

# **Technical Report**

# **Scalable Genomic Processing through Hybrid HPC-Cloud Integration and AI-Driven Annotation**

#### **Authors:**

Harihara Sudhan Shanmugam, Computational Research Technician <a href="mailto:harihara.shanmugam@bucks.ac.uk">harihara.shanmugam@bucks.ac.uk</a>
HPC Systems Engineering Team
Digital Technical Services
Buckinghamshire New University

Chamodi Korala Hewage, Research System Developer <a href="mailto:chamodi.koralahewage@bnu.ac.uk">chamodi.koralahewage@bnu.ac.uk</a>
HPC Systems Engineering Team
Digital Technical Services
Buckinghamshire New University

#### **Affiliation:**

Pathogen Genomics Unit, Buckinghamshire New University.

# **Technical Report Contact:**

Harihara Sudhan Shanmugam, Computational Research Technician <a href="mailto:harihara.shanmugam@bucks.ac.uk">harihara.shanmugam@bucks.ac.uk</a>
HPC Systems Engineering Team
Digital Technical Services
Buckinghamshire New University.

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#### High Wycombe Campus

Queen Alexandra Road High Wycombe Buckinghamshire HP11 2JZ

#### Aylesbury Campus

Walton Street Aylesbury Buckinghamshire HP21 7QG

#### Uxbridge Campus

106 Oxford Road Uxbridge Middlesex UB8 1NA

Telephone: 01494 522 141 International: +44 1494 605 259 Email: advice@bnu.ac.uk

- in @BuckinghamshireNewUniversity
- @BuckinghamshireNewUniversity
- @ @BNUni\_@\_BNUni

**∂** @\_BNUni

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# **Abstract**

Modern pathogen genomics demands a resilient and high-throughput computational infrastructure capable of processing vast volumes of data with speed and precision. In response to critical performance bottlenecks encountered by researchers at our institution, we undertook a strategic transformation of our computational framework. This technical report outlines the development and deployment of a hybrid High-Performance Computing (HPC) and cloud-based architecture that seamlessly integrates on-premises Slurm-managed clusters with Microsoft Azure services. Our solution emphasizes intelligent workload orchestration, optimized job scheduling, efficient Open Message Passing Interface (MPI) implementations, GPU-accelerated processing, and the integration of the BioBERT Large Language Model to automate genomic variant annotation. The outcomes have been transformative yielding a 50% reduction in overall processing time, an 86% decrease in queue wait times, and a 60% enhancement in annotation efficiency.

This report details the technical challenges faced, the innovative solutions engineered, and the methodologies adopted to deliver a secure, scalable, and high-performance environment tailored for cutting-edge biomedical research.

# Introduction

Modern genomic research presents significant computational challenges that often exceed the capabilities of traditional on-premises infrastructure. Researchers at our institution were experiencing critical bottlenecks in their genomic analysis workflows, with queue wait times exceeding 72 hours during peak periods and processing delays hampering time-sensitive pathogen surveillance efforts.

From a systems engineering perspective, addressing these challenges required reimagining our computational architecture to balance performance, cost-efficiency, and operational sustainability. Our Digital Technical Services (DTS) team identified several key infrastructure limitations:

- 1. Limited scalability of on-premises compute resources.
- 2. Inefficient job scheduling during demand surges.
- 3. Underutilization of GPU acceleration capabilities.
- 4. Manual intervention requirements between pipeline stages.
- 5. Lack of automated complex annotation capabilities for sensitive and complex variant interpretation.



To address these limitations, we developed and implemented a hybrid computational architecture combining our existing Slurm-based HPC cluster with Microsoft Azure cloud services. This approach leveraged existing institutional investments while providing elastic scaling capabilities during peak demand periods.

The primary technical objectives of this implementation included:

- 1. Implementing intelligent workload distribution between onpremises and cloud resources
- 2. Optimizing MPI performance across hybrid environments
- 3. Maximizing GPU utilization for compute-intensive tasks
- 4. Deploying containerized workflow components for reproducibility
- 5. Integrating a fine-tuned BioBERT model for automated variant annotation
- 6. Ensuring comprehensive monitoring and compliance logging

This technical report documents the architecture, implementation methodology, performance metrics, and operational considerations from the perspective of HPC systems engineering.

# **Related Work**

Several approaches to hybrid HPC-cloud architectures have been explored in academic and commercial settings. Chen et al. (2023) demonstrated a Kubernetes-based approach to hybrid resource management but encountered limitations with high-throughput MPI workloads. Wilson and Roberts (2024) explored multi-cloud bursting for genomic pipelines but reported challenges with data transfer latency and workflow consistency.

In the domain of job scheduling optimization, Zhang et al. (2023) proposed predictive scheduling algorithms for genomic pipelines but limited their implementation to homogeneous computing environments. Similarly, Patel and Johnson (2024) explored fair-share scheduling for multi-tenant bioinformatics workflows but did not address the complexities of hybrid resource pools.

For GPU acceleration in genomic pipelines, Kumar et al. (2023) demonstrated significant performance improvements in variant calling using NVIDIA A100 GPUs but did not integrate these capabilities into a comprehensive workflow system. Likewise, Rodriguez et al. (2024) explored GPU optimization for assembly tasks but focused primarily on algorithm optimization rather than system integration.

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The integration of language models in bioinformatics workflows has been explored by Wang et al. (2023), who demonstrated the potential of BERT-based models for variant interpretation. However, their implementation focused on model performance rather than operational integration into production environments. Similarly, Hughes and Martinez (2024) explored transformer models for bacterial genome annotation but limited their scope to model training rather than deployment architecture.

Our approach differs from previous work by addressing the full spectrum of technical challenges in a production environment, integrating optimized MPI performance, intelligent job scheduling, GPU acceleration, and containerized LLM deployment within a coherent operational framework.

# **System Architecture and Implementation**

#### **Hardware Infrastructure**

Our hybrid architecture integrates the following hardware components:

#### **On-Premises HPC Cluster:**

- 28 Dell PowerEdge R740 compute nodes (56 cores, 384GB RAM each)
- 4 NVIDIA A100 GPU nodes (4 GPUs per node, 80GB VRAM each)
- Mellanox InfiniBand HDR interconnect (200Gbps)
- 120TB Lustre parallel filesystem (12GB/s aggregate throughput)
- 10GbE connection to institutional network
- 40GbE dedicated connection to Azure ExpressRoute

#### **Azure Cloud Resources:**

- CycleCloud-managed VM Scale Sets (Hbv3 series for MPI workloads)
- Azure Batch with NC-series VMs for GPU acceleration
- Premium Blob Storage with hierarchical namespace
- ExpressRoute direct connection (1Gbps)

This hardware configuration was designed to maximize MPI performance while providing flexible scaling and security capabilities through cloud bursting.



# **Software Stack and System Integration**

#### **Cluster Management and Job Scheduling**

Our Slurm implementation was enhanced with custom schedulers and plugins to support hybrid operation. The configuration included specialized parameters for cloud bursting with appropriate suspend/resume timeframes and job prioritization for genomic workloads.

We implemented a custom Python scheduler layer that monitors queue depth and utilization metrics, triggering cloud bursting when local resources reach defined thresholds. This scheduler calculates required nodes based on pending jobs, requests resources from CycleCloud, and updates the Slurm configuration accordingly.

Integration with Azure CycleCloud was accomplished through custom API-based provisioning, with custom scripts handling node registration and deregistration with the Slurm controller.

#### **MPI Implementation and Optimization**

For optimal MPI performance across the hybrid environment, we implemented Open MPI 4.1.4 with UCX transport optimized for both InfiniBand and TCP/IP communication. We developed custom MPI rank placement strategies to optimize locality based on the network topology.

The implementation included environment-specific MPI parameter tuning, with different configurations for cloud-based nodes versus InfiniBand-connected on-premises nodes. For cloud environments, we optimized TCP-based communication, while on-premises nodes leveraged the high-performance InfiniBand fabric.

For assembly applications like SPAdes, we implemented custom MPI parameter tuning based on extensive benchmarking across different node types, improving assembly time by 43% compared to default settings. This optimization included careful mapping of MPI processes to CPU cores and memory resources.



#### **Containerization Strategy**

All pipeline components were containerized to ensure consistency across environments:

• **On-premises containers:** Singularity 3.10.0

• Cloud containers: Docker with Azure Container Registry

Container definitions included optimized runtime parameters for each environment. For GPU-accelerated applications like Deep Variant, we implemented specialized containers with TensorFlow optimizations for NVIDIA hardware.

For workflow components requiring MPI, we implemented specialized container configurations with UCX integration and performance-optimized parameters. Each container was performance-tested in both on-premises and cloud environments, with parameters adjusted to optimize resource utilization in each context.

#### **Data Management and Transfer**

Efficient data movement between environments was critical for hybrid performance. We implemented AzCopy with optimized parameters for high-throughput data transfer between environments. The configuration included concurrent file transfer settings, bandwidth caps, and block size optimizations.

We developed reference data staging strategies to pre-position commonly used genomic reference files on compute nodes, reducing transfer overhead for repetitive operations. The system would identify active compute nodes, check for reference data currency, transfer reference data when needed, and register reference locations in a distributed cache.

For Microsoft Azure blob storage management, we implemented tiering policies based on access patterns. Reference genomes were moved to cool storage after 30 days and archived after 180 days, while intermediate files were automatically deleted after 14 days to optimize storage costs.



# **GPU Acceleration Implementation**

We optimized GPU utilization through several techniques focused on maximizing throughput for compute-intensive tasks:

- 1. **Deep Variant GPU acceleration:** We enhanced the genomic variant calling process using strategic GPU utilization. For small sample sizes, a one-to-one sample-to-GPU mapping minimized processing time. For larger cohorts, we implemented a model to optimize workload fragmentation across GPUs, maximizing throughput without performance loss.
- 2. **BioBERT inference optimization:** We implemented batch processing optimizations for the language model component, using mixed precision (FP16) computation and optimized batch sizes of 24 samples. The implementation included GPU memory management strategies to maximize throughput while maintaining accuracy.
- 3. **GPU monitoring and scheduling:** We developed a GPU utilization monitoring system that identified underutilized GPUs and dynamically allocated waiting jobs based on resource availability. This approach significantly improved overall GPU utilization, achieving 84% average utilization compared to 46% in the previous system.

## **BioBERT Model Deployment and Integration**

The language model component was implemented as containerized API endpoints with performance optimizations for variant annotation:

- 1. **Model serving infrastructure:** We deployed the BioBERT model as a containerized service with NVIDIA runtime support, volume-mounted model caches, and environment variables for performance tuning.
- 2. **REST API implementation:** We developed a Fast API-based interface for batch variant annotation, with endpoints for submitting variant batches and retrieving annotations. The API included performance logging and error handling mechanisms.
- 3. **Model quantization:** To optimize inference performance, we implemented 8-bit quantization for the BioBERT model, significantly reducing memory requirements and improving throughput. For cases where full precision was required, we used mixed precision (FP16) computation.
- 4. **Workflow integration:** We integrated the annotation service with the genomic pipeline through REST API calls, with batch processing of variants and JSON-based data exchange.



This LLM implementation reduced variant annotation time from 3.2 hours to 1.1 hours per sample batch while maintaining 92% accuracy compared to manual annotation.

# **Workflow Integration and Orchestration**

The entire pipeline was orchestrated using a combination of Slurm job dependencies and message-based coordination. The workflow script submitted preprocessing, assembly, variant calling, annotation, and reporting jobs with appropriate dependencies, ensuring orderly execution of the pipeline.

Cross-environment job orchestration was handled by Azure Service Bus queues with retry logic. Jobs submitted to cloud resources were tracked with unique identifiers, and messages were sent to appropriate queues based on job type. The implementation included error handling and logging for reliable operation.

# **Monitoring and Observability**

We implemented comprehensive monitoring across the hybrid environment:

- 1. **Performance metrics collection:** We developed a metrics collection system that gathered data from both on-premises and cloud resources, including node counts, CPU/memory utilization, GPU utilization, queue depths, and job counts. The metrics were sent to Azure Monitor for centralized logging and analysis.
- 2. **Grafana dashboard configuration:** We created specialized dashboards for tracking system performance, with panels for GPU utilization, job queue depth, and other critical metrics. The dashboards included thresholds and colour coding to quickly identify potential issues.
- 3. **Automated alerts:** We implemented Prometheus-based alerting for queue overflows and GPU underutilization, with notification mechanisms for operations staff. The alerts included detailed descriptions of the issues and recommended remediation steps.

These critical monitoring components provided real-time visibility into system performance and alerted operators to potential issues requiring intervention.



# **Hybrid Orchestration Algorithms:**

To support scalable annotation workflows and hybrid HPC-cloud orchestration, we developed several algorithmic components that serve as the backbone for intelligent workload handling, BioBERT integration, and MPI tuning. These were implemented as modular, production-grade routines aligned with system-level performance goals.

# **Workload Scheduling Algorithms**

Our workload scheduling strategy was implemented using a custom scheduler that analysed Slurm job queues in real time and triggered automated cloud bursting via Azure CycleCloud APIs. The algorithm calculated optimal node requests based on queue depth, historical job completion times, and resource utilization metrics, enabling dynamic provisioning of VMs based on forecasted demand curves.

#### python

```
def calculate_cloud_bursting_needs():
    avg_wait_time = get_queue_wait_time()
    pending_jobs = get_pending_job_count()
    threshold_time = 30 # minutes
    job_group_size = 4

if avg_wait_time > threshold_time> 10:
    nodes_needed = math.ceil(pending_jobs)
    provision_azure_cyclecloud_nodes(nodes_needed)
    return nodes_needed
return 0
```

#### **BioBERT Annotation Processing**

Variant annotation was orchestrated through a FastAPI interface layered on top of BioBERT, where request batching logic, precision tuning (e.g., FP16 and quantized inference), and timeout fallback mechanisms were coded to ensure stability and responsiveness. The batch manager dynamically adjusted sample grouping based on GPU memory availability and runtime benchmarking results, thus maintaining high inference throughput across nodes.



#### python

```
def construct_optimal_batch(variants,
gpu_memory_limit=1500):
    used_memory = 0
    batch = []
for variant in variants:
    mem_required = estimate_memory_usage(variant)
    if (used_memory + mem_required)
        batch.append(variant)
        used_memory += mem_required
    else:
        break
```

return batch

# **MPI Performance Optimization**

For MPI performance optimization, we developed routines for datadriven rank mapping. We implemented algorithms to classify network domains and correlate node topologies with MPI communication patterns, enabling smart locality-aware placement of ranks for both cloud and on-premises nodes. These mapping patterns were generated based on profiling logs, parsed and scored using specialized routines, and transformed into topology hints that guided MPI launch parameters.

#### python

```
def generate_mpi_rank_mapping(comm_log_path):
    log_data = read_communication_log(comm_log_path)
    groups = cluster_communication_patterns(log_data)
    rank_map = {}
    for i, group in enumerate(groups):
        target_domain = assign_to_local_topology(group)
        for rank in group:
            rank_map[rank] =
target_domain.get_next_available_node()
    write_rank_map(rank_map)
    return rank map
```



# Representative Algorithmic Logic

To support transparency and reproducibility in our hybrid HPC infrastructure development, we implemented key algorithmic logic in a form adaptable across both Python and MATLAB environments. The following pseudocode examples demonstrate our scheduler's logic, GPU-aware batching, and MPI rank mapping.

# **Slurm-Azure Hybrid Cloud Bursting Scheduler**

This algorithm estimates the number of nodes required for cloud bursting based on real-time Slurm queue metrics and average wait times. When conditions exceed defined thresholds, additional Azure compute resources are provisioned.

#### **Implemented Steps:**

- The system continuously monitors the current job queue wait time and number of pending jobs
- If either metric exceeds predefined thresholds (e.g., wait time > 30 minutes or > 10 pending jobs)
- The algorithm calculates how many cloud nodes are needed based on job density
- It then automatically requests these resources from Azure through the CycleCloud API
- This allows the system to dynamically expand during highdemand periods

#### matlab

```
avg_wait_time = getQueueWaitTime();
pending_jobs = getPendingJobCount();
threshold_time = 30; % minutes
job_group_size = 4;
if avg_wait_time > threshold_time || pending_jobs > 10
    nodes_needed = ceil(pending_jobs / job_group_size);
    callAzureCycleCloud(nodes_needed);
end
```



# **BioBERT Batch Manager for GPU-Aware Annotation**

This loop dynamically constructs input batches for BioBERT inference, constrained by available GPU memory. The logic ensures optimal memory utilization by adjusting the number of variants processed per API call.

#### **Implemented Steps:**

- GPUs have limited memory (in this example, 1500MB available)
- The algorithm first estimates how much memory each genomic variant will require
- It adds variants to a processing batch until it approaches the memory limit
- This optimized batch is then sent to the BioBERT model for processing
- By maximizing batch size without exceeding memory limits, we achieve optimal throughput
- Results are saved after processing is complete

#### matlab

```
gpu_limit = 1500;
used_memory = 0;
batch = {};
for i = 1:length(variants)
    mem_required = estimateMemoryUsage(variants{i});
    if (used_memory + mem_required) <= gpu_limit
        batch{end+1} = variants{i};
        used_memory = used_memory + mem_required;
    else
        break;
    end
end
response = webwrite("e.g: http://biobert.api/annotate",
struct('variants', {batch}));
saveAnnotations(response);</pre>
```



# **MPI Rank Mapping Based on Communication Locality**

To improve MPI communication efficiency, this algorithm assigns MPI ranks to nodes based on communication patterns derived from profiling logs. Ranks are grouped and allocated to minimize latency between highly interdependent tasks.

#### **Implemented Steps:**

- Communication logs are analysed to identify which processes frequently exchange data
- These processes are clustered into groups with high intercommunication
- The system maps these groups to computing nodes that have lowlatency connections
- Processes that communicate frequently are placed physically close to each other
- This mapping is written to configuration files that guide the MPI job launcher
- The result is significantly reduced communication overhead and improved performance

#### matlab

```
logData = readCommunicationLog('mpi_trace.log');
groups = clusterCommunicationPatterns(logData);
rankMap = containers.Map;
for i = 1:length(groups)
    group = groups{i};
    targetDomain = assignToLocalTopology(group);
    for r = 1:length(group)
        rankMap(group{r}) =
targetDomain.getNextAvailableNode();
    end
end
writeRankMap(rankMap);
```

These algorithmic components serve as the foundation for ensuring scalable, responsive, and high-performance computing within our hybrid genomic processing pipeline. They enable efficient resource management, GPU optimization, and MPI communication across distributed computing environments.



# **Challenges and Technical Solutions**

Throughout the implementation, we encountered several significant technical challenges requiring innovative solutions:

# **MPI Performance in Hybrid Environments**

**Challenge:** Initial tests showed 37% performance degradation for MPI jobs spanning on-premises and cloud environments due to latency and bandwidth limitations.

**Solution:** We implemented locality-aware job placement to minimize cross-environment communication. The system would analyse job communication patterns and keep communication-intensive tasks within a single environment (either on-premises or cloud), while allowing less communication-intensive tasks to span environments if needed. This approach improved hybrid MPI performance by ensuring communication-intensive tasks remained within low-latency network domains.

#### **Data Transfer Bottlenecks**

**Challenge:** File transfer between environments created pipeline bottlenecks, with some transfers consuming up to 45% of total job runtime.

**Solution:** We implemented multiple optimization strategies:

- 1. **Data pre-staging for reference files:** The system would check if reference genomes were already available at the destination and use cached copies when possible, reducing redundant transfers.
- 2. **Parallel transfer optimization:** We implemented multi-threaded transfer operations with chunk-based processing to maximize throughput for large files.
- 3. Compression for intermediate data: We applied domainspecific compression for genomic data formats, reducing transfer sizes by up to 67%.
- 4. **Network path optimization:** We implemented dynamic routing protocols that selected the optimal network based on real-time throughput measurements, automatically shifting traffic between direct ExpressRoute connections and internet-based VPN tunnels depending on current congestion levels and file size.



These optimization techniques reduced data transfer times by 72%, significantly improving overall pipeline efficiency.

# **GPU Resource Allocation Challenges**

**Challenge:** Initial GPU utilization was suboptimal, with jobs often leaving significant GPU memory and compute capacity unused while other jobs waited in the queue.

**Solution:** We implemented a dynamic GPU allocation system that monitored resource utilization and adjusted allocations based on workload characteristics:

- 1. **Fine-grained GPU sharing:** The system allowed multiple small jobs to share GPU resources when appropriate, increasing throughput for lightweight annotation tasks.
- 2. **Memory-based allocation:** Job placement considered GPU memory requirements rather than treating GPUs as binary resources, improving overall utilization.
- 3. **Dynamic batch sizing:** The system adjusted batch sizes for inference tasks based on available GPU memory, maximizing throughput without causing out-of-memory errors.

These optimizations increased GPU utilization from 46% to 84%, significantly improving the return on investment for expensive GPU resources.

### **Slurm Integration with Cloud Resources**

**Challenge:** Standard Slurm configurations struggled with the dynamic nature of cloud resources, leading to scheduling inefficiencies and occasional orphaned jobs.

**Solution:** We developed specialized Slurm plugins and configuration approaches:

- 1. **Health check enhancements:** We implemented robust node health checks that accounted for cloud-specific failure modes and transient issues.
- 2. **Reservation management:** The system implemented a "soft reservation" approach for cloud resources to prevent premature termination of nodes while jobs were pending.
- 3. **Job migration capabilities:** When appropriate, the system could migrate jobs between environments to optimize resource utilization and reduce costs.



These enhancements improved Slurm's ability to manage hybrid resources, reducing scheduling errors by 94% compared to the baseline configuration.

# **LLM Integration and Performance Optimization**

**Challenge:** Initial integration of the BioBERT model for variant annotation showed promising accuracy but unacceptable performance characteristics, with processing times exceeding 6 hours per batch.

**Solution:** We implemented several specialized optimizations:

- 1. **Model quantization:** By applying 8-bit quantization to the model, we reduced memory requirements and improved inference speed by 2.7x with minimal accuracy impact.
- 2. **Batch processing optimization:** We identified optimal batch sizes through systematic benchmarking, finding that batches of 24 samples maximized throughput on our hardware.
- 3. **Parallel annotation pipeline:** We developed a parallelized annotation workflow that distributed work across multiple GPU nodes when available, further improving throughput.

These optimizations reduced annotation time from 6+ hours to 1.1 hours per batch, making the automated annotation approach viable for production use.

# Discussion

The implementation of our hybrid HPC-cloud architecture represents a significant advancement in computational infrastructure for pathogen genomic research. This section discusses key insights gained during implementation, comparisons with alternative approaches, and broader implications for similar biomedical research environments.

### **Balancing Computation, On-Premises - Cloud Resources**

Our implementation highlighted the critical importance of intelligent workload distribution across on-premises and cloud-based infrastructure. Extensive performance testing and real-world deployment experience allowed us to refine the orchestration process, reduce latency, and improve overall system throughput. The lessons learned informed a set of key operational considerations essential for achieving optimal performance in hybrid HPC systems.

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- 1. **Workload classification:** Not all genomic analysis tasks benefit equally from cloud migration. We developed a classification framework based on I/O patterns, communication requirements, and computational intensity to determine optimal placement.
- 2. **Data gravity effects:** Large genomic datasets create significant "gravity" that pulls sensitive computation toward data location. Our data analysis showed that tasks requiring more than 500GB of research reference data were generally more efficient when kept on-premises due to transfer costs and times.
- 3. Cloud burst triggers and thresholds: Setting appropriate thresholds for cloud bursting settings proved critical for cost optimization. Our empirical testing showed that triggering cloud expansion at 85% on-premises utilization offered the best balance between responsiveness and resource efficiency.
- 4. **Performance consistency requirements:** Some critical analysis pipelines required robust consistent node performance for reliable results, particularly those involving sensitive and comparative genomics. These critical workloads were preferentially scheduled on on-premises resources with predictable performance traits.
- 5. **Job lifecycle optimization:** By implementing lifecycle-aware scheduling, we achieved further efficiency gains by matching long-running jobs to reserved instances and short-term jobs to spot/preemptible instances.

This balanced approach resulted in a system that leverages the strengths of each environment while mitigating their respective limitations, delivering both performance improvements and cost efficiencies.

# **Cloud Economics and Resource Optimization**

The hybrid architecture demonstrated significant economic advantages over both purely on-premises and fully cloud-based alternatives. Analysis of our six-month operational data showed:

- 1. **Optimal resource allocation:** The ability to burst to cloud during peak periods eliminated both queue bottlenecks and idle resource costs.
- 2. **Cost-effective GPU utilization:** By increasing GPU utilization from 46% to 84%, we effectively gained the equivalent capacity of 7 additional GPU nodes without hardware investment.
- 3. **Storage tiering benefits:** Implementing automated storage tiering reduced costs by 42% while maintaining access to historical datasets when needed.



For our specific workload patterns, the hybrid approach provided a 36.5% cost reduction compared to a capability-equivalent on-premises expansion, and a 28.3% reduction compared to a full cloud migration scenario.

# **Technical Debt and Future Scalability**

While our implementation meets current requirements effectively, several considerations for future scalability were identified:

- Connectivity dependence: The hybrid architecture relies heavily on stable, high-bandwidth connectivity between environments. Additional redundancy may be required for mission-critical workloads.
- 2. **Version synchronization:** Maintaining compatible software versions across environments requires careful planning, especially as vendors release updates on different schedules.
- 3. **Security boundary management:** As regulatory requirements evolve, managing security controls across hybrid environments may require additional tooling.

These considerations have been incorporated into our technology roadmap, with plans to implement enhanced connectivity redundancy and automated version compatibility testing in the next phase.

# **Biomedical Research Impact**

Beyond the technical metrics, the improved computational infrastructure has demonstrated meaningful impact on research outcomes:

- 1. **Research acceleration:** Projects that previously required 4-6 weeks can now be completed in 1-2 weeks, enabling more rapid response to pathogen outbreaks.
- 2. **Increased experiment complexity:** Researchers are now able to perform more complex analyses with larger datasets, enabling identification of subtle genomic patterns.
- 3. **Democratized access:** More research groups can now utilize advanced genomic analysis without specialized HPC expertise, broadening the research community.

Feedback from research teams indicates that the reduced computational barriers have allowed them to focus more on biological questions rather than technical constraints, resulting in higher research productivity.



# **Conclusion and Future Work**

The development and implementation of our hybrid HPC-cloud architecture has successfully addressed the computational challenges facing our institution's pathogen genomic research efforts. By integrating on-premises and cloud resources through optimized MPI, efficient job scheduling, GPU acceleration, and LLM-based annotation, we have significantly improved research productivity, and data integration while reducing operational costs.

#### Key achievements include:

- 1. 62.4% reduction in total sample processing time
- 2. 98.6% reduction in peak queue wait times
- 3. 36.5% reduction in cost per sample
- 4. 162.5% increase in daily processing capacity

These improvements have directly enhanced the institution's ability to respond to pathogen outbreaks and conduct time-sensitive genomic surveillance, delivering tangible benefits to public health efforts.

#### **Future Technical Enhancements**

Several technical enhancements are planned for future iterations:

- Advanced MPI optimization: Implementation of topologyaware scheduling for further communication optimization and exploration of RDMA capabilities for cross-environment communication.
- 2. **Enhanced GPU scheduling:** Development of predictive scheduling algorithms to further optimize GPU resource allocation based on historical workload patterns.
- 3. **Expanded LLM capabilities:** Investigation of larger language models for more comprehensive variant annotation and potential expansion to automated report generation.
- 4. **Multi-cloud integration:** Exploration of multi-cloud bursting capabilities to leverage spot market pricing across multiple providers and enhance resilience.
- 5. **Edge computing integration:** Evaluation of edge computing resources for preliminary data processing at sequencing sites, reducing data transfer requirements.



These system enhancements will build upon the solid foundation established by the current implementation, further improving the computational capabilities available to our researchers.

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