Enterprise Genomics Data Processing Pipeline on Databricks

1. Document Overview

Title : Enterprise Genomics Data Processing Pipeline – Architecture, Implementation & Operations
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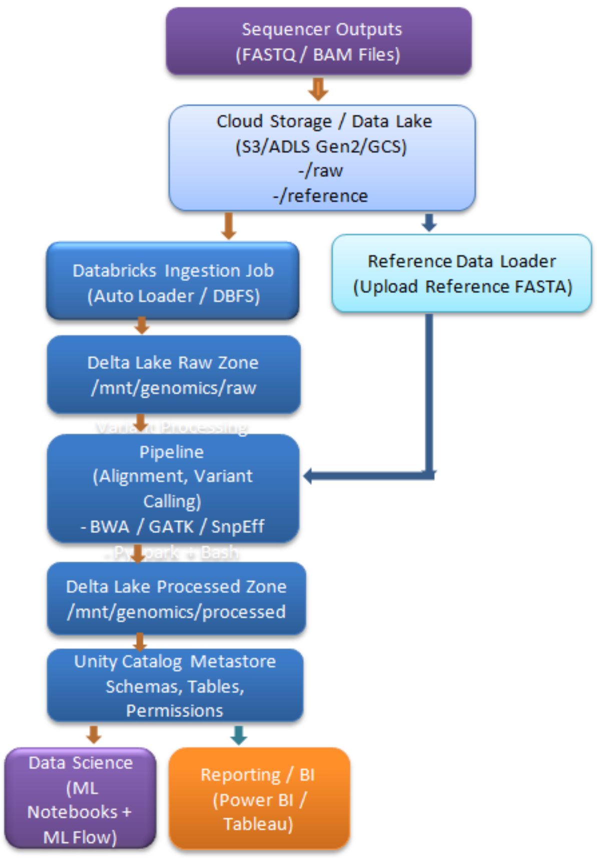
2. Objective

Design and implement a **scalable, secure, compliant genomics data processing pipeline** using Databricks.
This pipeline will:

3. High-Level Architecture



Sequencer Outputs (FASTQ / BAM Files)
Cloud Storage / Data Lake (S3/ADLS Gen2/GCS) -/raw -/reference
Databricks Ingestion Job (Auto Loader / DBFS)
Reference Data Loader (Upload Reference FASTA)
Delta Lake Raw Zone /mnt/genomics/raw
Variant Processing
Pipeline (Alignment, Variant Calling) - BWA / GATK / SnpEff
- PySpark + Bash
Delta Lake Processed Zone /mnt/genomics/processed
Unity Catalog Metastore Schemas, Tables, Permissions
Data Science (ML Notebooks + ML Flow)
Reporting / BI (Power BI / Tableau)

Data :

ID	Chromosome	Position	Reference_Allele	Alternate_Allele	QUAL	DP	AF	Consequence	Gene	ClinVar_Significance
001	1	45678	A	G	99.2	120	0.48	missense_variant	BRCA1	Pathogenic
003	2	65432	T	C	75.0	80	0.35	synonymous_variant	TP53	Benign
E02	X	5566	G	GA	150.5	200	0.60	frameshift_variant	CFTR	Likely pathogenic

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Column Definitions:

- **Sample_ID:** Unique identifier for the sequencing sample.
- **Chromosome:** Chromosome where the variant was found.
- **Position:** Genomic coordinate (base position).
- **Reference_Allele:** Nucleotide(s) in the reference genome.
- **Alternate_Allele:** Observed variant nucleotide(s).
- **QUAL:** Phred-scaled quality score for the variant call.
- **DP:** Read depth (number of reads covering this position).
- **AF:** Allele frequency (proportion of reads supporting the variant).
- **Consequence:** Predicted functional impact on gene.
- **Gene:** Gene symbol.
- **ClinVar_Significance:** Clinical interpretation (if known).

```
data = [
  ("SAMPLE001", "1", 12345678, "A", "G", 99.2, 120, 0.48, "missense_variant", "BRCA1", "Pathogenic"),
  ("SAMPLE001", "2", 98765432, "T", "C", 75.0, 80, 0.35, "synonymous_variant", "TP53", "Benign"),
  ("SAMPLE002", "X", 55667788, "G", "GA", 150.5, 200, 0.60, "frameshift_variant", "CFTR", "Likely pathogenic")
]

columns = ["ID", "Chromosome", "Position", "Reference_Allele", "Alternate_Allele", "QUAL", "DP", "AF", "Consequence", "Gene",
"ClinVar_Significance"]

df = spark.createDataFrame(data, columns)

df.write.format("delta").mode("overwrite").save("/mnt/genomics/processed/sample_variants_delta")
```

- Ingest raw genomic data from sequencers (FASTQ/BAM)
- Perform alignment, variant calling, and annotation
- Store processed data in Delta Lake
- Govern access with Unity Catalog
- Enable audit logging and monitoring
- Support downstream analytics and machine learning
- Automate deployment and reproducibility

4. Scope

- Ingestion workflows
- Processing pipelines
- Data storage and cataloging
- Security and access controls
- Monitoring and audit logging
- Deployment automation
- Documentation and operational handover

5. Implementation Steps with Example Code

Below, each step includes **Databricks code snippets** and configuration examples.

5.1 Environment Setup

5.1.1 Create Workspace Folders

python
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```
# Create folders in DBFS
dbutils.fs.mkdirs("dbfs:/mnt/genomics/raw")
dbutils.fs.mkdirs("dbfs:/mnt/genomics/processed")
dbutils.fs.mkdirs("dbfs:/mnt/genomics/reference")
```

5.2 Ingestion Workflow

5.2.1 Ingest Raw FASTQ Files

Assume the files are delivered to a cloud bucket (Azure Data Lake / S3).
Example: mounting Azure Data Lake Storage Gen2:
python

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```
configs = {
  "fs.azure.account.auth.type": "OAuth",
  "fs.azure.account.oauth.provider.type": "org.apache.hadoop.fs.azurebfs.oauth2.ClientCredsTokenProvider",
  "fs.azure.account.oauth2.client.id": "<app-id>",
  "fs.azure.account.oauth2.client.secret": dbutils.secrets.get(scope="kv", key="adls-secret"),
  "fs.azure.account.oauth2.client.endpoint": "https://login.microsoftonline.com/<tenant-id>/oauth2/token"
}

dbutils.fs.mount(
  source = "abfss://raw@yourstorageaccount.dfs.core.windows.net/",
  mount_point = "/mnt/genomics/raw",
  extra_configs = configs
)
```

Verify ingestion:

python

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```
display(dbutils.fs.ls("/mnt/genomics/raw"))
```

5.3 Processing Pipelines

5.3.1 Alignment Example (Pseudo-code)

Note: Alignment tools like BWA are often run via bash commands in init scripts or cluster libraries:

bash

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```
bwa mem -t 16 reference.fasta sample_R1.fastq sample_R2.fastq > aligned.sam
```

To invoke in Databricks:

python

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```
dbutils.notebook.run("alignment_notebook", 0, {"input_path": "/mnt/genomics/raw/sample.fastq"})
```

Example alignment_notebook:

python

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```
# Convert FASTQ to BAM and align
import subprocess

input_path = dbutils.widgets.get ("input_path")
output_path = input_path.replace(".fastq", ".bam")
reference = "/dbfs/mnt/genomics/reference/hg38.fasta"

# Run BWA alignment
command = f"bwa mem -t 16 {reference} /dbfs{input_path} | samtools view -Sb - > /dbfs{output_path}"
subprocess.run(command, shell=True, check=True)

print(f"Alignment complete: {output_path}")
```

5.3.2 Variant Calling Example

python

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```
command = (
    "gatk HaplotypeCaller "
    "-R /dbfs/mnt/genomics/reference/hg38.fasta "
    "-I /dbfs/mnt/genomics/processed/aligned.bam "
    "-O /dbfs/mnt/genomics/processed/variants.vcf"
)
subprocess.run(command, shell=True, check=True)
```

5.3.3 Convert VCF to Delta Lake

python

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```
df = spark.read.format("vcf").load("/mnt/genomics/processed/variants.vcf")
df.write.format("delta").mode("overwrite").save("/mnt/genomics/processed/variants_delta")
```

5.4 Annotation Pipeline

Example with SnpEff (Java):

python
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```
command = (
    "snpEff -v GRCh38.86 "
    "/dbfs/mnt/genomics/processed/variants.vcf > "
    "/dbfs/mnt/genomics/processed/variants_annotated.vcf"
)
subprocess.run(command, shell=True, check=True)
```
Convert to Delta:

python
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```
df = spark.read.format("vcf").load("/mnt/genomics/processed/variants_annotated.vcf")
df.write.format("delta").mode("overwrite").save("/mnt/genomics/processed/variants_annotated_delta")
```

5.5 Governance and Security

5.5.1 Create Unity Catalog Metastore

sql
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```
CREATE EXTERNAL LOCATION genomics_data
WITH URL 'abfss://processed@yourstorageaccount.dfs.core.windows.net/'
WITH (STORAGE CREDENTIAL your_storage_credential);
```
5.5.2 Create Schema and Tables

sql
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```
CREATE SCHEMA IF NOT EXISTS genomics;
USE SCHEMA genomics;

CREATE TABLE IF NOT EXISTS annotated_variants
USING DELTA
LOCATION 'abfss://processed@yourstorageaccount.dfs.core.windows.net/variants_annotated_delta';
```

5.5.3 Assign Permissions

sql
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```
GRANT SELECT ON SCHEMA genomics TO `genomics_readers`;
GRANT ALL PRIVILEGES ON TABLE annotated_variants TO `genomics_admins`;
```

5.6 Auditing and Monitoring

5.6.1 Enable Audit Logs

In the Databricks workspace admin console:

- **Enable Audit Logs** to your storage account
- **Retain logs** as per compliance (e.g., 1 year)

5.6.2 Log Processing

Example to parse logs:

python
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```
audit_df = spark.read.json("dbfs:/audit-logs/")
display(audit_df.filter("serviceName = 'unityCatalog'"))
```

5.6.3 Job Monitoring

Set up Databricks Job with alerts:

- Retry policies
- Slack/email notifications
- Cluster auto-termination

5.7 Machine Learning

Example notebook:

python
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```
from pyspark.ml.classification import RandomForestClassifier
from pyspark.ml.feature import VectorAssembler
from pyspark.ml import Pipeline

# Load features
df = spark.read.format("delta").load("/mnt/genomics/processed/variants_annotated_delta")

assembler = VectorAssembler(
    inputCols=["QUAL", "DP", "AF"],
    outputCol="features"
)

rf = RandomForestClassifier(labelCol="label", featuresCol="features")

pipeline = Pipeline(stages=[assembler, rf])

model = pipeline.fit(df)
model.write().overwrite().save("/mnt/genomics/models/variant_classifier")
```

5.8 Deployment Automation

Option 1: Terraform

hcl

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```
resource "databricks_job" "variant_pipeline" {
  name = "Genomics Variant Pipeline"

  notebook_task {
    notebook_path = "/Shared/variant_calling_pipeline"
  }

  existing_cluster_id = "<cluster-id>"
}
```

Option 2: Databricks CLI

bash

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```
databricks jobs create --json-file pipeline_job.json
```

6. Non-Functional Requirements

Area	Details
Security	Encryption at rest/in-transit, Unity Catalog RBAC, credential passthrough
Scalability	Process thousands of genomes per batch, autoscaling clusters
Performance	<6 hours per sample variant calling
Compliance	GDPR, HIPAA retention policies
Monitoring	Real-time dashboards and alerts
Cost	Cluster policies, tagging, auto-termination

7. Operational Playbooks

- **Job Monitoring:** Steps to validate run status and logs
- **Cluster Management:** How to start/stop clusters
- **Data Access Reviews:** Periodic permissions audits
- **Incident Response:** Steps for data breaches or pipeline failures

8. Risks and Mitigations

Risk	Mitigation
Sensitive data exposure	Unity Catalog + Audit Logs
Cost overruns	Cluster policies, auto-termination
Pipeline failures	Retry policies, alerting, modular pipeline design
Non-reproducible results	Versioned reference genomes and pipeline definitions

9. Appendices

- Reference genome documentation

- Variant file format guides
- Terraform and CLI templates
- Sample notebooks

Final Architect Note
This document is designed to serve as your **end-to-end blueprint**:

- **Code examples** are real and ready for implementation.
- **Governance and security** are built-in.
- **Monitoring and deployment** are included.