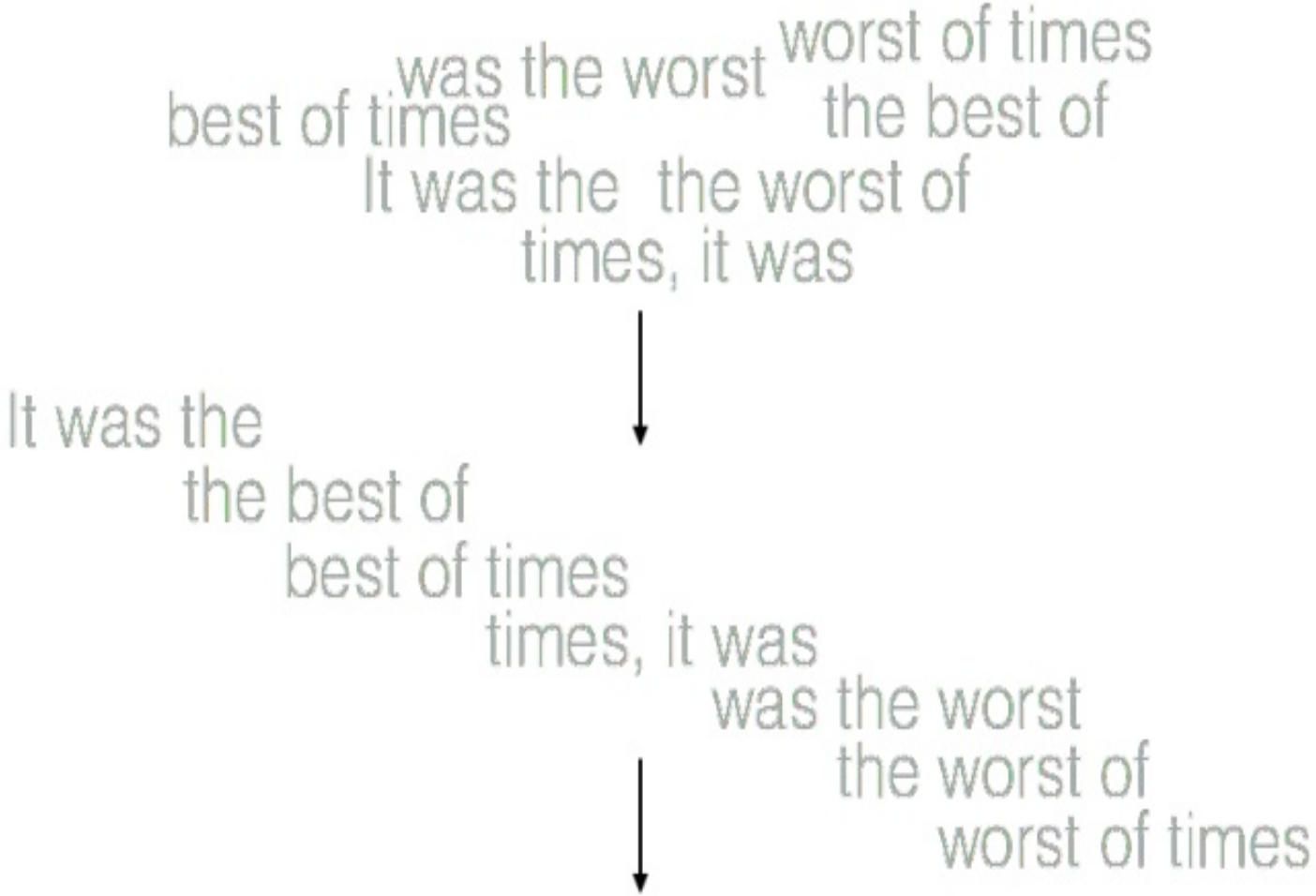
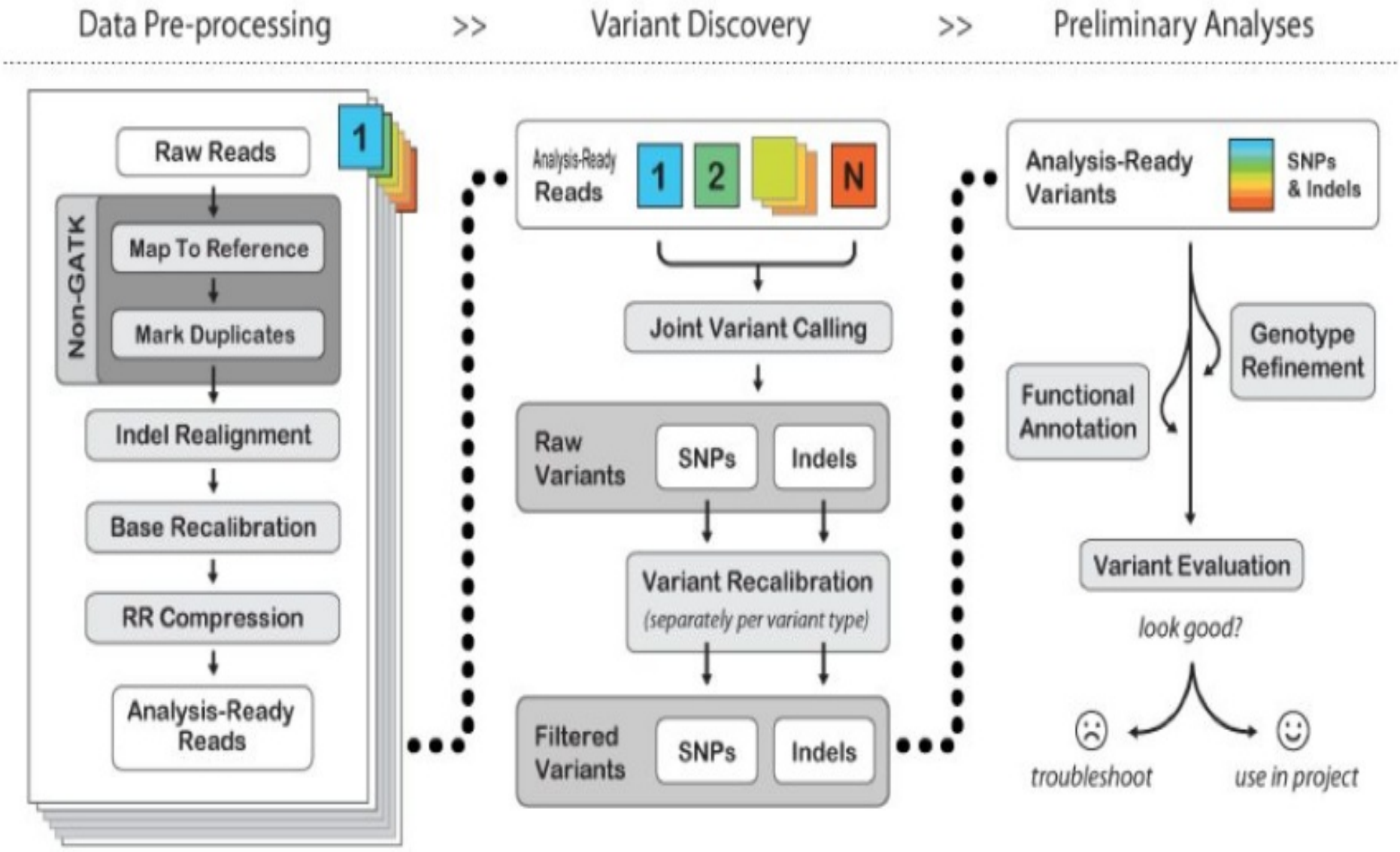


The Sequence Re-assembly Process

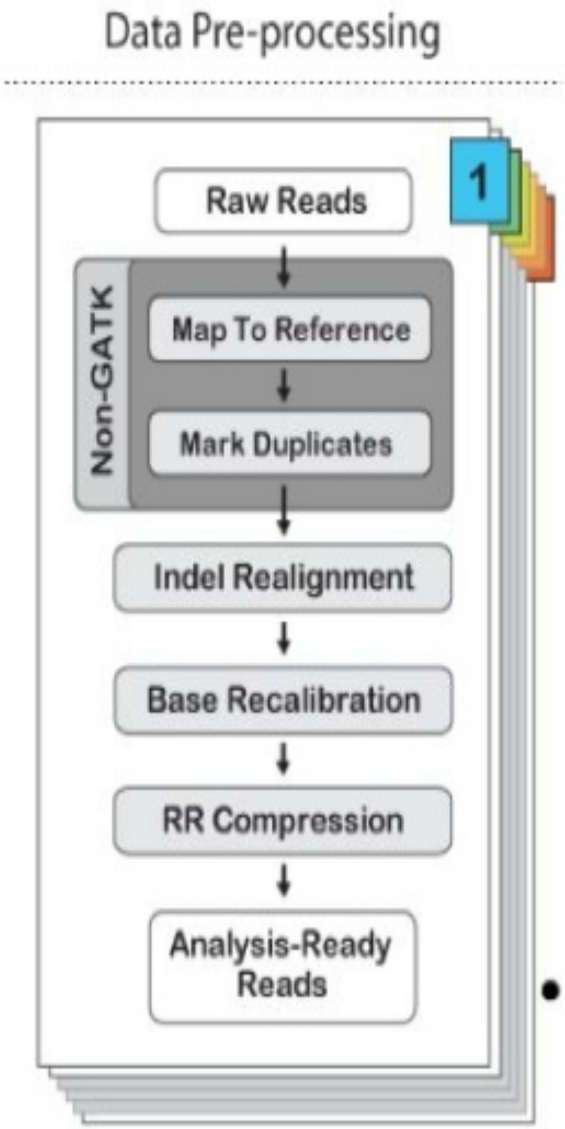


It was the best of times, it was the worst of times…

End-to-end variant analysis



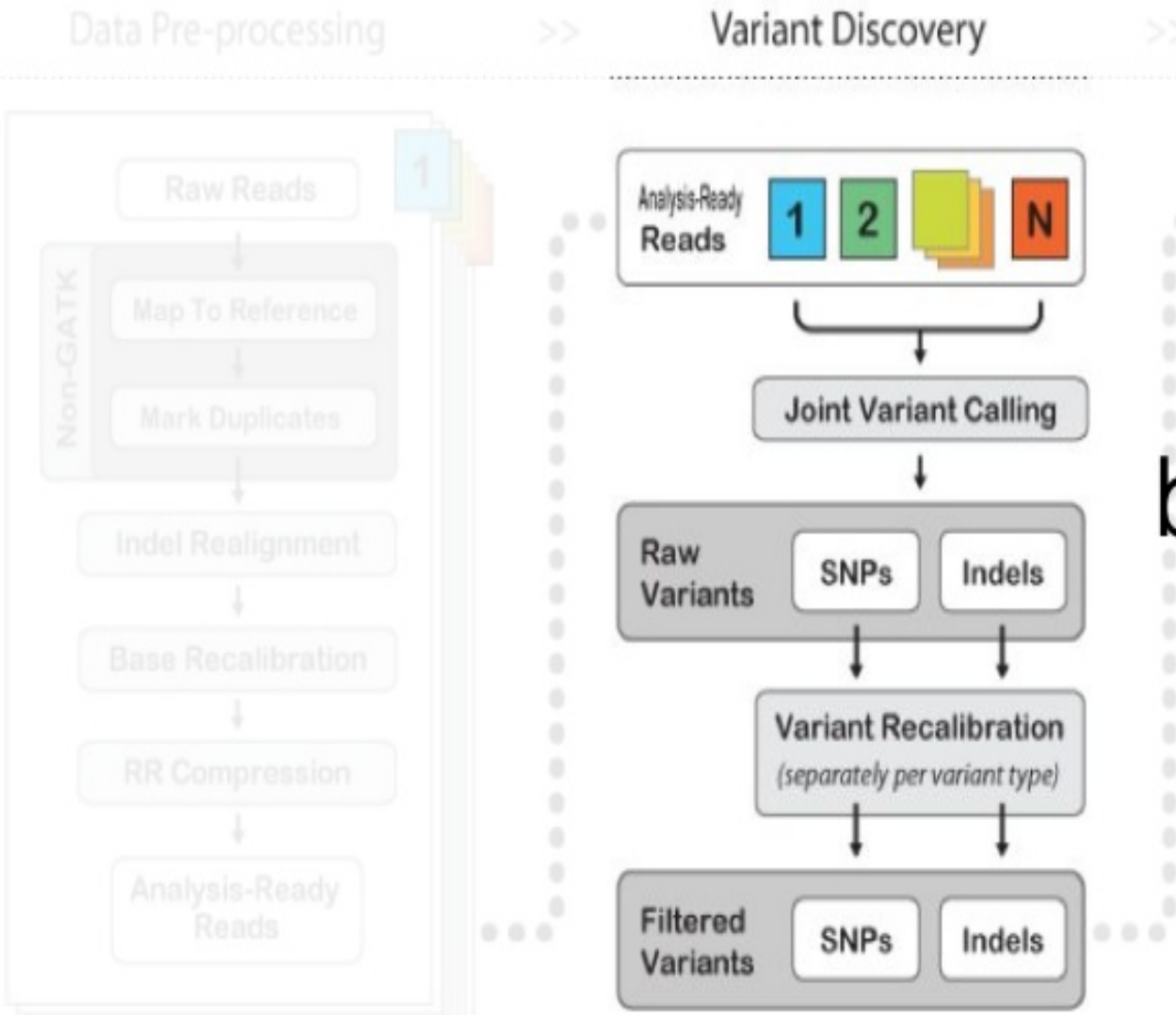
End-to-end variant analysis



Align and clean up errors in raw reads

150 hrs/sample

End-to-end variant analysis



Generate diffs between samples

1 week/100 samples

Genomics is built around flattened tools

Genomics is built around legacy file formats:

- E.g., SAM/BAM → alignment, VCF → variants, BED/GTF/etc → features
- Manually curated text/binary flat files

These formats dictate:

- What accesses can be optimized (read a full row)
- What predicates can be evaluated (small number of genomic loci)
- How we write genomic algorithms (sorted iterator over genome)

BAM File Format

```
Header: n = 500
Reference 1
Sample 1
1:c20,TCGA,4M;2: c20,
GAAT,4M1D;3:c20,CCGAT,
5M;4:c20,TTGCAC,6M;5:
c20,CCGT,3M1D1M; …
```

Why avoid flat architectures?

Flat architectures tend to expose bad programming interfaces:

- What access patterns do our flat files lock us into?
- GATK: *sorted iterator over the genome*

What do flat architectures break?

1. Trivial: low level abstractions are not productive
2. Trivial: flat architectures create technical lock-in
3. Subtle: low level abstractions can introduce bugs

Green field genomics: start with a schema!

```
record AlignmentRecord {
    union { null, Contig } contig = null;
    union { null, long } start = null;
    union { null, long } end = null;
    union { null, int } mapq = null;
    union { null, string } readName = null;
    union { null, string } sequence = null;
    union { null, string } mateReference = null;
    union { null, long } mateAlignmentStart = null;
    union { null, string } cigar = null;
    union { null, string } qual = null;
    union { null, string } recordGroupName = null;
    union { int, null } basesTrimmedFromStart = 0;
    union { int, null } basesTrimmedFromEnd = 0;
    union { boolean, null } readPaired = false;
    union { boolean, null } properPair = false;
    union { boolean, null } readMapped = false;
    union { boolean, null } mateMapped = false;
    union { boolean, null } firstOfPair = false;
    union { boolean, null } secondOfPair = false;
    union { boolean, null } failedVendorQualityChecks = false;
    union { boolean, null } duplicateRead = false;
    union { boolean, null } readNegativeStrand = false;
    union { boolean, null } mateNegativeStrand = false;
    union { boolean, null } primaryAlignment = false;
    union { boolean, null } secondaryAlignment = false;
    union { boolean, null } supplementaryAlignment = false;
    union { null, string } mismatchingPositions = null;
    union { null, string } origQual = null;
    union { null, string } attributes = null;
    union { null, string } recordGroupSequencingCenter = null;
    union { null, string } recordGroupDescription = null;
    union { null, long } recordGroupRunDateEpoch = null;
    union { null, string } recordGroupFlowOrder = null;
    union { null, string } recordGroupKeySequence = null;
    union { null, string } recordGroupLibrary = null;
    union { null, int } recordGroupPredictedMedianInsertSize = null;
    union { null, string } recordGroupPlatform = null;
    union { null, string } recordGroupPlatformUnit = null;
    union { null, string } recordGroupSample = null;
```

Schema
Data Models

A schema provides a narrow waist

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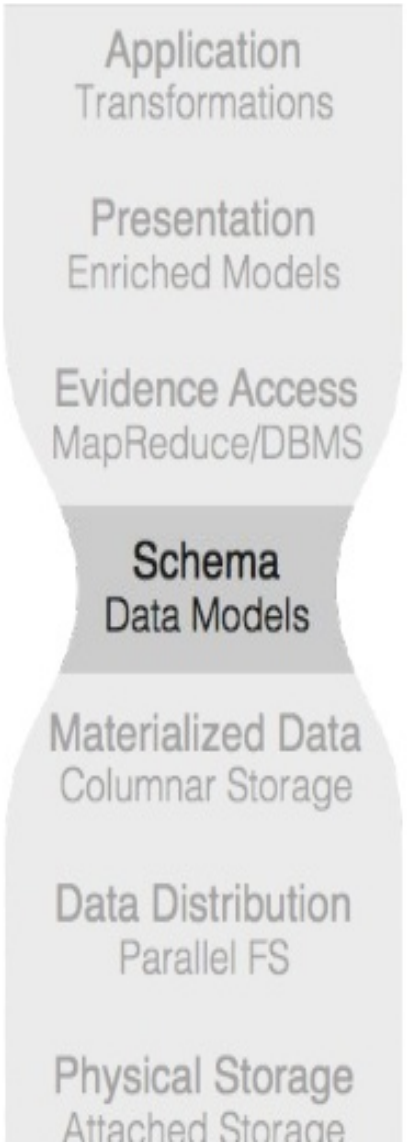
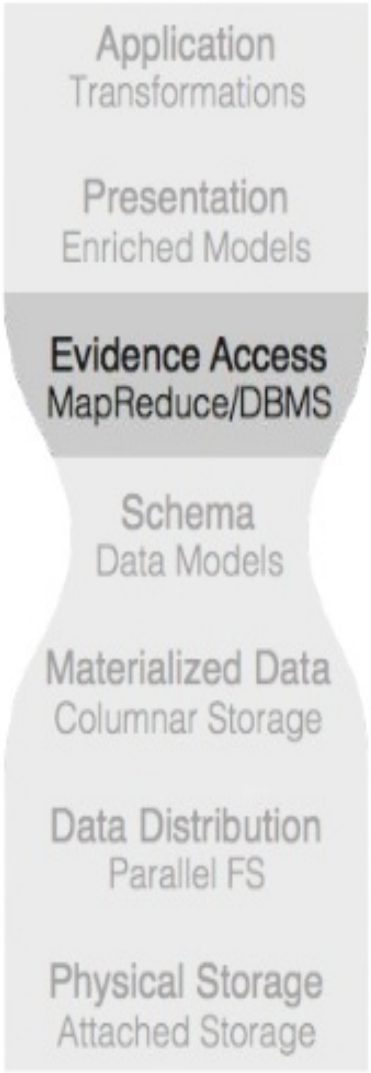


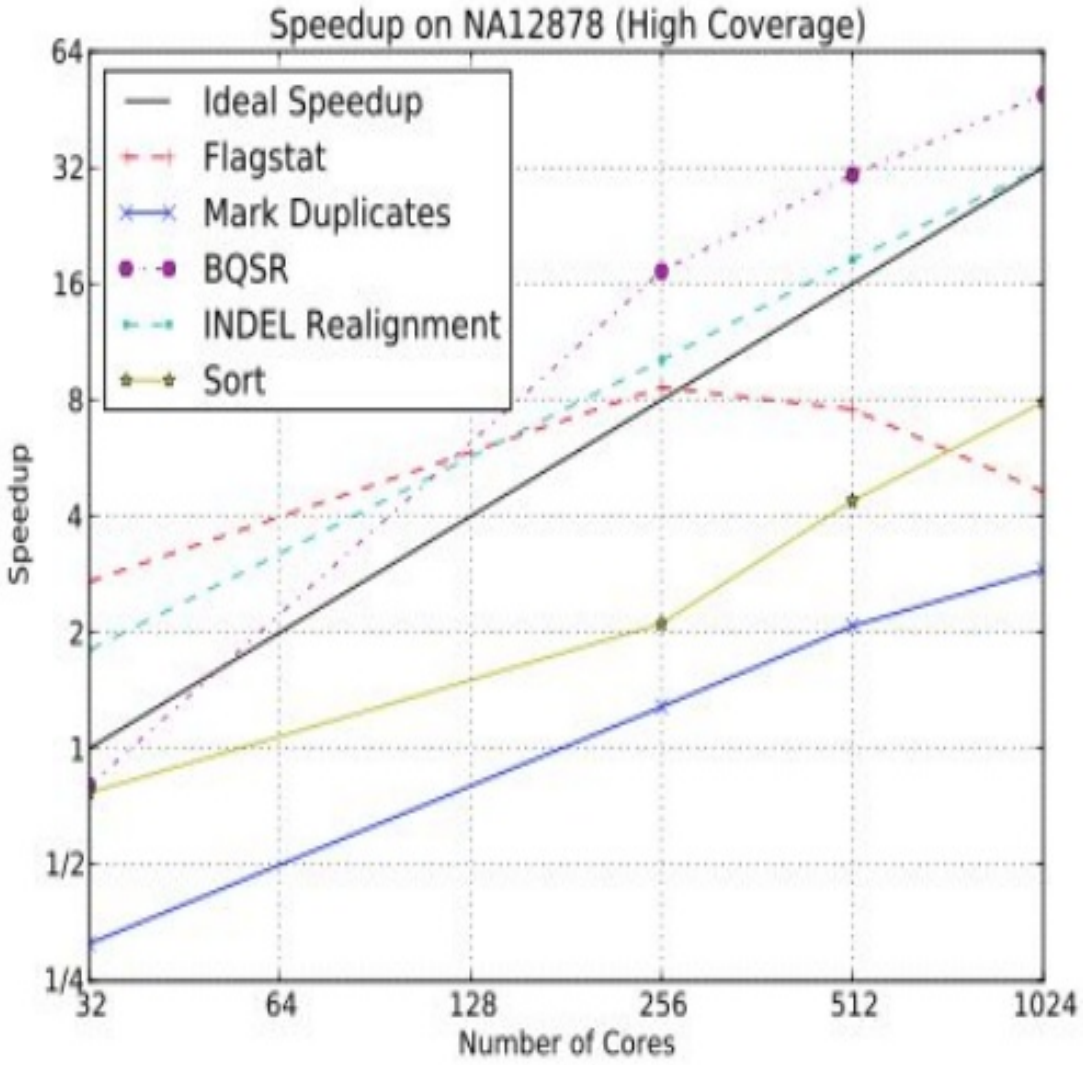
We can use our stack to accelerate common queries!

- In genomics, we commonly have to find observations that overlap in a coordinate plane
- This coordinate plane is genomics specific, and is known a priori
- We can use our knowledge of the coordinate plane to implement a fast overlap join

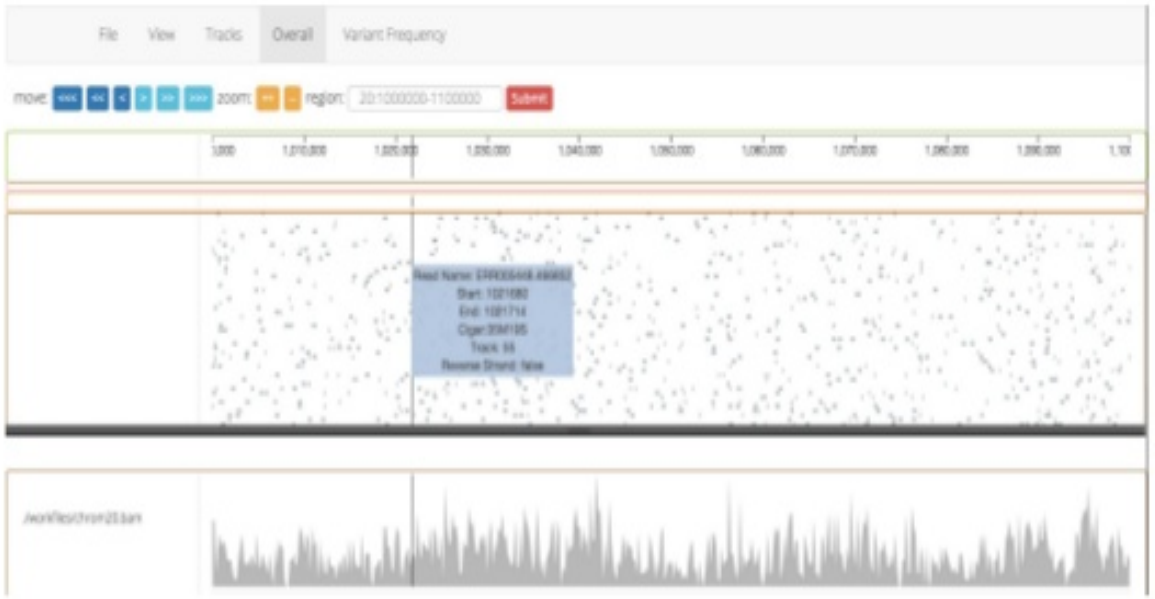


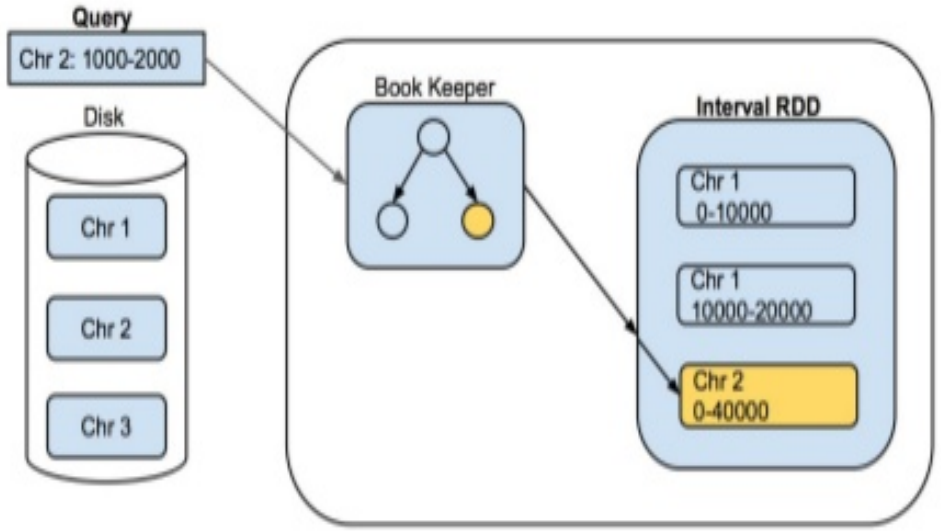
ADAM/Spark Yields Horizontal Scalability

- 30–50x speedup over traditional implementations
- Speedup extends to O (200MB / node)
- 3x improvement in analysis cost



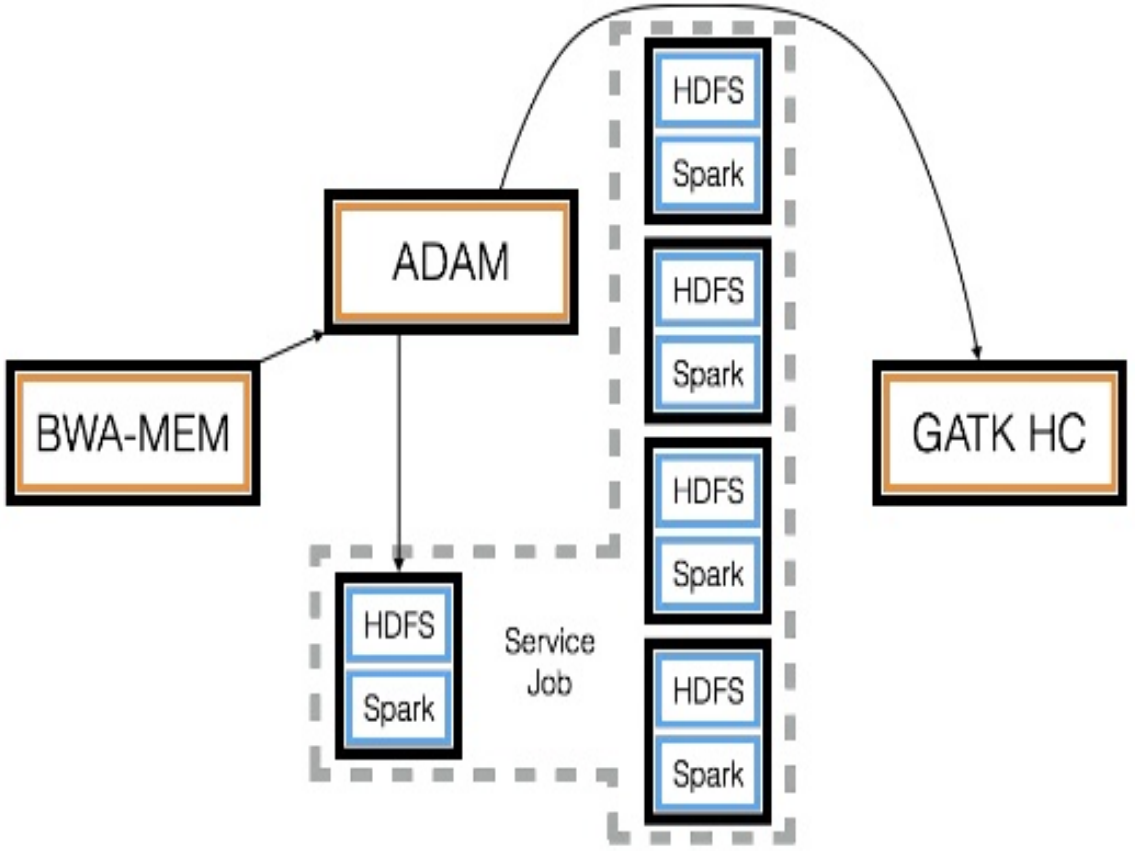
This means we can support genomic EDA as well...





- Narrow waist in stack → can swap in/out stages
- If I want to run interactive queries against genomic loci, swap in an RDD implementation that is optimized for point/range queries

Using ADAM+Spark+Toil



- On-going validation of ADAM on Toil against existing “best practice” tools
- Using Simons Genome Diversity Project:
  - 260 individuals from 127 ethnic groups: more than 100TB of genomic data

Toil: Pipeline Architecture for Massive Workflows

- Work led by UCSC/BD2K Center
- Massively Scalable — tested on 32,000 cores
- Resumable after failure of *any* node
- Portable: installed with a single command
  - Amazon, OpenStack, Azure, HPC, and Google (soon)
- Simple: built entirely in Python
- Open-source → github.com/BD2KGenomics/toil

Develop workflows locally…

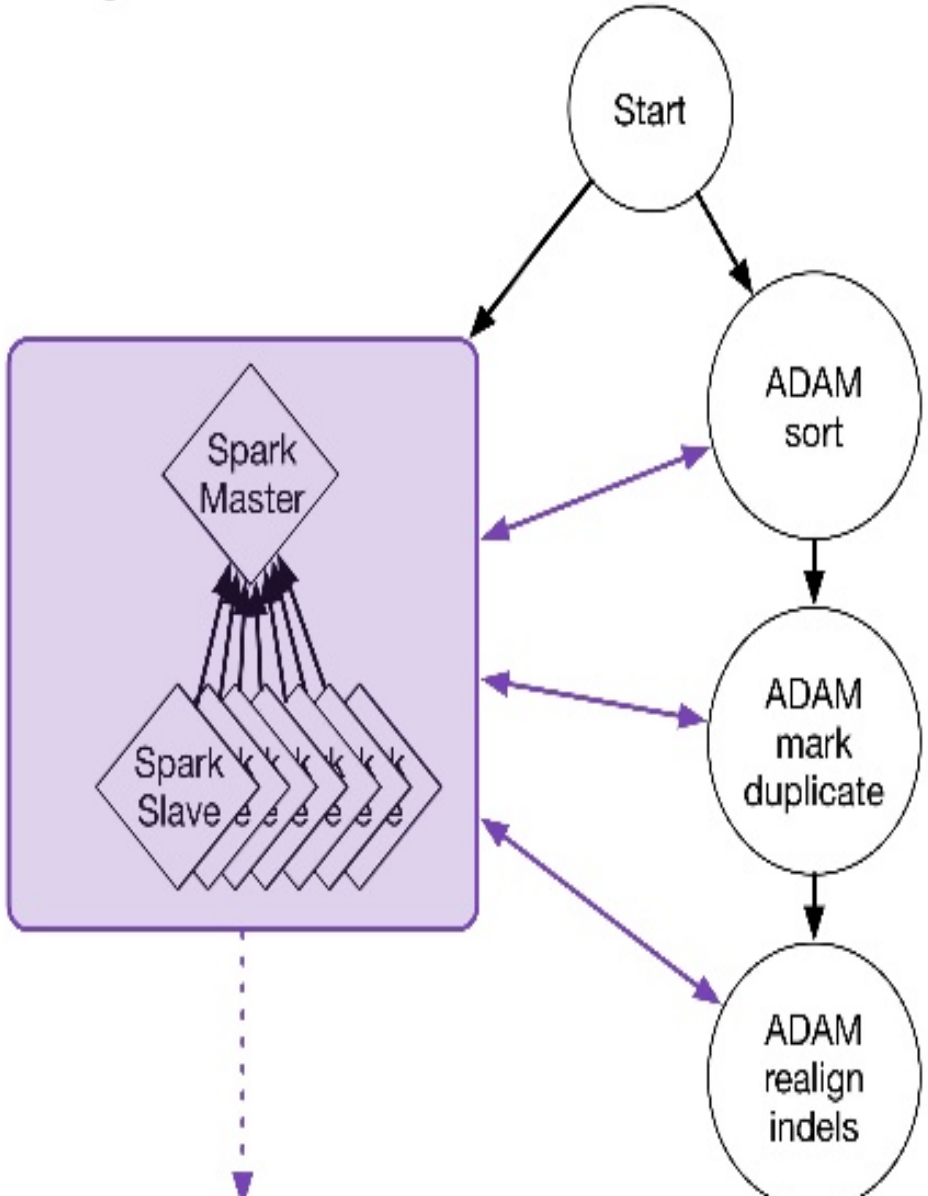
Deploy at scale without changing source code!

Toil is a DAG metascheduler

- Users decompose a workflow into jobs and data:
  - Job → python function or class
  - Toil runs jobs on a single node by delegating to a sub-scheduler
  - Files get written to persistent FileStore for communication between jobs running on different nodes, use local cache to improve performance
- Supports many underlying schedulers/file stores
- When running in the cloud, jobs can be autoscaled
  - Happens transparently to the running jobs

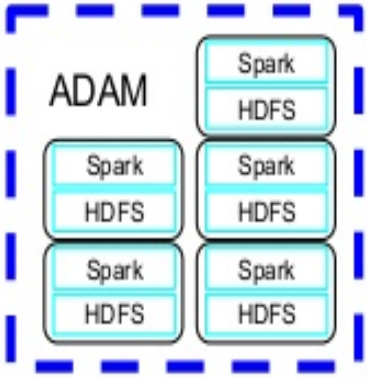
Accommodating “clusters” in a job-oriented workflow

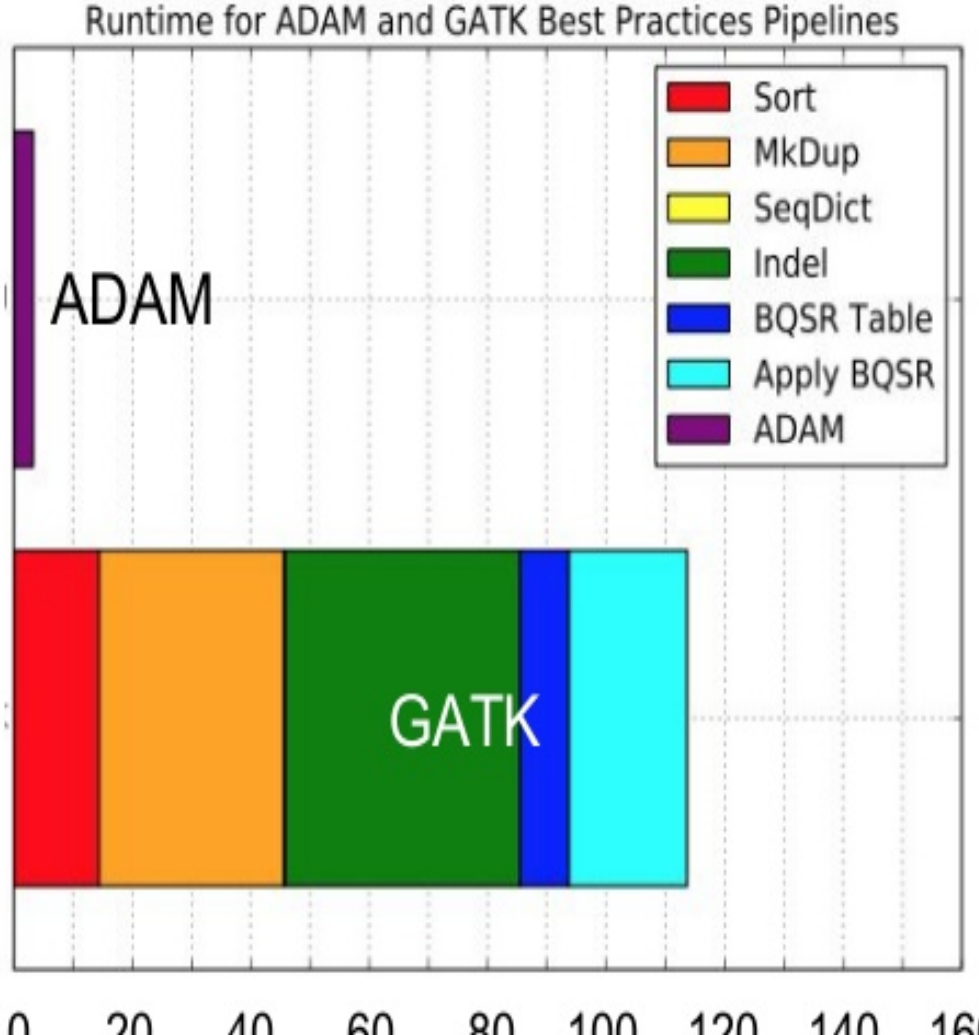
- Hint: a cluster is just a collection of single node jobs!
  - However, the fate of all of the jobs are tied!
- Service jobs persist for the whole lifetime of the task that spawned them
- Spark has a clean mapping to a set of services



ADAM Evaluation

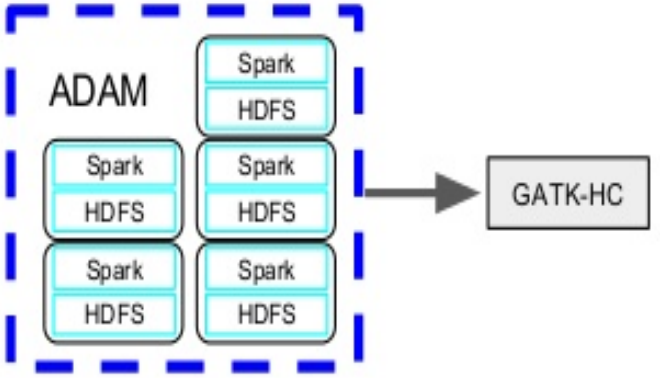
- ADAM produces statistically equivalent results to the GATK best practices pipeline
- Read preprocessing is >30x faster and 3x cheaper
- In the process of recalling the Simons Genome Diversity Project using ADAM
- We have a working pipeline using both HG19 and GRCh38

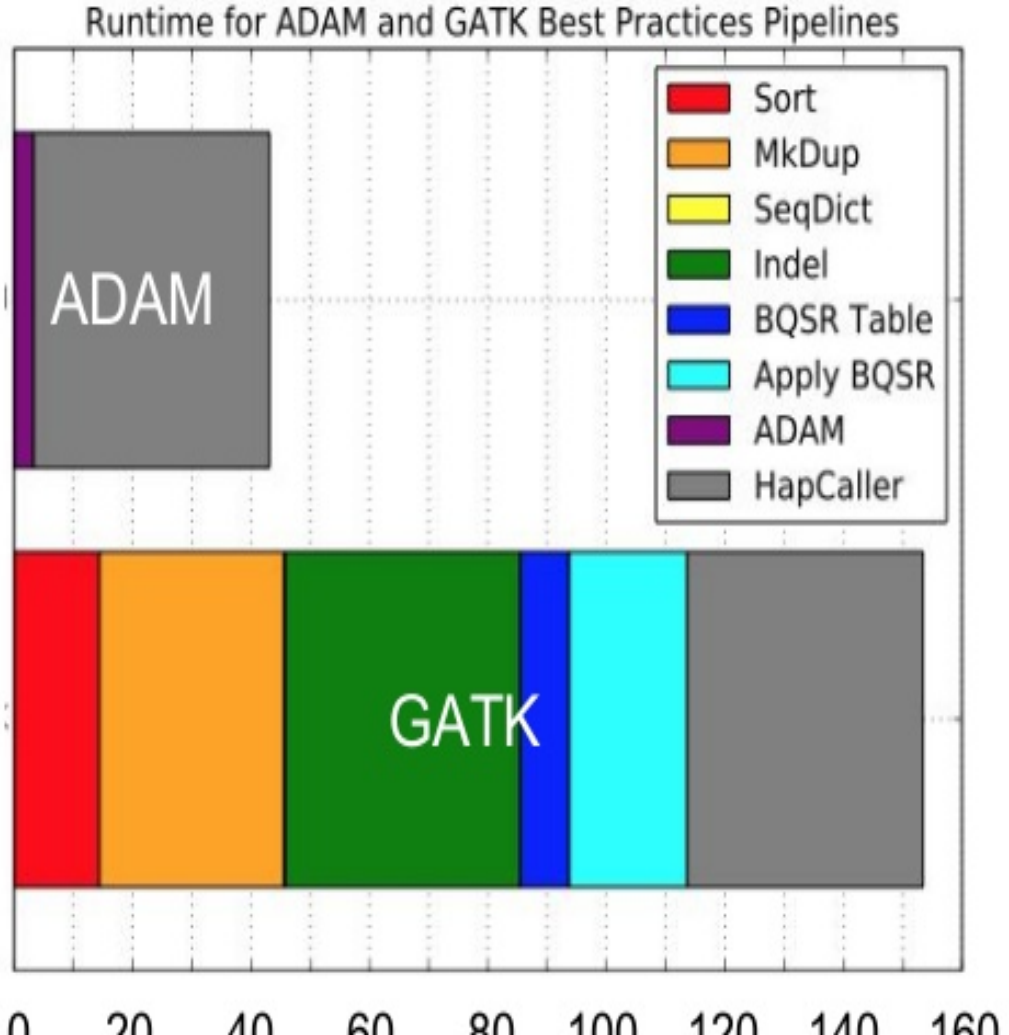




ADAM Evaluation

- ADAM produces statistically equivalent results to the GATK best practices pipeline
- Our end-to-end pipeline is 3.5x faster while also being 4x cheaper
- In the process of recalling the Simons Genome Diversity Project using ADAM
- We have a working pipeline using both HG19 and GRCh38





Check out the code!

ADAM: https://github.com/bigdatagenomics/adam

Check out a demo!

https://databricks.com/blog/2016/05/24/genome-sequencing-in-a-nutshell.html

Run ADAM in Databricks CE!

http://goo.gl/xK8x7s

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- **Cloudera:** Uri Laserson, Tom White
- **Microsoft Research:** Ravi Pandya, Bill Bolosky
- **UC Santa Cruz:** Benedict Paten, David Haussler, Hannes Schmidt, Beau Norgeot, Audrey Musselman-Brown, John Vivian
- And many other open source contributors, especially Neil Ferguson, Andy Petrella, Xavier Tordior, Deborah Siegel, Denny Lee
- Total of 52 contributors to ADAM/BDG from >12 institutions, 23 contributors to Toil from 5 institutions