Variant Calling Using GATK (Genome Analysis Toolkit)

Architecture of large projects in bioinformatics

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Presentation outline

1. Introduction
2. Definitions
3. Genome Analysis Toolkit
4. Variant Calling
   - HaplotypeCaller
5. Conclusion

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Introduction

- Massive data sets make developing analysis tools challenging.
- Many professionals are limited due to the complexity of accessing and manipulating NGS data.
- GATK optimizes for correctness, stability, CPU and memory efficiency, and supports distributed and shared memory parallelization.

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Definitions

- **Variant**: A variation in the DNA sequence compared to a reference genome.
- **Variant Calling**: The process of identifying and characterizing genetic variants from next-generation sequencing data.
- **SNP (Single Nucleotide Polymorphism)**: A variation at a single position in a DNA sequence among individuals, where each variation is present to some appreciable degree within a population.

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What is GATK?

- Open-source programming framework.
- Developed by the Broad Institute.
- Widely used in bioinformatics for variant discovery and genotyping.
- Provides a suite of tools for processing high-throughput sequencing data.

GATK technical details

GitHub repository at github.com/broadinstitute/gatk/.

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Requirements for running GATK:

- Java 17
- Python 2.6 or greater (frontend)
- Python 3.6.2, with additional Python packages (some tools and workflows)
- R 3.2.5 (plots in some tools)

All are found in prepared Docker images.

Licensing

License at project website and dockerhub repository:

- BSD 3-clause

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License at project repository:

- Apache 2.0

How is GATK Used?

- Identifying single nucleotide polymorphisms (SNPs)
- Detecting insertions and deletions (indels)
- Calling germline and somatic mutations
- Filtering variants based on quality metrics
- Somatic short variant calling
- Copy number (CNV) and structural variation (SV)
- Other tasks like processing and quality control

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Workflow

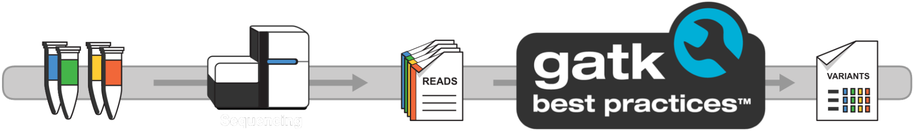

Figure: General workflow for finding variants.

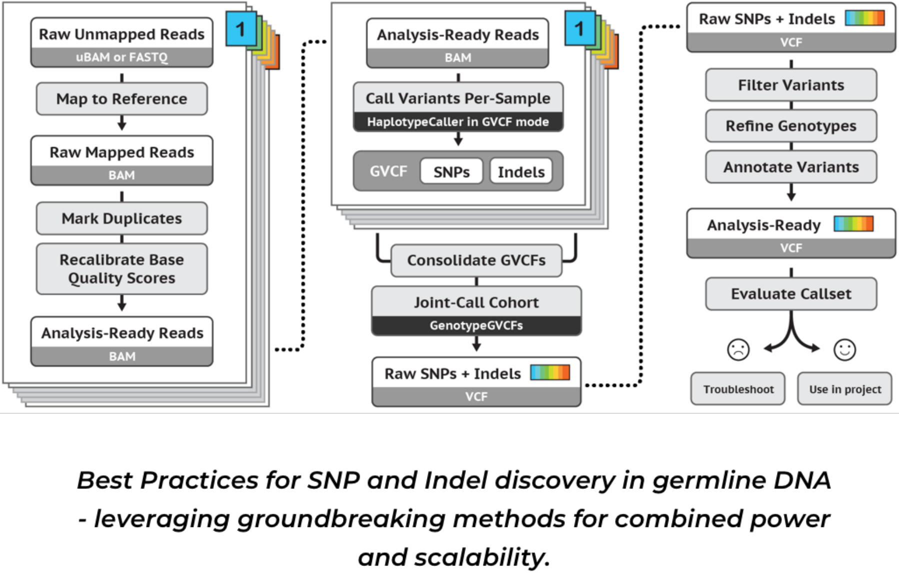

Figure: GATK Best Practices workflow.

HaplotypeCaller algorithm

1. **Define active regions.** Finds regions with the most variation.

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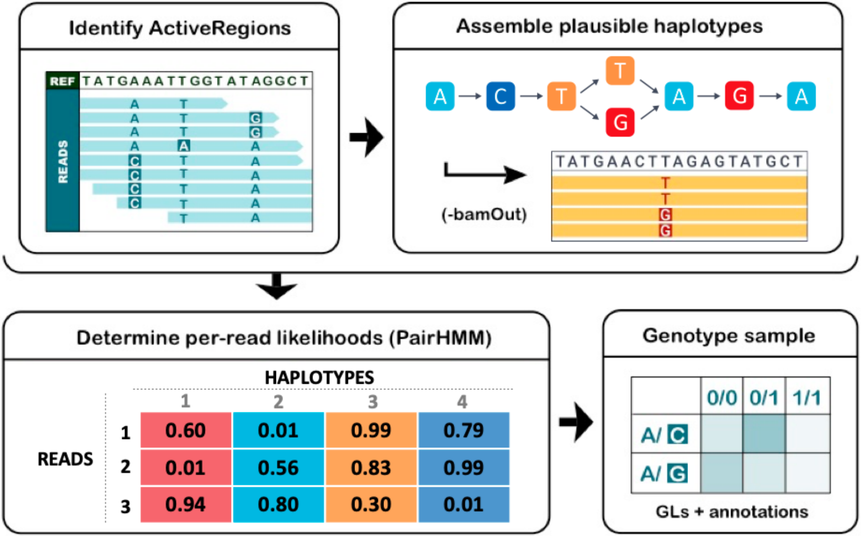
3. **Determine likelihoods of the haplotypes given the read data.** Computes how much evidence is there in the reads for each haplotype.
4. **Assign sample genotypes.** Computes likelihoods for each genotype.



		HAPLOTYPES			
		1	2	3	4
READS	1	0.60	0.01	0.99	0.79
	2	0.01	0.56	0.83	0.99
	3	0.94	0.80	0.30	0.01

	0/0	0/1	1/1
A/ C			
A/ G			

Figure: HaplotypeCaller workflow.

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Conclusion

GATK plays a crucial role in variant calling and genomic analysis. Its robust algorithms and tools enable accurate identification of genetic variants from next-generation sequencing data, facilitating various research and clinical applications.

GATK has been incorporated into large-scale sequencing projects like the 1000 Genomes Project and The Cancer Genome Atlas, highlighting its importance.

Thank you for your attention.

Sources

- https://gatk.broadinstitute.org/
- McKenna et al., The Genome Analysis Toolkit: a MapReduce framework for analyzing next-generation DNA sequencing data. Genome Res. 2010 Sep;20(9):1297-303. doi: 10.1101/gr.107524.110. Epub 2010 Jul 19. PMID: 20644199; PMCID: PMC2928508
- https://github.com/broadinstitute/gatk/