Community based approaches to scaling variant calling pipelines

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Complex, rapidly changing pipelines

Whole genome, deep coverage v1

Warning: the material on this page is considered out of date by the GSA team.

Best Practice Variant Detection with the GATK v2

Warning: the material on this page is considered out of date by the GSA team.

RETIRED: Best Practice Variant Detection with the GATK v3

Best Practice Variant Detection with the GATK v4, for release 2.0

Mark_DePristo Posts: 150 Administrator, GSA Official Member admin
July 2012 edited April 24 in Methods and Workflows

HaplotypeCaller now so sensitive, it cries at the movies

We know you don't want to miss a single true variant, so for this release, we've put a lot of effort into making the HaplotypeCaller more sensitive. And it's paying off: in our tests, the HaplotypeCaller is now more sensitive than the UnifiedGenotyper for calling both SNPs and indels when run over whole genome datasets.

Large number of specialized dependencies

```
#######################################
# HugeSeq                             #
# The Variant Detection Pipeline      #
#######################################

-- DEPENDENCIES

+ ANNOVAR version 20110506
+ BEDtools version 2.16.2
+ BreakDancer version 1.1
+ BreakSeq Lite version 1.3
+ BWA version 0.6.1
+ CNVnator version 0.2.2
+ GATK version 1.6-9
+ JDK version 1.6.0_21
+ Modules Release 3.2.8
+ Perl
+ Picard Tools version 1.64
+ Pindel version 0.2.2
+ Plantation version 2
+ pysam version 0.6
+ Python version 2.7
+ Simple Job Manager version 1.0
+ Tabix version 0.1.5
+ VCFtools version 0.1.5
```

https://github.com/StanfordBioinformatics/HugeSeq

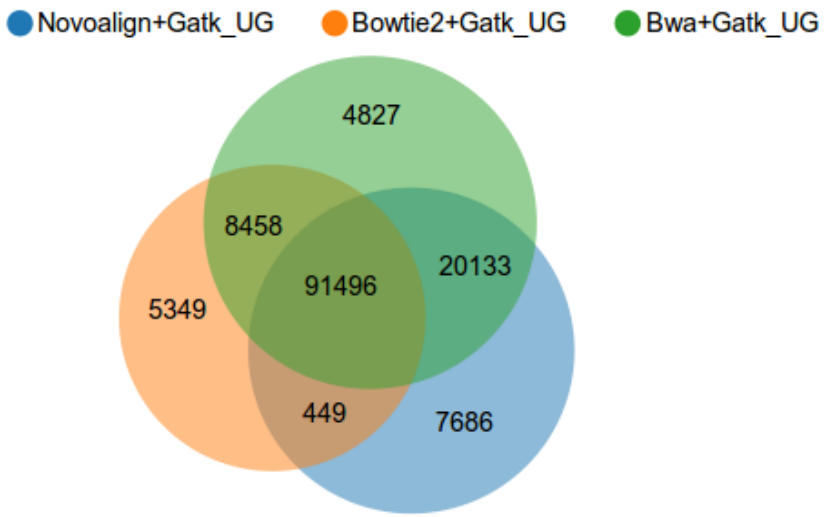
Quality differences between methods

Variant Calling Test

Discuss

We compare combinations of variant calling pipelines across different data sets. Browse our public facing reports to see how various aligner + variant caller combinations perform against each other. Test your own combination of tools by creating your own report. Below is a sample conconcordance view on our "Illumina 100bp Paired End 30x Coverage" data set.

Variant Concordance - "illumina-100bp-pe-exome-30x"



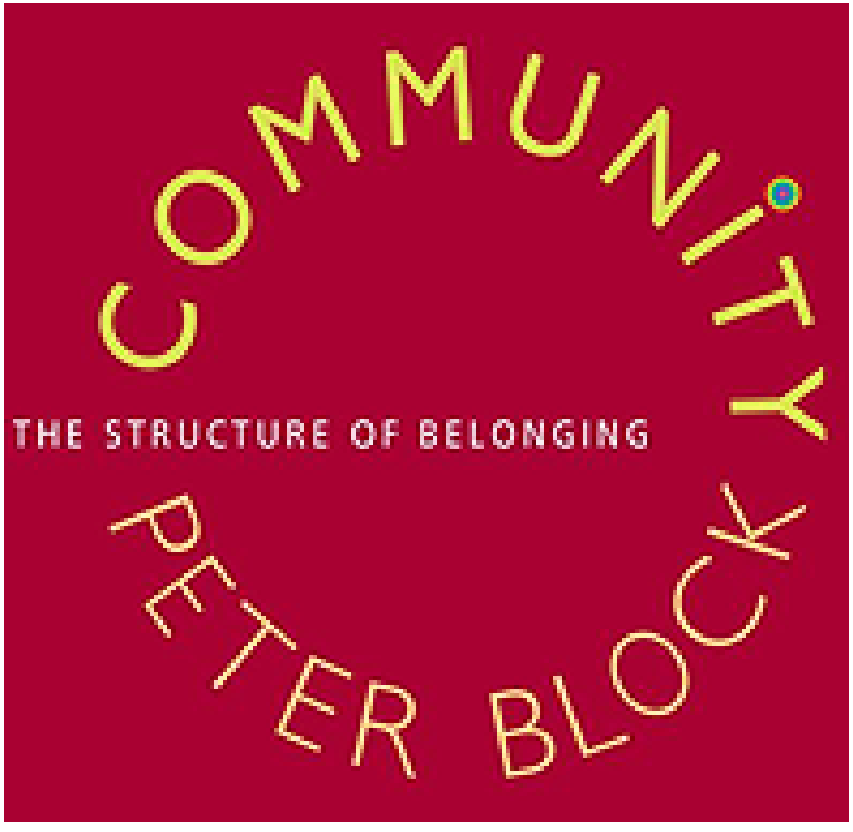
http://www.bioplanet.com/gcat

Scaling on full ecosystem of clusters

Platform LSF

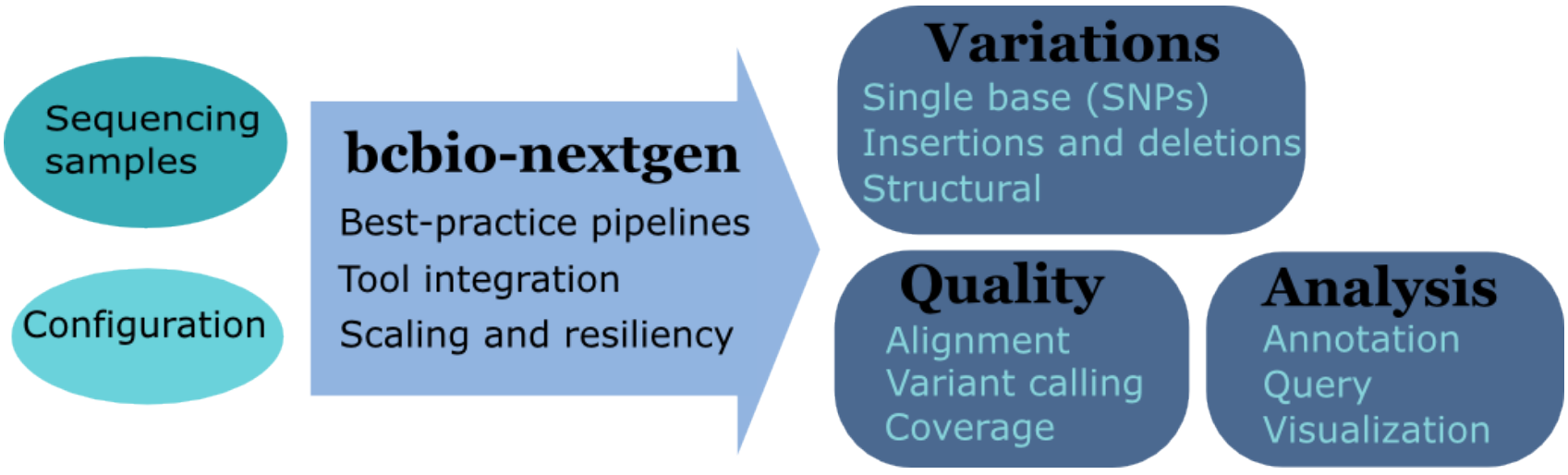
Torque

Solution



http://www.amazon.com/Community-Structure-Belonging-Peter-Block/dp/1605092770

Overview


Sequencing samples
Configuration
bcbio-nextgen
Best-practice pipelines
Tool integration
Scaling and resiliency
Variations
Single base (SNPs)
Insertions and deletions
Structural
Quality
Alignment
Variant calling
Coverage
Analysis
Annotation
Query
Visualization

Development goals

- Community developed
- Quantifiable
- Scalable

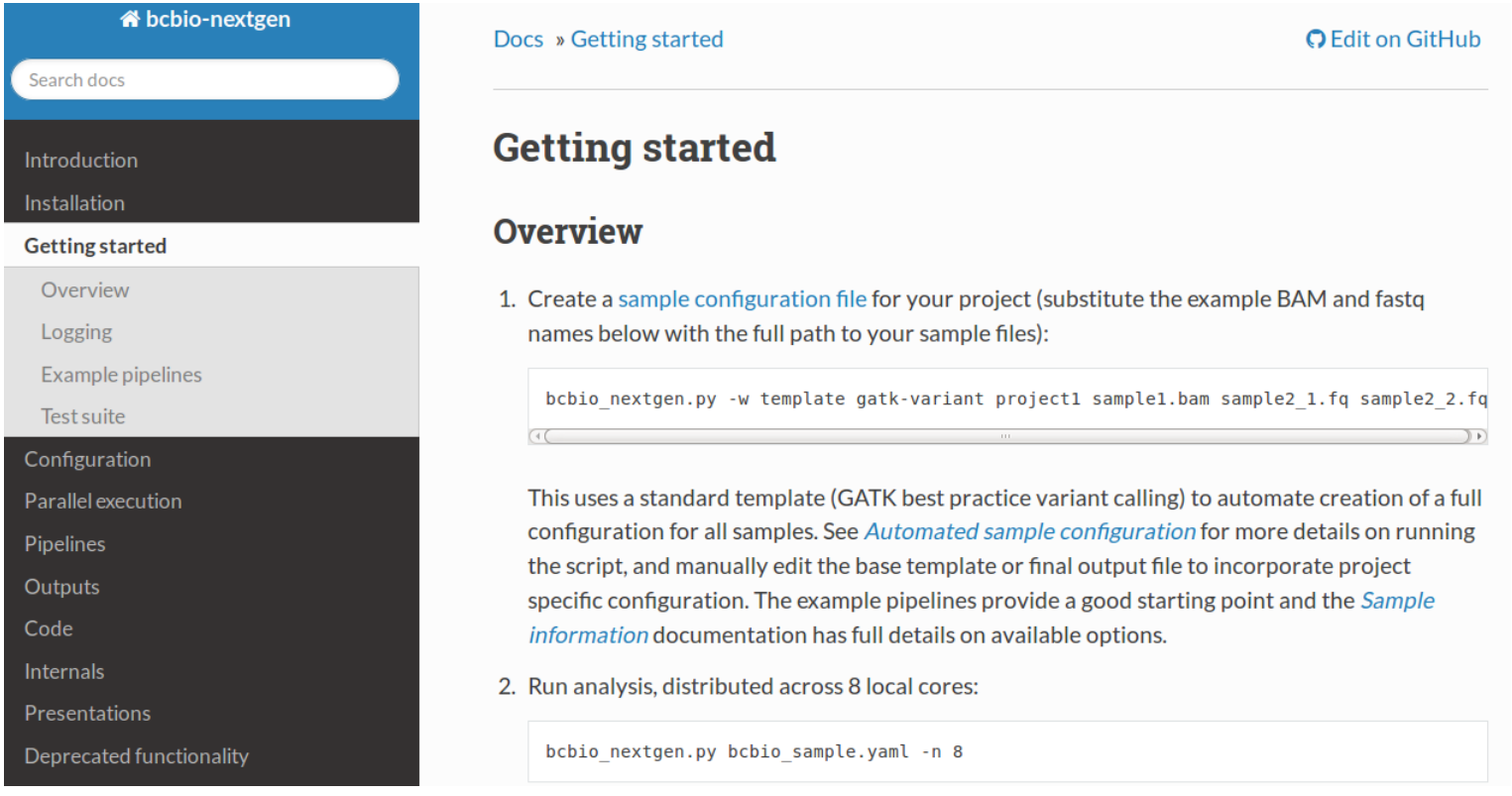
Community: installation

Automated Install

Bare machine to ready-to-run pipeline, tools and data

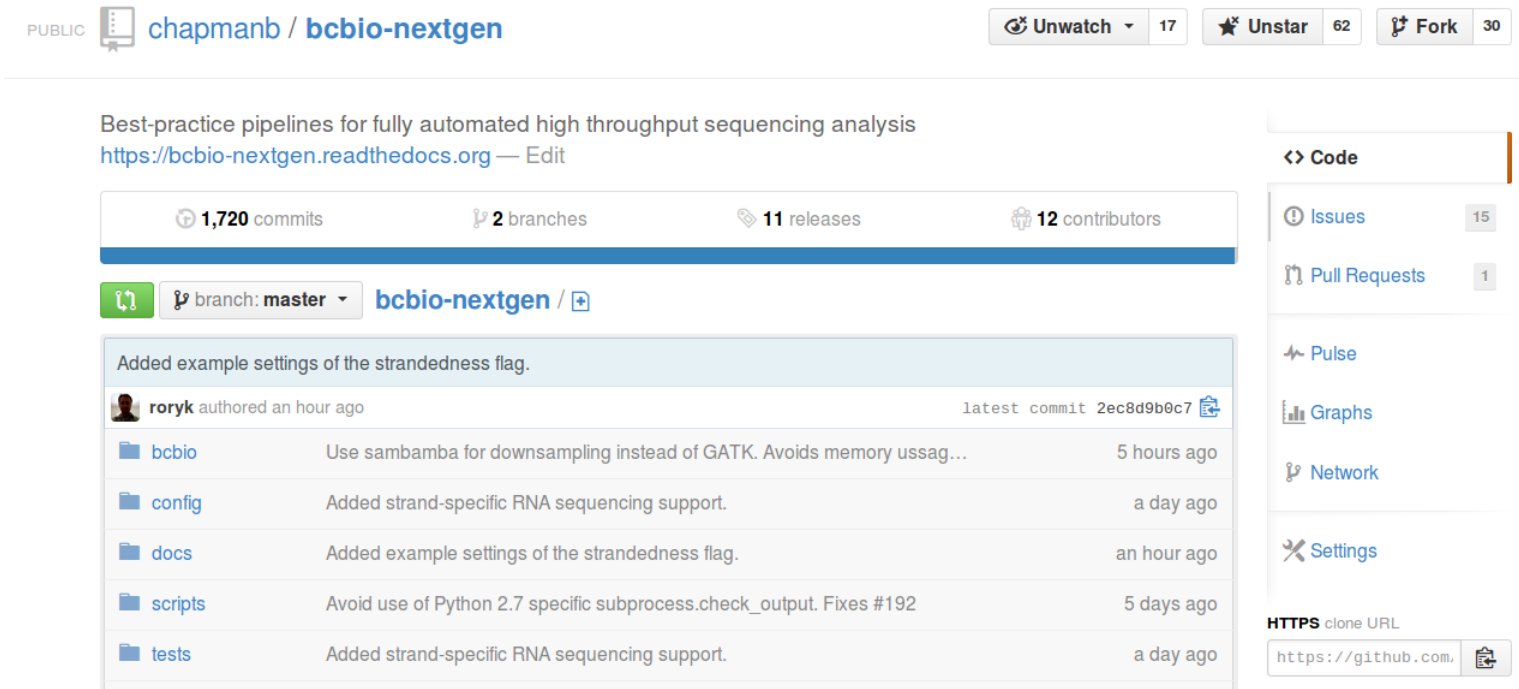
- CloudBioLinux: http://cloudbiolinux.org
- Homebrew: https://github.com/Homebrew/homebrew-science
- Conda: http://j.mp/py-conda

Community: documentation



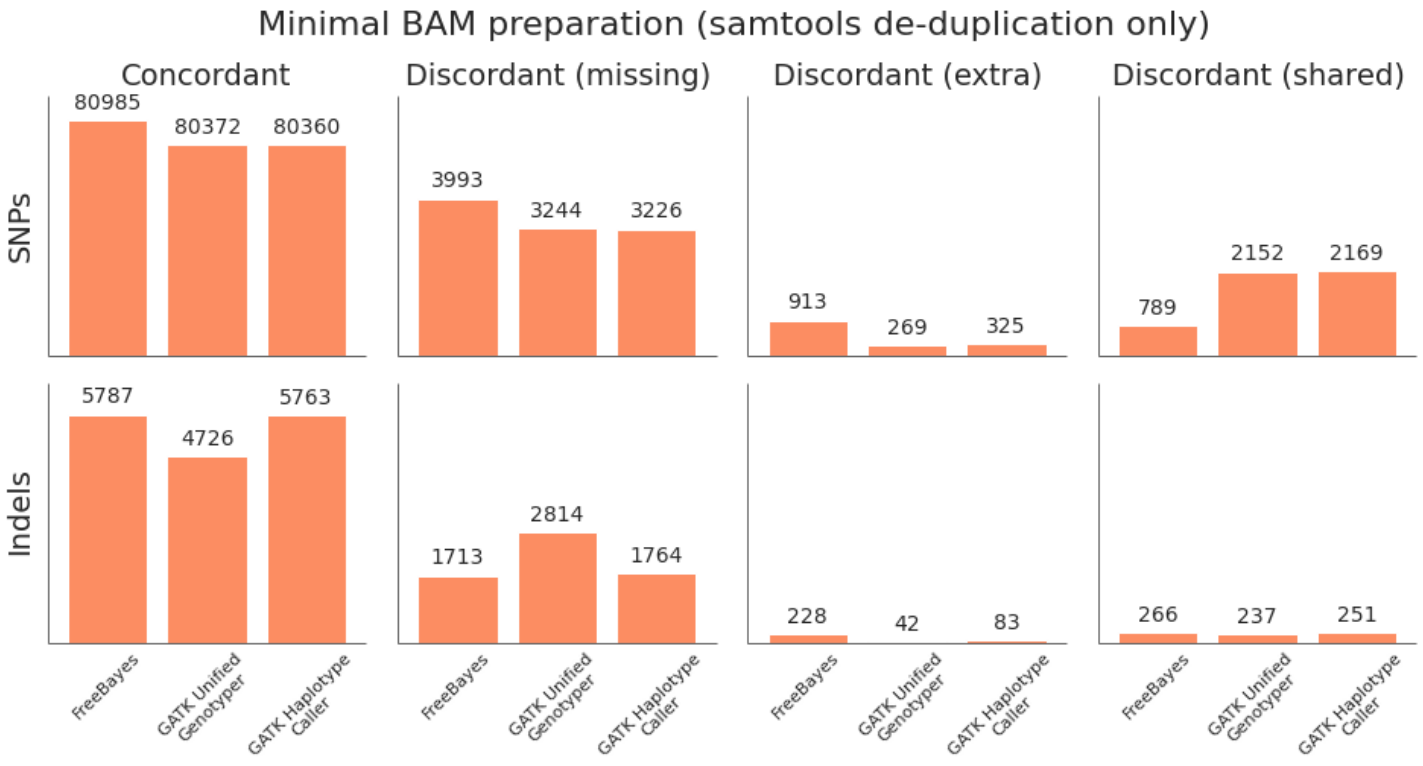
https://bcbio-nextgen.readthedocs.org

Community: contribution



https://github.com/chapmanb/bcbio-nextgen

Quantify quality

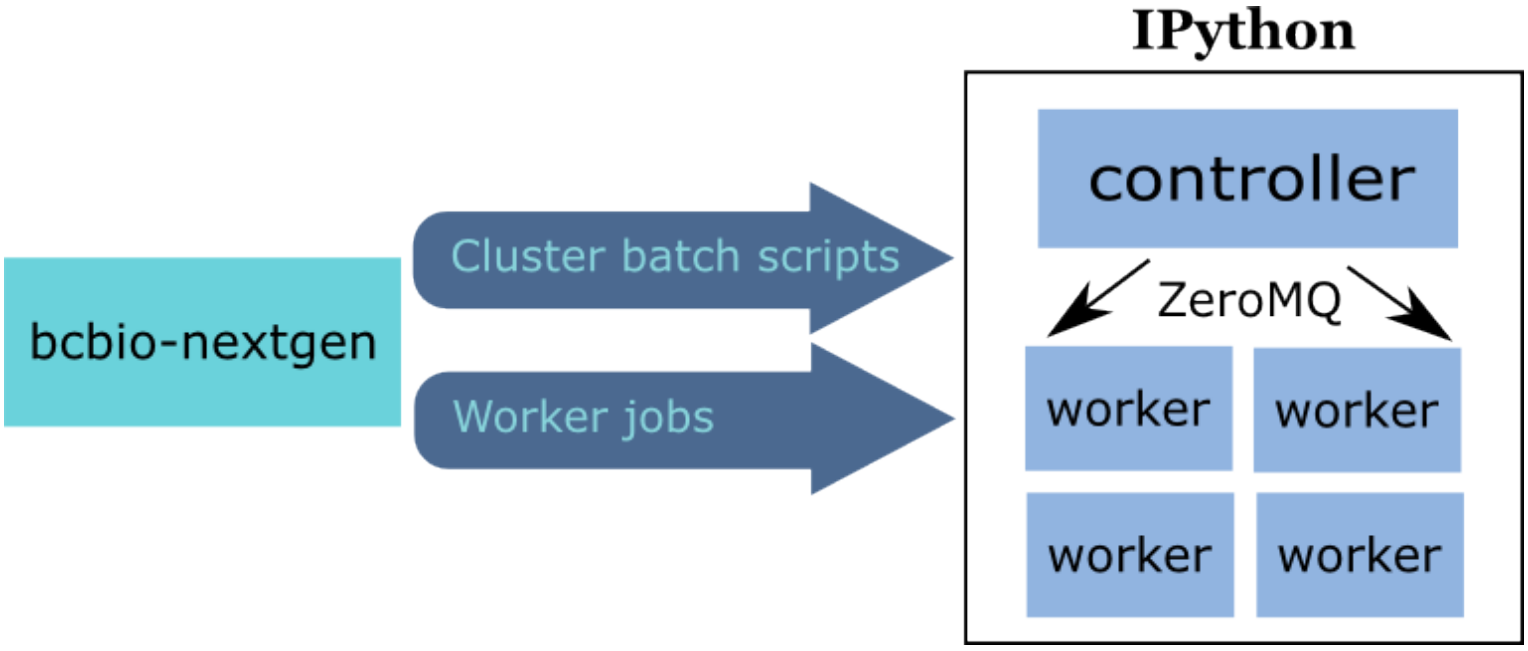


- Reference materials: http://www.genomeinabottle.org/
- Quantification details: http://j.mp/bcbioeval2

Validation

- Unit tests for implementation and methods
- Expand to:
  - Cancer tumor/normal
    http://j.mp/cancer-var-chal
  - Family/population calling
  - Structural variations

Scaling overview

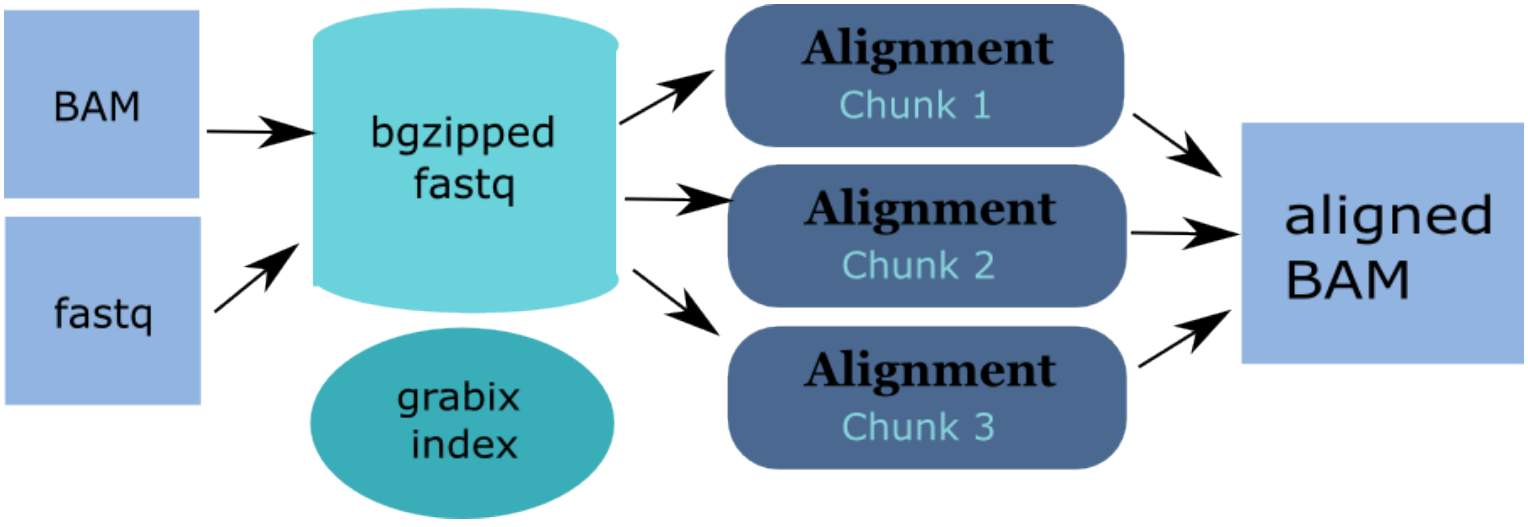


- Infrastructure details: `http://j.mp/bcbioscale`
- IPython: `http://ipython.org/ipython-doc/dev/parallel/index.html`

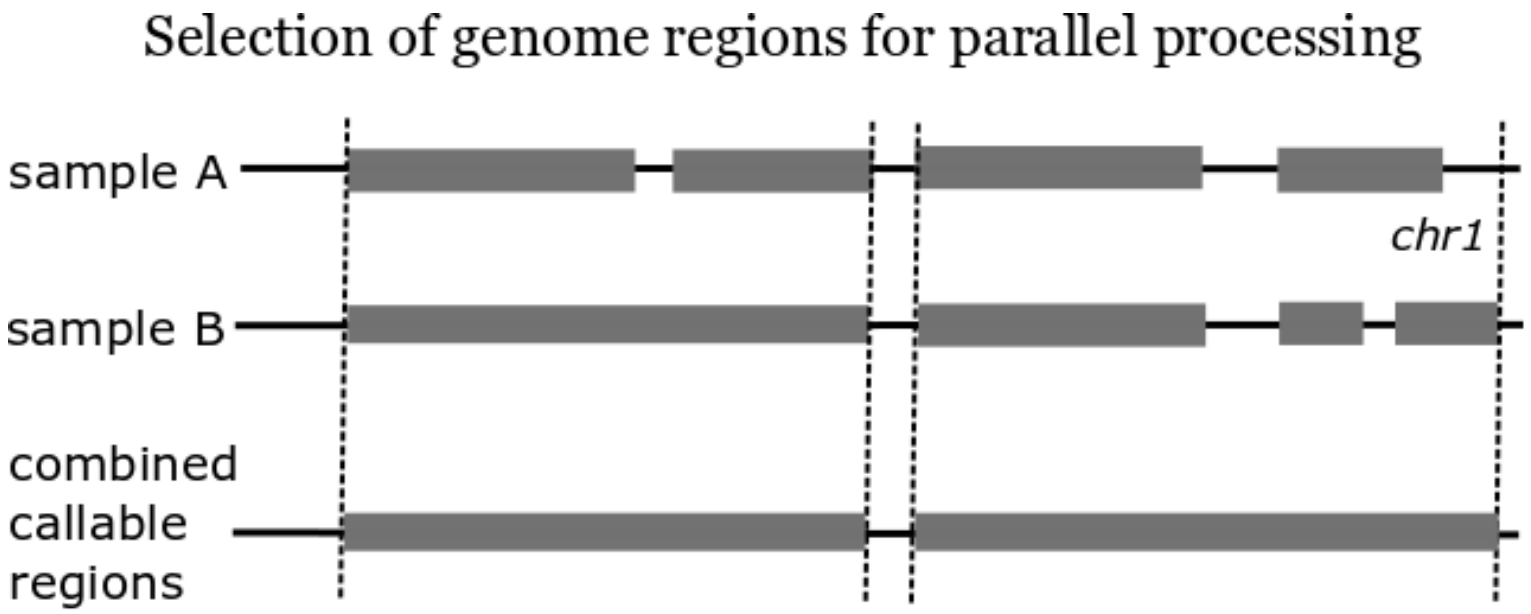
Current target environment

- Cluster scheduler
  - SLURM
  - Torque
  - SGE
  - LSF
- Shared filesystem
  - NFS
  - Lustre
- Local temporary disk
  - SSD

Alignment parallelization



Variant calling and BAM preparation parallelization



Multicore parallelization

BAM manipulation

Sambamba

https://github.com/lomereiter/sambamba

Prep analysis database (SQLite)

GEMINI

https://github.com/arq5x/gemini

Memory usage

Configuration

```
bwa:
  cmd: bwa
  cores: 16
samtools:
  cores: 16
  memory: 2G
gatk:
  jvm_opts: ["-Xms750m", "-Xmx2750m"]
```

Batch file

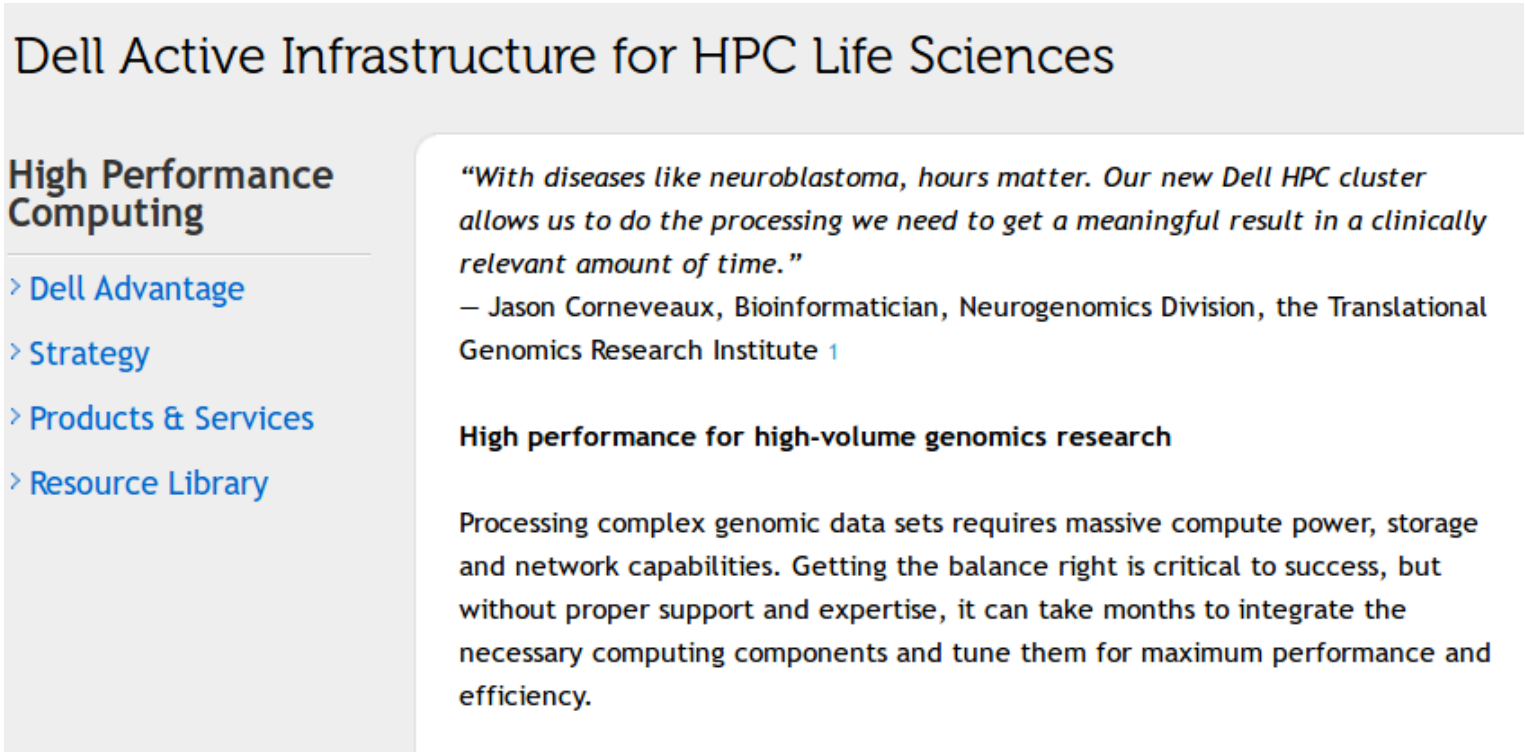
```
#PBS -l nodes=1:ppn=16
#PBS -l mem=45260mb
```

Filesystem IO

Pipes and streaming algorithms

```
("{bwa} mem -M -t {num_cores} -R '{rg_info}' -v 1 "
 "{ref_file} {fastq_file} {pair_file} "
 "| {samtools} view -b -S -u - "
 "| {samtools} sort -@ {num_cores} -m {max_mem} "
 "- {tx_out_prefix}")
```

Dell System



Dell Active Infrastructure for HPC Life Sciences

High Performance Computing

- Dell Advantage
- Strategy
- Products & Services
- Resource Library

"With diseases like neuroblastoma, hours matter. Our new Dell HPC cluster allows us to do the processing we need to get a meaningful result in a clinically relevant amount of time."
— Jason Corneveaux, Bioinformatician, Neurogenomics Division, the Translational Genomics Research Institute 1

High performance for high-volume genomics research

Processing complex genomic data sets requires massive compute power, storage and network capabilities. Getting the balance right is critical to success, but without proper support and expertise, it can take months to integrate the necessary computing components and tune them for maximum performance and efficiency.

Glen Otero, Will Cottay

http://dell.com/ai-hpc-lifesciences

Evaluation details

Samples

- 60 samples
- 30x whole genome
- Illumina
- Family-based calling

System

- 400 cores
- 3Gb RAM/core
- Lustre filesystem
- Infiniband network

Timing: Alignment

Step	Time	Processes
Alignment preparation	13 hours	BAM to fastq; bgzip; grabix index
Alignment	30 hours	bwa-mem alignment
BAM merge	7 hours	merge alignment parts
Alignment post-processing	9 hours	Calculate callable regions

Timing: Variant calling

Step	Time	Processes
Post-alignment BAM preparation	12 hours	De-duplication
Variant calling	23 hours	FreeBayes
Variant post-processing	2 hours	Combine variant files; annotate: GATK and snpEff

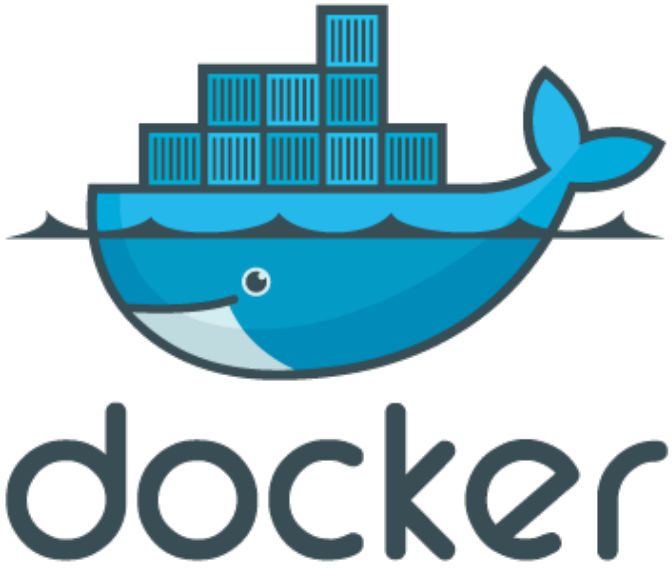
Timing: Analysis and QC

Step	Time	Processes
BAM merging	6 hours	Combine post-processed BAM file sections
GEMINI	3 hours	Create GEMINI SQLite database
Quality Control	5 hours	FastQC, alignment and variant statistics

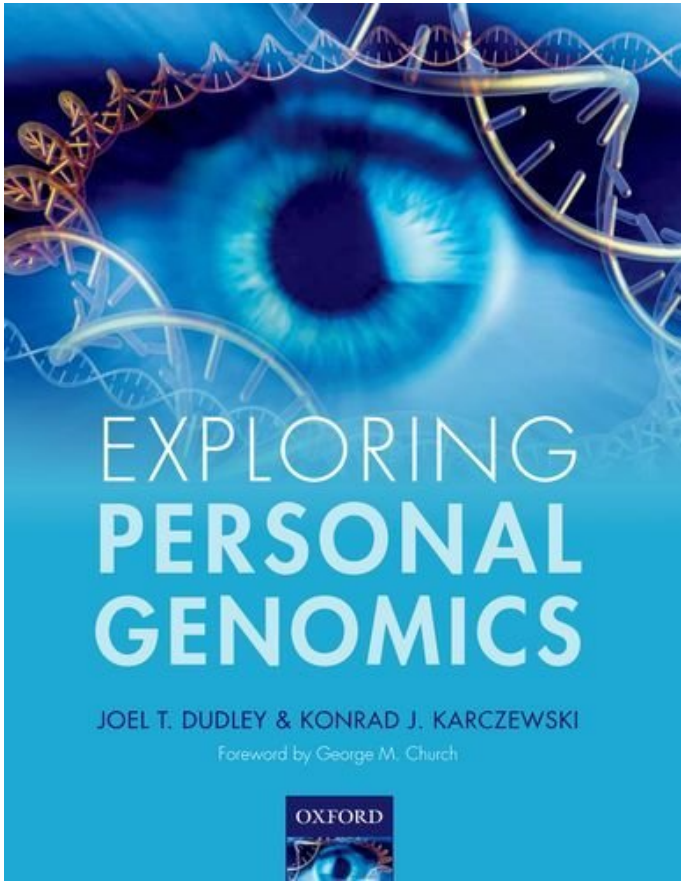
Timing: Overall

- 4 1/2 total days for 60 samples
- ~2 hours per sample at 400 cores
- In progress: optimize for single samples

Virtualization and reproducibility



Accessible



http://exploringpersonalgenomics.org/

Summary

- Community developed pipelines > challenges
- Focus
  - Assessing quality: good science
  - Community: easy to install and contribute
  - Scalability: finish in time
- Widely accessible

https://github.com/chapmanb/bcbio-nextgen

http://j.mp/bcbiolinks