Genomics Deployments: Enabling Precision Medicine with IBM Spectrum Scale

Sandeep Patil
IBM STSM, Master Inventor

Acknowledgement

IBM

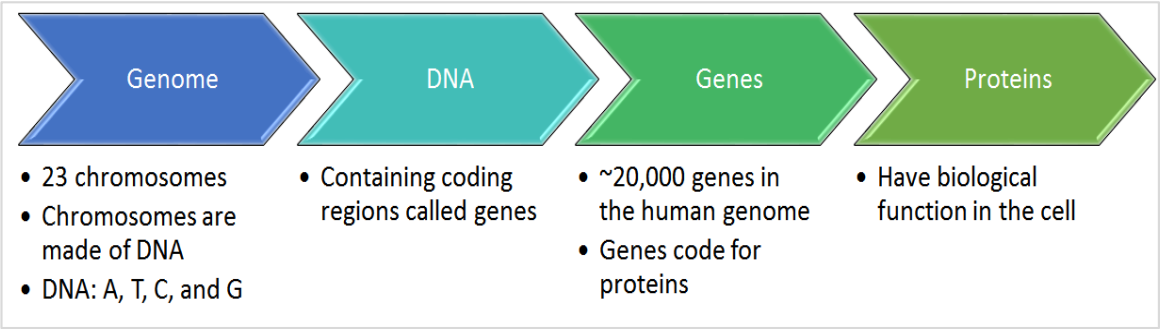
Frank N Lee, Ulf Troppens, Yael Shani, Carl Zetie, Kevin Gildea, Piyush Chaudhary, Theodore Hoover Jr, Kumaran Rajaram, Joanna Wong, Monica Lemay, Luis Bolinches

Agenda

- Genomic Introduction
  - What is Genomics
  - Genomics – An Emerging Market
- Understanding Genomic Sequencing Workloads
- Requirements on Infrastructure
- Solution Approach
- Solution Architecture
- Performance for GATK based on proposed solution

Genomics - Introduction

- Genomics is a branch of biotechnology focusing on genomes.
- Genomics involves applying the techniques of genetics and molecular biology to sequence, analyze or modify the DNA of an organism.
- It finds its use in a number of fields, such as, diagnostics, personalized healthcare, agricultural innovation, forensic science and others.

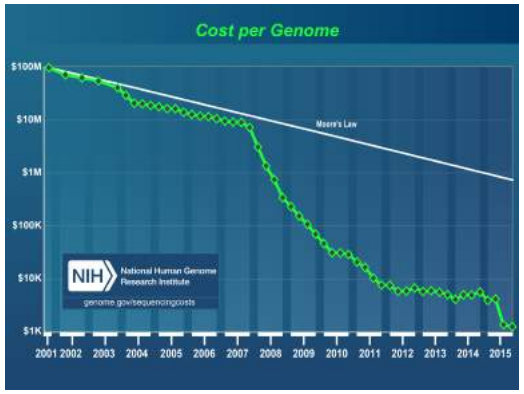


Frost & Sullivan: Global Precision Medicine Growth Opportunities, Forecast to 2025

Genomics – Path Towards Precision Medicine

Why Genomics is becoming more relevant ?

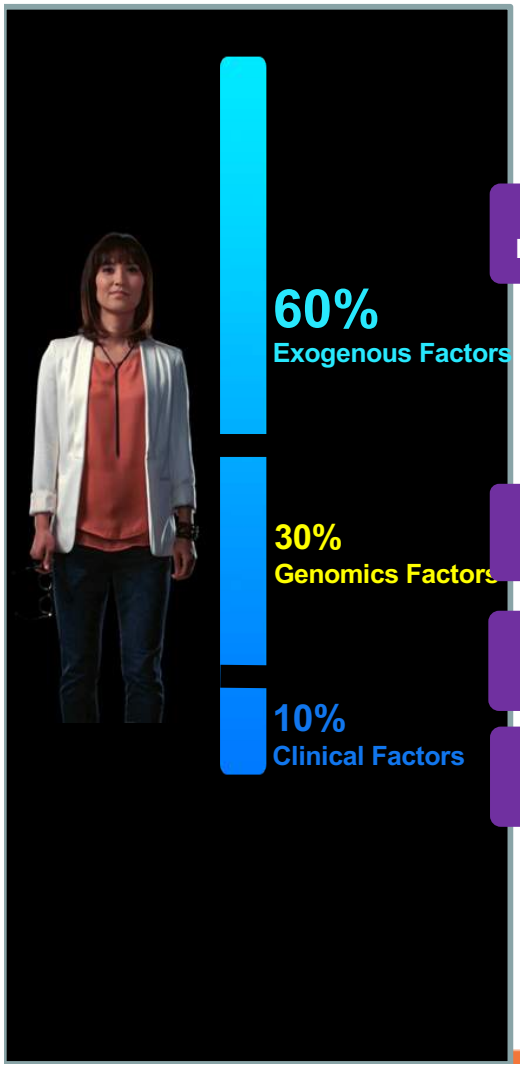
- **Feasibility:** Decreased cost of sequencing.
  - First sequencing of the whole human genome in 2003 cost roughly $2.7 billion
  - Today Genome sequence can cost around 1000 to 1500 USD
  - DNA sequencing players target to get it down to 100 USD
- **Value:**
  - Genomics is bringing in an era of proactive and personalized medicine (among other fields) – Potential of disruption.
- **Investment:**
  - The market for genomic products and services is growing at 10% and is predicted to become a $20 billion opportunity.
  - Growth in the Genomics market is majorly attributed to increasing government initiatives and increasing research.



https://www.genome.gov/27565109/the-cost-of-sequencing-a-human-genome/

MarketsandMarkets Report

Moon Shot: Building Cognitive Platform for HC/LS



Internet of Things
Real World Evidence

Genomics
Multi-omics

Medical Imaging

Clinical

What is the platform here for precision medicine?

FAST

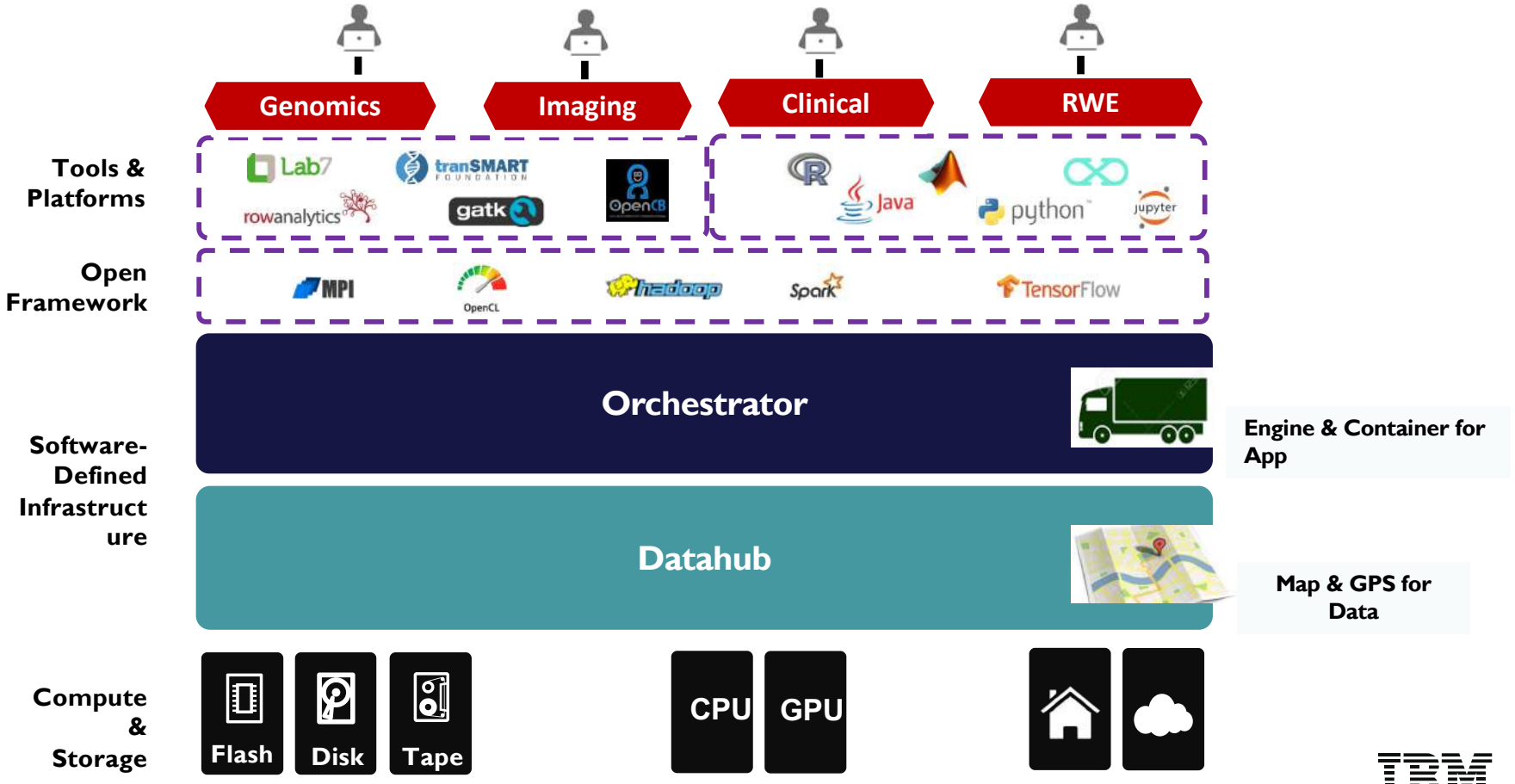
EASY

AFFORDABLE

COLLABORATIVE

IBM

Reference Architecture for the Foundation



For Data Hub Part: Questions for Storage Community

Questions that come in mind….

- **Customer:** Is there a reference architecture or approach.
- **Solution Architect :** How do I solutionize storage for Genomics … What is the workload requirements ?
- **Storage Developer**: what I developed meets the genomics requirement… What is the workload looks like ?
- **Storage Tester:** did my testing cover the requirements for genomic workload…What is the workload, what are the tools,

Questions for Storage Community (Cont.)

Answer to the Questions in mind :

Need to understand the Genomics Sequencing Workload from Storage Perspective !

Genomic Sequencing Workload– High Level

Key Characteristics of Genomic Workload

- Genomics requires a significant focus on big data management as the sequencing of the genome results in the production of a large amount of data.

- Genomic data analysis requires 3 process steps:
  1. Sequencers convert the physical sample to raw data. ‘
  2. Raw data is put in a sequence corresponding to the genome.
  3. Analytics (example: matching mutations with certain diseases), is then performed.

Requires easy to use and scalable IT Infrastructure for:
1) Owning, managing and accessing PBs of file storage
2) High throughput batch processing to analyze data.

Genomic Sequencing Workload to Storage Requirement Mapping

(based on GATK3 pipeline reference)

- ✓ Need to ingest millions of files (Small to medium size)
- ✓ Continuous guaranteed writes from multiple sequences
- ✓ Ingest protocol by sequencer systems is (SMB / NFS)

- ✓ CPU Intensive
- ✓ Pattern of writes followed by reads
- ✓ Predominantly sequential I/O
- ✓ Few large file access (GB file size)
- ✓ Access Protocols: POSIX/NFS

- ✓ Memory Intensive
- ✓ Write intensive and Write I/O is predominantly sequential I/O
- ✓ Read I/O is random access
- ✓ Few output files – MB to GB file size
- ✓ Access Protocols: POSIX/NFS

- ✓ CPU intensive
- ✓ Memory intensive
- ✓ Mix of sequential and random file access.
- ✓ Read and Write I/O to many files with varying file sizes (KB – GB) Access Protocols: POSIX/NFS

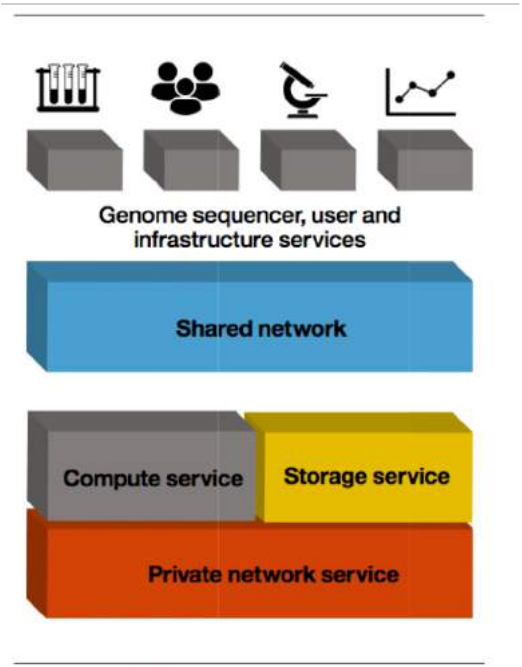
- ✓ Read Intensive
- ✓ Multi Region/Multi-Sites
- ✓ Authenticated and Secure
- ✓ Metadata Support
- ✓ Access Protocols: SMB/NFS/Object
- ✓ Faster access across WAN

Need for Optimal Solution.

- Need to think end to end which included Compute, Network and Storage as the key building blocks.
- The infrastructure (Compute, Network & Storage) should allow elasticity to scale-in / scale-out of the building blocks similar to “Lego” blocks.
- For Storage Building Block : Need for a high performance file storage with multiple access interfaces/protocols – Not a typical Network Attach Storage (NAS) as genomic sequencing workload is not a NAS workload but a **Technical Computing** workload.

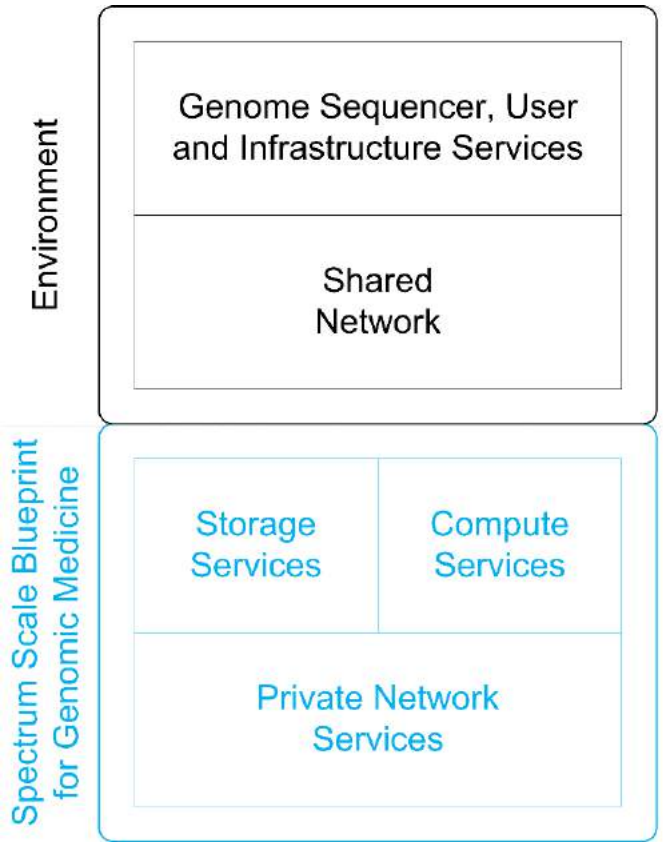
Need for Elasticity like ‘Lego’ Blocks … Choosing the Composable Infrastructure Principal

- Composable solutions are built in a way that disaggregates the underlying building blocks viz. compute, storage, and network services.
- These disaggregated services provide the required granularity allowing the infrastructure that can be sliced, diced, expanded and contracted at will and based on the actual need.
- It facilitates ease in deployment with well defined configuration and tuning templates per building block.
- Genomic workloads benefit from composable principals as one can grow and shrink the building blocks based on the needs.



Composable building block for genomics.

For Genomics – A Composable Building Block Approach



Shared Network

- **High-speed NFS , SMB , Object Data Access,** connected to shared campus network.
- **User Login** to submit and manage batch jobs and to access interactive applications.

Compute Services

- Scale-able **Compute Cluster** to analyze genomics data.

Storage Services

- Scale-able **Storage Cluster** to store, manage and access genomic data.

Private Network Services

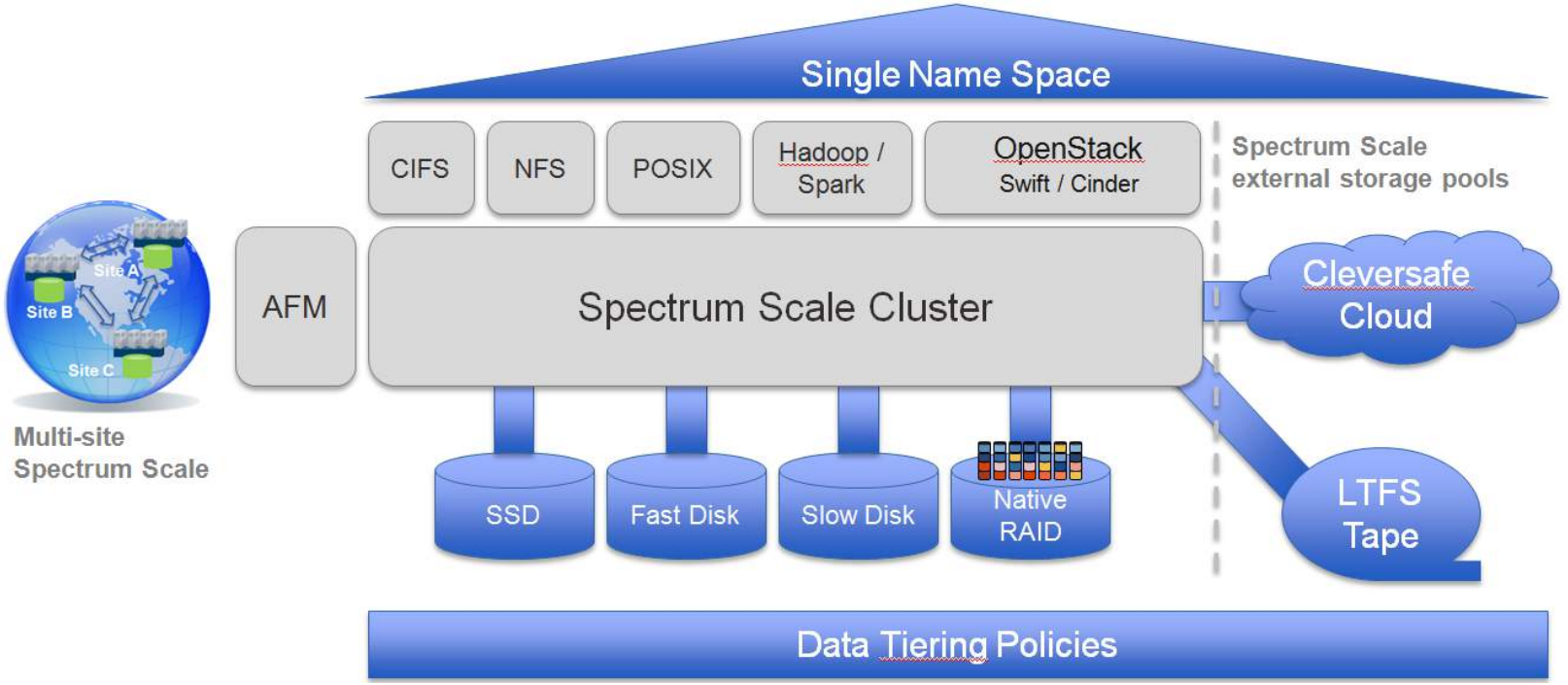
- **High-speed Data Network,** not connected to data center network.
- **Provisioning Network** and **Service Network** for administrative login and hardware services, optionally connected to shared campus network.

Storage Service: Need for High Performance File Storage aligning to Composable Infrastructure Principals

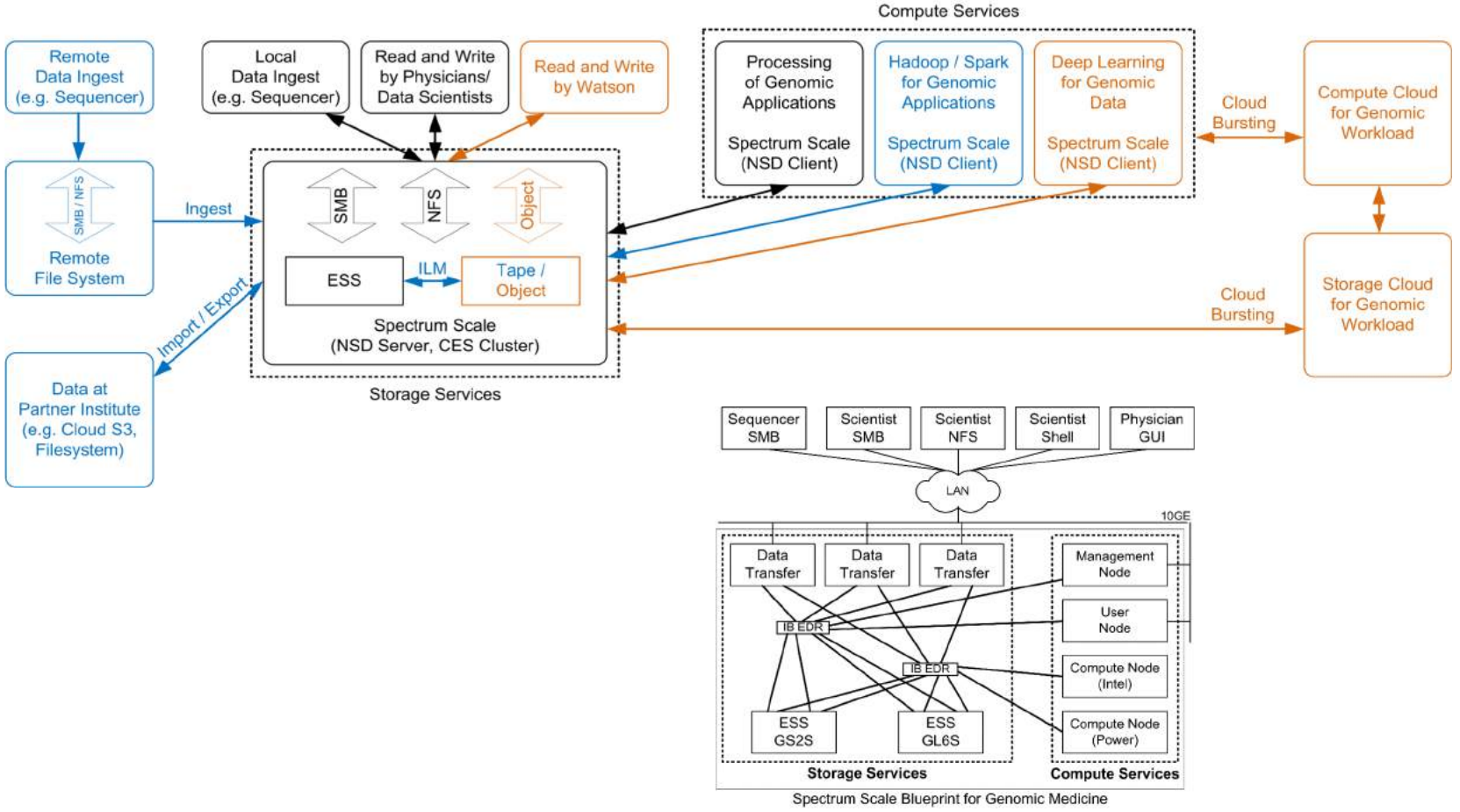
- **Key requirements per genomic sequencing workload**
  - High Performance & high throughput is key – Technical Computing workload , HPC-like , not a typical NAS workload.
  - Should support scale-in and scale-out to adhere to composable infra principals.
  - Ability to support different type of storage backend (need to be software defined)
  - Support global namespace across different stages of sequencing.
  - Multiprotocol support like NFS,SMB,HDFS,POSIX,Object for data ingestion, collaboration and computing the sequencing.
  - Easy ability for archive to low cost tier (like Tape), cloud integration.

Storage Solution: Taking the "Software Defined" approach and choosing a clustered filesystem that meets the above requirements

Choosing a High Performance Clustered Filesystem for Storage – IBM Spectrum Scale By Design is The Ideal Candidate !



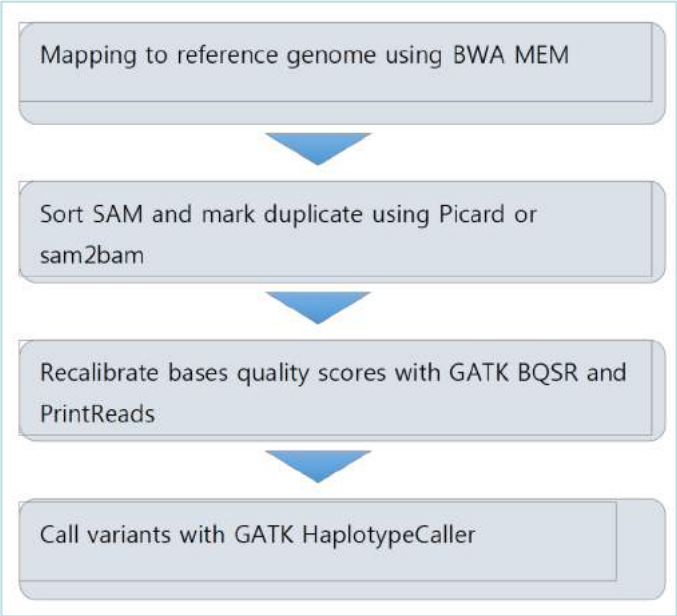
Solution Architecture: Putting it all together



Spectrum Scale Blueprint for Genomic Medicine

Accelerated Performance for Genomics Sequencing

GATK Workflow – Execution Time on Profiling Environment using the Proposed Solution Architecture for single sample



	Solexa WGS Broad dataset with b37 reference
BWA-Mem	303 min 47 sec
sam2bam (storage mode)	35 min 53 sec
GATK BaseRecalibrator (java setting -Xmn10g -Xms10g -Xmx10g)	87 min 21 sec
GATK PrintReads (java setting -Xmn10g -Xms10g -Xmx10g)	97 min 1 sec
GATK HaplotypeCaller (java setting -Xmn10g -Xms10g -Xmx10g)	261 min 37 sec
GATK mergeVCF (java setting -Xmn10g -Xms10g -Xmx10g)	0 min 51 sec

Profiling environment:

- 1x Power8 Node (IBM 8247-22L with SMT=8) with 256GB memory to execute whole workflow.
- 1x IBM ESS GS4 storage based on SSD (>= 23 GB/s write bandwidth and >= 30 GB/s read bandwidth)
- Dual rail FDR InfiniBand aggregating to ~13 GB/s

Note: Execution time was measured on the testbed configuration (detailed in profiling environment). The actual Genomics application performance will depend on testbed configuration, tunings, and other factors.

Spectrum Scale for Genomics - Collaterals

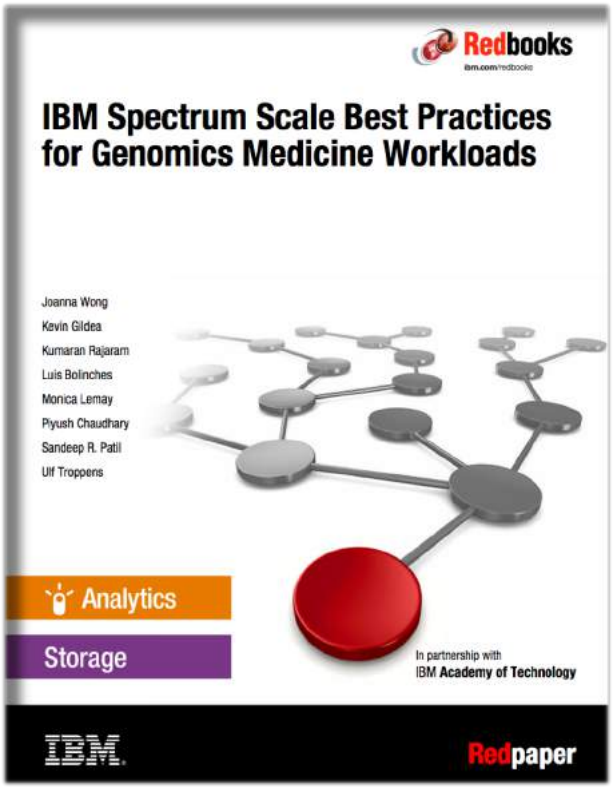
- **Solution Brief: Deeper, Faster insights with compostable building blocks based in IBM Spectrum Scale**
  - Gives a quick overview of the solution its advantages and references.
  - Download from: https://public.dhe.ibm.com/common/ssi/ecm/ts/en/tss03239usen/systems-hardware-system-storage-ts-solution-brief-tss03239usen-20180105.pdf

- **An IDC InfoBrief:** A Modular Approach to GENOMICS INFRASTRUCTURE at Scale in Healthcare and Life Sciences
  - Download from: https://www-01.ibm.com/common/ssi/cgi-bin/ssialias?htmlfid=37016937USEN

Blueprint : Best Practices Guide

- **Spectrum Scale Best Practices Guide for Genomics Medicine Workload**

1) Solution Overview
2) Best Practices for Compute Services
3) Best Practices for Storage Services
4) Best Practices for Private Network Services



Download from: https://www.redbooks.ibm.com/Redbooks.nsf/RedpieceAbstracts/redp5479.html?Open

References

- Genome Analysis Toolkit Variant Discovery in High-Throughput Sequencing Data. https://software.broadinstitute.org/gatk/
- IBM Redpaper: IBM Spectrum Scale Best Practices for Genomics Medicine Workloads: http://www.redbooks.ibm.com/abstracts/redp5479.html
- Performance optimization of Broad Institute GATK Best Practices on IBM reference architecture for healthcare and life sciences: https://www-01.ibm.com/common/ssi/cgi-bin/ssialias?htmlfid=TSW03540USEN
- IBM Reference Architecture for Genomics: Speed, Scale, Smarts: http://www.redbooks.ibm.com/abstracts/redp5210.html?Open

Thank You!

Workload profile for each GATK processing step for one sample

	BWA-Mem	sam2bam (storage mode)	GATK BaseRecalibrator	GATK PrintReads	GATK HaplotypeCaller	GATK mergeVCF
CPU	Intensive. Close to 100% CPU utilization	~93% (initial phase) and ~40% in later phases	~70% CPU utilization	~70% CPU utilization	~40% CPU utilization	Less than 1% CPU utilization
Memory	Low memory consumption	Higher memory consumption with ~223 GB consumed	Total of 18 x Java threads with each thread customized with 10 GB ➔ 180 GB	Total of 18 x Java threads with each thread customized with 10 GB ➔ 180 GB	Not memory intensive	Not memory intensive
File data I/O access pattern	Pattern of writes followed by reads, Predominantly sequential I/O.	Write I/O predominantly sequential I/O. Read I/O is random access in units of 512 KiB	Predominantly read intensive. Read is mix of sequential and random I/O	Mix of read and write. Write I/O is mostly 512 KiB with mix of sequential and random. Read is mostly sequential	Mix of read and write. Write I/O is mix of sequential and random. Read is mostly sequential	Mix of read and write. Read and write I/O is predominantly sequential I/O.
File I/O bandwidth	<= 200 MB/s (read and write)	Write < 2.5 GB/s. Sustained read < 300 MB/s. High degree of pagepool cache hits during reads (< 36 GB/s).	<= 100 MB/s (read and write)	Write < 150 MB/s and read < 75 MB/s.	Write < 100 MB/s and read < 100 MB/s.	Write < 1.5 GB/s and read < 2 GB/s.
File Metadata	<=2 inode updates	Initial phase <= 60 inode updates. Later phase, <=2 inode updates.	~24 file open and ~24 file closes.	~24 file open and ~24 file closes.	~20 file open and ~20 file closes.	~2 file open and ~2 file closes.
Output file(s)	Single output file (*.sam) <= 380 GB file size	Two output files. ~77 GB (.bam) and ~9 MB (.bam.bai).	Total of 52 files. 26 x ".table.log-4" files (<200 KB) and 26 x "*.table" files (< 300 KB)	Total of 78 files. 26 x "*.recal_reads*.bam" files (< 15 GB), 26 x "*.bai" files (< 750 KB), and 26 x "*.recal_reads*.bam.log" files (< 200 KB)	Total of 78 files. 26 x "*.raw_variants*.vcf" files (< 6 GB), 26 x "*.raw_variants*.vcf.log" files (< 400 KB), and 26 x "*.raw_variants*.vcf.idx" files (< 20 KB)	Single output file (*.raw_variants.vcf) with ~66 GiB file size

Source: IBM Redpaper: IBM Spectrum Scale Best Practices for Genomics Medicine Workloads: http://www.redbooks.ibm.com/abstracts/redp5479.html