SCAN: A Smart Application Platform for Empowering Parallelizations of Big Genomic Data Analysis in Clouds

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***Abstract*—Cloud computing is often adopted to process big data for genome analysis due to its elasticity and pay-as-you-go features. In this paper, we present SCAN, a smart application platform to facilitate parallelization of big genome analysis in clouds. With a knowledge base and an intelligent application scheduler, the SCAN enables better understanding of bio-applications' characteristics, and helps to orchestrate huge, heterogeneous tasks efficiently and cost-effectively. We conducted a simulation study and found that the SCAN platform is able to improve the performance of genome analysis and reduce its cost in a wide variety of circumstances.**

***Keywords*-genome analysis; application platform; cloud computing; parallelization**

I. Introduction

Cancer is a disease of the genome. Systematic studies of the cancer genome can provide us with a global view of the molecular architecture of complex traits, which is useful for the identification of genes, pathways, and cell signal networks that may dictate tumour clinical behaviour and treatment response [1]–[3]. Because cancer cells have a large variety of relatively rare mutations, a computational challenge arises to process hundreds of millions of short DNA sequences (corresponding to billions of DNA nucleotides) in a cost-effective way.

Today cloud computing is often employed to provide huge computational resources for the needs of genome analysis on an on-demand basis. Genome analysis normally encompasses a chain of various biological applications, which may engage thousands of analytic tasks with hundreds of thousands of copies of heterogeneous data in different sizes derived from geographically diverse sources. Though current cloud computing systems are able to adapt to workload changes by provisioning required resources automatically, there is still plenty of room to improve the performance and reduce the total cost for processing big genomic data.

There are two major issues with cloud-based big genomic data analysis. Firstly, most genome analytic processes are currently executed sequentially in clouds when there are huge opportunities for application parallelization. This opportunity is missed because we lack a smart scheduler that can "understand" the genomic applications and identify opportunities for concurrency. Secondly, very often analysis processes spend large proportions of their running time on blocked I/O due to the volume of data that must be fetched or retrieved, both to/from the analysis user and to/from intermediate storage used to communicate between analysis processes.

To address the above issues, We need a smart scheduling mechanism to orchestrate the huge number of analysis processes and make them execute effectively in clouds. For example, it could assign analysis tasks with their required computing resources in a "just enough and just on time" manner, so that the utilisation of cloud computing resources can be optimised. we also need an intelligent mechanism that can supply data when required with the progress of analysis execution. For example, it could upload required genome reference files just before they are needed to avoid a long waiting time, or fragment large sequencing datasets into suitable small pieces to enable parallel execution and thus speed up the whole process.

SCAN, a smart application platform to empower parallelization for big data processing in a cloud environment, is proposed in this paper. The SCAN is a generic platform that can be applied to any type of big data processing. However, our efforts focus on exploring the research challenges within the context of big genomic analysis and in the research area of translational cancer research through well-defined examples and the application tools, i.e., Genome Analysis Toolkit (GATK). GATK is one of most popular software tools today that is used to process genomic data. Together with a sequencing machine and pre-processing by other software tools that map the machine's output onto a reference genome, it can achieve many different functions for genomic data analyses. We thus select GATK tools for our evaluation.

Other genomic data processing share the same kernel of the SCAN platform.

The SCAN platform has two key components. The first component distributes large amounts of biological data required by analysis processes in an intelligent manner. This is informed by an application knowledge base which includes information about various bio-applications and their characteristics, such as input data format, parameter settings, performance suggestions, etc. By querying the knowledge-base, the SCAN can determine, for example, the most suitable file size for each type of genomic data analysis based on the resource cost and performance requirements. It can then suggest to subdivide a big input data file into some number of small input files for parallel processing. The second key component of the SCAN platform applies smart algorithms to determine what cloud resources to hire, and how to distribute resources between different analysis jobs, aiming to execute analysis tasks in the cloud as efficiently as possible.

In this paper, we present the design and development of the SCAN platform. We also describe a reward-based job scheduling mechanism to orchestrate large numbers of heterogeneous genome analysis tasks. Finally, the benefits of the SCAN platform is demonstrated through a simulation study. The evaluation results indicate that the SCAN platform can improve overall genomic data analysis performance and can significantly reduce the attendant cost. The contributions of this work are:

1) A smart application platform is developed to facilitate big genomic data processing in clouds.
2) A knowledge-based data distribution mechanism is implemented to parallelize big genomic data processing.
3) A scheduling algorithm is designed to better support resource elasticity of genome analysis in cloud environments.
4) Simulation experiments are conducted to examine the benefits of running the GATK application using the SCAN platform.

The remainder of this paper is structured as follows: in Section II we describe the design and development of the SCAN platform architecture and its key components, and provide detailed information on SCAN's smart algorithms. In Section III-B the prototype implementation is discussed. In Section IV we study SCAN's performance in a simulated cloud. In Section V related work is discussed before the conclusion of the paper in Section VI.

II. Design

Genome analysis normally involves a number of different analysis applications, which may incorporate multiple levels of biological information such as phenotype, genotype, expression profiles, proteomics, protein interaction, metabolic analysis and physiological measurements, etc. The main challenge addressed in the design of the SCAN is that different stages of a particular analysis pipeline may require substantially different amounts and types of input data and computing resources. For example, mapping of deep sequencing data to genome annotation via a relational database such as ENSEMBL relies on the ability to perform frequent joins across multiple tables containing millions of rows, while computation of downstream statistics is often dependent on repeated numerical calculations over permuted data in order to provide a null distribution [4]. The SCAN provides the required data and cloud computing resources smartly in order to improve the performance and reduce the cost of genome analysis.

A. Basic Requirements

In this section, we analyse basic requirements of the design of the SCAN platform as follows:

1) Catering to diverse application requirements: SCAN manages various bio-applications, each with different computing resource requirements, and each dealing with different kinds of data. For example, a sequence aligner may process sequence data in FASTQ format and may need many CPUs, whilst the GATK handles aligned sequence data in BAM files and may need a large amount of main memory [5], [6].
2) Allowing parallel and concurrent control: Different applications also support different degrees and modes of parallelism (for example, local multithreading, coarse-grained multi-process sharding and fine-grained distributed computing). Therefore it is important that SCAN can compare the benefits of and coordinate these different modes, including communicating with the underlying cloud infrastructure to commission appropriate resources.
3) Staging of data files: the SCAN has to process various data files of different sizes. It is essential to provide a method of manipulating or fetching the required data for each application process. For example, for optimal performance, the GATK analysis should operate on a 2GB BAM file; however, whole genome sequencing data normally runs to over 100GB, which must therefore be sharded.
4) Maintaining a knowledge base: the SCAN needs to assemble information about cost and performance of different bio-applications within different cloud infrastructures in order to form an optimal execution plan.

B. SCAN Data Flow

Genome analysis may need to analyse large amounts of Next Generation Sequencing (NGS) data in order to identify the driver mutation of tumour samples, and then to associate the mutation with protein functions within a cell signal network. Biological processes are organised and controlled by complex interactions between many individual components, and thus inherently involve intricate networks. The

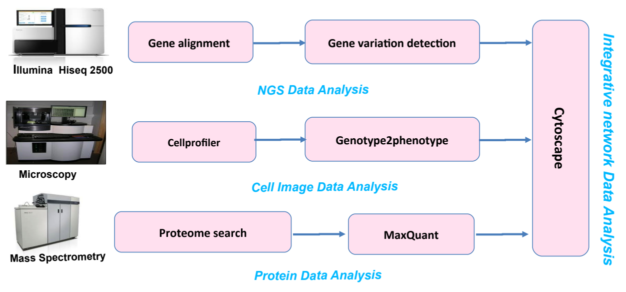


Figure 1. SCAN Data Flow Digram.

properties of these networks underlie virtually all aspects of cell function and can, for example, predict disease outcome and responses to treatment.

The SCAN is thus designed to analyse either exome data or Whole Genome Sequencing (WGS) data from the Illumina HiSeq platform referring to some public genomic or proteomic data. It may also analyse proteomic data and high throughput imaging data together with the genomic data [7]. Figure 1 shows the SCAN data flow digram and the applications in details. We design the SCAN to work with standard formats to enable interoperability with other tools. For example, the read mapping produces sorted SAM output and the variant caller takes sorted SAM input, and generates a standard VCF file.

C. *SCAN Ontology and Genomic Application Knowledge*

Having information about applications is critical for efficiently planning genome analysis. This information is used for application data preparation, parameter setting, workflow orchestration and cloud resource allocation. In order to organise information to help the SCAN to "understand" various biological and clinical applications, we define a semantic model to represent heterogeneous information in a meaningful way.

The SCAN semantic model is composed of a domain ontology (DO), a cloud ontology (CO) and the SCAN linker. The definition in BNF syntax is as follows:

```
Active Ontology ::=
     'Ontology('  [ domain ] ')'
     | 'Ontology('[cloud ]')'
     | 'SCAN('{linker}')'
```

Those ontologies provide an expressive information model to describe genome analysis and the cloud domain. They enable information to be logically self-organised and automatically processed.

D. *SCAN Reward Algorithm*

We designed reward functions to motivate SCAN's scheduling decisions. We assume that a large number of independent users are submitting analysis pipeline requests to a cloud, and that they all offer reward on the same terms (i.e. there are no users with more urgent work than others willing to offer a premium for fast execution). We use either the *time-oriented* reward scheme and the *throughput-oriented* scheme. Any cloud manager can select a suitable scheme for allocating resources based on user's policy.

- Time-oriented Reward: Under the time-oriented reward scheme, users offer a reward proportional to input data size for completion of their whole analysis pipeline, with a constant penalty per unit time the work is delayed. Thus the reward R given for finishing an analysis with input data size d in total time t is related by constants R_{max} and $R_{penalty}$:

$$R(d,t) = d(R_{max} - tR_{penalty})$$

This scheme represents the case where the primary undesirable factor is the time wasted by users waiting for analysis pipelines to complete: they are paid proportional to time, and so the penalty for delaying work is similarly a linear function of time.

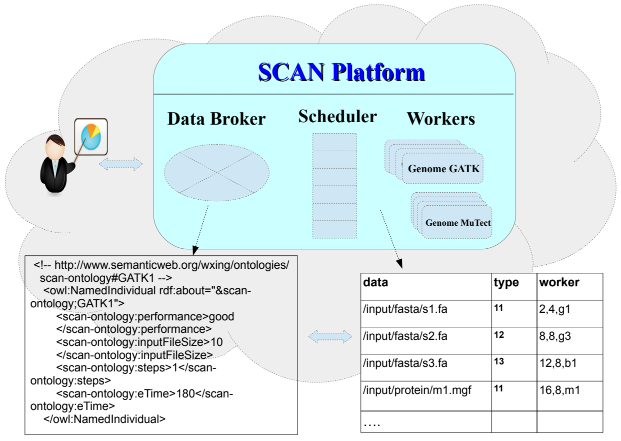
- Throughput-oriented Reward: Under the throughput-oriented reward scheme, users offer a reward proportional to the *rate* at which analysis requests are completed, and thus inversely proportional to the duration of the complete pipeline execution. It can be given in terms of input data size d and analysis time t in terms of a scaling factor R_{scale}:

$$R(d,t) = \frac{dR_{scale}}{t}$$

This scheme represents the case where the user is more concerned with relative speedup than with the total time consumed for a particular run: whilst the time-oriented scheme values any minute it can save equally, the throughput-oriented scheme rewards according to the *proportion* of runtime that was eliminated.

III. The Development of SCAN

The SCAN is designed as an integrative application platform which supports four types of data processes: i) genomic data process; ii) proteomic data process; iii) cell imaging data process; and iv) integrative data analysis. It therefore employs a set of biological application tools for those four types of data processes, including Burroughs-Wheeler Aligner (BWA) for gene alignment, GATK for gene variations detection, the Global Proteome Machine for proteomic data analyses, MaxQuant, CellProfiler for cell image analyses, and Cytoscape for omic data integration [8]–[11]. The key objective of the SCAN platform is to match the data and computing resources demanded by a variety of genomic applications or by different volumes of cancer data efficiently and economically.



```
<!-- http://www.semanticweb.org/wxing/ontologies/
  scan-ontology#GATK1 -->
   <owl:NamedIndividual rdf:about="&scan-
ontology;GATK1">
        <scan-ontology:performance>good
        </scan-ontology:performance>
        <scan-ontology:inputFileSize>10
        </scan-ontology:inputFileSize>
        <scan-ontology:steps>1</scan-
ontology:steps>
        <scan-ontology:eTime>180</scan-
ontology:eTime>
   </owl:NamedIndividual>
```

data	type	worker
/input/fasta/s1.fa	11	2,4,g1
/input/fasta/s2.fa	12	8,8,g3
/input/fasta/s3.fa	13	12,8,b1
/input/protein/m1.mgf	11	16,8,m1
….		

Figure 2. Overview of SCAN Architecture.

A. SCAN Architecture

Considering all the requirements presented in Section II-A, we present the SCAN as a smart application platform (shown in Figure 2). It comprises three key components: a) Data Broker, b) SCAN Scheduler, and c) SCAN Workers. The Data Broker splits and distributes large datasets for various applications, so that the SCAN is able to run subtasks in parallel. The SCAN Scheduler maintains analytic task queues and pools of SCAN workers that may be used to execute those tasks or subtasks. Tasks are scheduled by a "reward" algorithm with the aim to maximise profit (the difference between resource costs and user reward for work completion). The SCAN Workers are varied in terms of their application software stack (for example, operating systems and installed applications available) and their hardware configuration (for example, the number of (virtual) CPU cores they are assigned or the amount of physical memory they are permitted to use). In the following, we will discuss these three components in more detail.

1) Data Broker: The Data Broker is designed to fragment or merge large sets of input data for massive analytic tasks so that the SCAN can parallelize genome analysis. The SCAN can intelligently fragment the input data of each step of analysis workflows based on the information provided in a knowledge-base. For example, it can divide a large input file into many small input files so that a big data process can be executed by several parallel analysis processes, choosing the degree of parallelism based on a user cost policy.

The data broker has two key components: an application knowledge base to guide data preparation of each task, and data sharders to fragment various genomics data into suitable chunks. The knowledge-base is built by using semantic web technology, i.e., ontology and the instances. There are three key functions of the data broker are described as follows:

(i) The Creation of SCAN Knowledge-base: We have created an OWL (Web Ontology Language) ontology that describes biological data and its associated bio-applications, resources, capabilities and the relationships among them [12], [13]. The ontology is based on the Gene Ontology (GO) described in [14] and extends the GO to include descriptions about biological data types and formats, bio-applications, cloud middleware services, computing and storage resources, networks, and usage policies. Besides the ontology, we add various instances of tasks of omics data analysis, including genome analysis, proteome analysis, imaging analysis, and integrative analysis running in a cloud. For example, the instances of genome analysis include workflows like data variation detection analysis and miRNA fusion detection workflows.

The knowledge-base is initially created by profiling some of the most common genome applications. In this case, there is no profiling information. We can just use history information about a particular application as the start point, then SCAN knowledge-base can update its knowledge accordingly. After that, the knowledge base will be expanded by using information from logs of each task running on the SCAN platform. For example, we profiled GATK performance under different hardware configurations and with different inputs [15]. The datasets include genome inputs of different sizes, ranging from 1GByte to 9GBytes. We can then conclude that total execution time linearly increases with the input file size and that different GATK analysis tools scale differently with thread count, generating different parallelism recommendations depending on the reward offered by the user. Based on these profiling results, we can express the GATK input datasets in the SAN ontology in RDF/OWL format as follows:

```
.....
    <owl:NamedIndividual rdf:about="&scan-ontology;GATK1">
      <rdf:type rdf:resource="&scan-ontology;Application"/>
        <scan-ontology:inputFileSize>10
        </scan-ontology:inputFileSize>
        <scan-ontology:steps>1</scan-ontology:steps>
        <scan-ontology:RAM>4</scan-ontology:RAM>
        <scan-ontology:eTime>180</scan-ontology:eTime>
        <scan-ontology:CPU>8</scan-ontology:CPU>
    </owl:NamedIndividual>
.....
```

In order to enrich the knowledge base, The SCAN keeps the log information of each task scheduled to run in a cloud. The log information will be used to further populate the SCAN knowledge-base. We show below an example of the knowledge-base expansion when some GATK tasks are run under the SCAN:

```
.....
       <!-- http://www.semanticweb.org/wxing/ontologies
       /scan-ontology#GATK1 -->

    <owl:NamedIndividual rdf:about="&scan-ontology;GATK1">
     <rdf:type rdf:resource="&scan-ontology;Application"/>
        <scan-ontology:inputFileSize>10
        </scan-ontology:inputFileSize>
        <scan-ontology:steps>1</scan-ontology:steps>
        <scan-ontology:RAM>4</scan-ontology:RAM>
        <scan-ontology:eTime>180</scan-ontology:eTime>
        <scan-ontology:CPU>8</scan-ontology:CPU>
    </owl:NamedIndividual>
    <!-- http://www.semanticweb.org/wxing/ontologies
    /scan-ontology#GATK2 -->

    <owl:NamedIndividual rdf:about="&scan-ontology;GATK2">
     <rdf:type rdf:resource="&scan-ontology;Application"/>
        <scan-ontology:CPU>8</scan-ontology:CPU>
        <scan-ontology:steps>1</scan-ontology:steps>
        <scan-ontology:RAM>4</scan-ontology:RAM>
        <scan-ontology:eTime>200</scan-ontology:eTime>
        <scan-ontology:inputFileSize>5
        </scan-ontology:inputFileSize>
    </owl:NamedIndividual>

    <!-- http://www.semanticweb.org/wxing/ontologies
    /scan-ontology#GATK3 -->

    <owl:NamedIndividual rdf:about="&scan-ontology;GATK3">
    <rdf:type rdf:resource="&scan-ontology;Application"/>
        <scan-ontology:steps>1</scan-ontology:steps>
        <scan-ontology:CPU>8</scan-ontology:CPU>
        <scan-ontology:eTime>280</scan-ontology:eTime>
        <scan-ontology:RAM>4</scan-ontology:RAM>
        <scan-ontology:inputFileSize>20
        </scan-ontology:inputFileSize>
    </owl:NamedIndividual>

    <!-- http://www.semanticweb.org/wxing/ontologies
    /scan-ontology#GATK4 -->

    <owl:NamedIndividual rdf:about="&scan-ontology;GATK4">
    <rdf:type rdf:resource="&scan-ontology;Application"/>
        <scan-ontology:eTime>80</scan-ontology:eTime>
        <scan-ontology:steps>1</scan-ontology:steps>
        <scan-ontology:CPU>8</scan-ontology:CPU>
        <scan-ontology:inputFileSize>4
        </scan-ontology:inputFileSize>
        <scan-ontology:RAM>4</scan-ontology:RAM>
    </owl:NamedIndividual>
</rdf:RDF>
```

(ii) Querying the SCAN Knowledge-base for Sharding Data: The Data Broker will query the SCAN knowledge-base to decide the suitable chunk size of input files of tasks whenever there is a new GATK task in the SCAN platform. It then will call Data Sharders to chunk (different types of) genomic data into pieces accordingly and submit those tasks to the Scheduler.

In general, the SCAN will be smarter to suggest the combination of the most suitable input data size and available cloud computing resources when more log information has been collected from previous tasks executed on the platform.

The decision is based on a set of workflow execution conditions, including the actual information needed (specified as a SPARQL query), and other aspects like the availability of the source [16]. For example, in our prototype we have defined the class `AlignedGenomicData` that represents inputs to the GATK pipeline. This class has a property `CPU` that is `requiredBy` GATK workflows.

Since in our ontology we have defined over 10 different genome analysis workflows (as instances of the class `GenomeAnalysis`), the Data Broker sends a query to select the most suitable one for deciding the size of a input file. The query is done in SPARQL, and retrieves the suggested values of those instances of `GATK`, along with its *CPU* and *RAM* resource attributes. Below is a SPARQL query for the GATK instances in the SCAN knowledge-base:

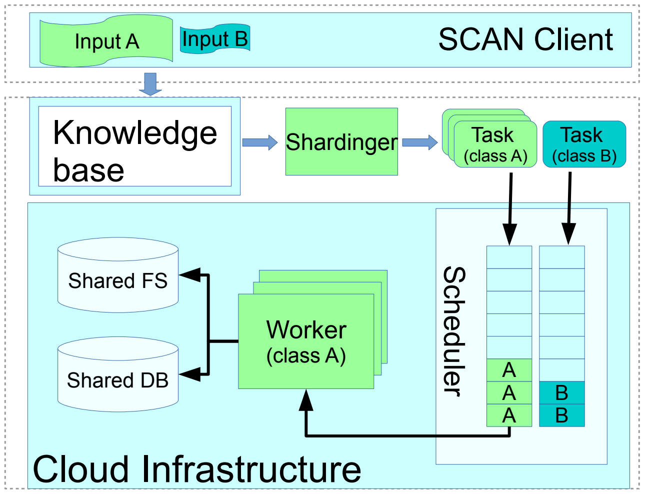


Figure 3. The Key Components and the Implementation.

```
PREFIX  SCAN: <http://www.semanticweb.org/wxing/ontologies
    /scan-ontology#GATK>
FROM    <scan-wxing.owl>
SELECT  ?InputData
WHERE   { ?s SCAN:inputFileSize "sharding"?    .
          OPTIONAL { ?x:resourceRequired "clouds"   .
                     ?y SCAN:computingResource  ``CPU" .
                     ?z onG:computingResource ``RAM'' . }
```

The selected GATK instances are ranked according to the values of their execution time and the size of input files.

(iii) Sharding Input Data for Genomic Tasks in a Cloud: Genome data size for a particular analysis varies widely. The SCAN is equipped with Data Sharders for each type of genomic data, such as FASTQ and BAM files. They can, for example, divide a 100GB FASTQ file into 25 4GB files, and create 25 data analysis subtasks. On the other hand, the SCAN can merge many small input files into one big file, for example, for the GATK task called VariantsToVCF. The SCAN knowledge-base will advise the appropriate shard size.

2) SCAN Scheduler: The SCAN provides a scheduler for deploying batch-oriented workloads, such as the GATK pipeline, against an elastic cloud environment. It provides a set of work queues and a worker pool that services each one. As shown in Figure 3, the scheduler keeps track of available workers and pending tasks, and assigns tasks to the workers.

The Scheduler accepts analytic tasks from users, exports information to clouds and supports a variety of scaling parameters that the cloud manager can adjust at runtime. It also controls cloud resource hiring. For each work item reaching the front of a task queue, and which is therefore about to be assigned to a worker, the SCAN must decide: should a worker (or workers, if process-level parallelism is used) be hired from the elastic cloud to run it immediately, or should it be delayed until an existing worker becomes available?

To make decisions, the SCAN implements a *cost function*, which maps the number of machines currently active and their configuration to the cost per unit time of keeping them running, and a *reward function*, which maps task latency and task size onto a reward measured in the same units (latency measures the time from a task entering the queue for the first analysis stage to completing the last stage). The task's size is a format-specific concept, but generally reflects the number of records of input data supplied.

The cost function consists of tiers, representing a class of resources that can be hired at a given price. For example, if the deployment belonged to an academic institution, they might describe their institution's private cloud as a tier of resources at negligible cost, their University's private cloud as a tier with higher cost with availability bounded by the available physical decisions are taken.

The reward function may express concepts such as a deadline, where reward falls to zero as the results are useless thereafter, and bonuses for rapid completion, where reward slopes upwards before plateauing when execution is fast enough that the customer is not willing to pay for more.

Denoting the reward function $R(latency, records)$, and the number of records in job *j* as $recs_j$, we can then define the *delay cost DC* of delaying queue *Q* by *delay* time units:

$$\begin{gathered} DC(delay) = \sum_{j \in Q} R(ETT(j), \\ recs_j) - R(ETT(j) + delay, recs_j) \end{gathered} \tag{1}$$

$ETT(j)$ gives the Estimated Total Time for the job *j* to run, given its progress so far and the occupancy of this queue and those of future pipeline stages. This is the sum of time already passed since the job started and the estimated queueing and execution times for future pipeline stages.

We estimate execution time for pipeline stage *i*, denoted EET_i, using a linear function of the number of job input records derived from profiling data. We also estimate the time we expect a general job to spend in the queue for stage *i*, EQT_i. Writing the job *j*'s current stage S_j, we have:

$$ETT(j) = elapsed_j + \sum_{i=S_j} (EQT_i + EET_i(j)) \tag{2}$$

3) SCAN Workers: SCAN Workers are responsible for executing tasks as instructed by the scheduler. The workers are very simple entities: they are assigned SCAN tasks, which they run until completion, and provide feedback concerning their resource utilization to the scheduler. Each worker has a software stack suitable for a particular application and a certain hardware configuration. SCAN Workers can host most genomic applications by using cloud virtualisation technology. Currently we have implemented GATK, BWA, and Maxquant workers for the SCAN platform.

B. SCAN Prototype Implementation

The current SCAN implementation realises the design using the SCAN knowledge-base; a custom-built scheduler; and existing Linux and Windows services for the workers, CIFS for the shared filesystem and Apache Cassandra for the database. The SCAN knowledge-base is built using an OWL/RDF ontology and its instance store; SPARQL is used to query the store. The scheduler is implemented in Python, using the CherryPy web framework to process HTTP requests. Its interface is realized using HTTP RPCs. It maintains an in-memory pool of available workers and a FIFO queue of pending tasks per class. Workers do not need any custom SCAN software to provide their required interface. They accept tasks using existing remote control mechanisms, such as ssh.

Within the EU FP7 CELAR project [17], the SCAN has been implemented in conjunction with CELAR cloud middleware development [18]. The CELAR cloud is a fully automated and highly customisable system for elastic provisioning of resources in cloud computing platforms. It aims at providing an elasticity layer for applications that need to be able to take advantage of the elastic, pay-as-you-go resource provisioning nature of cloud infrastructures in a transparent and customizable manner. The SCAN interacts with two key cloud components of the CELAR, which are the CELAR Manager and the CELAR Decision Module. The CELAR Manager is a cloud component to orchestrate and execute the deployment of the applications in the cloud, and the Decision Module takes automated control measures, based on application behaviour and the user-defined requirements.

By employing CELAR middleware components, such as the CELAR cloud manager and the decision making module, the SCAN can query the analysis performance characteristics and issue scaling commands to the underlying cloud infrastructure. However, the SCAN can function independent of the CELAR. General speaking, the SCAN can work with any kind of cloud platforms and various cluster systems.

IV. Evaluation

To demonstrate the benefits of the SCAN platform for big genome data analysis, we conduct simulations to compare the performance and cost of GATK tasks running with and without SCAN's smart scaling and resource allocation algorithms. In the current prototype implementation, we exhibit SCAN to integrate two biological applications that supports a SCAN analysis to draw the two applications' results together. One of the applications uses the Broad Institute's Genome Analysis Toolkit (GATK) to detect variations between a given set of DNA reads (in BAM format) and a reference genome. Its analysis takes place across seven different phases with distinct resource requirements but identical software requirements. In this section we describe our model of the GATK application and the scaling algorithms in a cloud for our evaluation.

1) GATK Application: A typical genomic data process is to determine whether a DNA sample taken from a patient exhibits genetic mutations known to cause cancer, and if it does, which specific variety of the disease. We employ the GATK application which is typically used to build a pipeline consisting of multiple *stages*. The first stage consumes the user's input data, whilst every other stage depends on the full output of its predecessor. We consider a particular 7-stage pipeline that is commonly used to diagnose genetic mutations in input data compared to a known reference genome: the user submits aligned DNA or RNA reads, typically in Binary Aligned Map (BAM) format, and at the end of the pipeline receives a list of suspected mutations compared to the reference genome.

Many of the GATK tools used in this pipeline require a great deal of I/O bandwidth, but they are ultimately compute- or memory-bound rather than I/O-bound. A genomic sequence file can varied in size, from 100MB to 500GB, which will greatly affect the needs of computing and memory resources. The SCAN makes the inputs of GATK steps according to the suggestions from the knowledge base. In our case, the inputs will be 2GB for each task. Most (but not all) GATK tools can be accelerated by local multi-threading: ordinarily this is manually controlled by the user, but in this paper it will be controlled by our resource allocation algorithm. In both cases the degree of multi-threading must be chosen when the stage starts execution, and cannot be adjusted thereafter, but can differ from pipeline stage to stage.

We model GATK pipeline stages with single-threaded execution time that is a linear function of the size of the first stage's input data. Thus for each pipeline stage i we can specify coefficients a_i and b_i such that execution time E_i can be given in terms of input data size d:

$$E_i(d) = a_i d + b_i$$

We compute multi-threaded execution time assuming that the single-threaded execution time for a particular stage may be split by a constant factor c_i into a sequential part and a part which scales perfectly. Thus threaded execution time using t threads $T_i(t, d)$ relates to $E_i(d)$ by:

$$T_i(t, d) = c_i \frac{E_i(d)}{t} + (1 - c_i) E_i(d)$$

Thus the maximum possible speedup achievable by adding threads is limited in accordance with Amdahl's law. The values of a_i, b_i and c_i were determined for each pipeline stage by linear regression of offline profiling data. The profile measured the time taken to analyse a variety of input sizes and thread counts. We found these simple models represented the profiling data very accurately.

A. Experimental Configuration

Most of cancer genome data centres are with a hybrid infrastructure, that is they have their own decimated resources, and they will use public cloud resource when they need more computing resources for some cases. We thus setup a hybrid cloud for our evaluation which consist of two tiers: a *private* tier (624 CPU cores and 64GB RAM per node) and a *public* tier. Using cores at either tier has a constant cost per core per unit time, with private cores being cheaper than public cores. The private tier represents the owned compute resources which are commonplace in scientific institutions with HPC requirements, with the cost representing depreciation of the owned machines or an internal incentive for fair sharing. The public tier represents cores or machines hired from a public cloud computing provider such as Amazon EC2, or perhaps a national-level academic shared computing facility. Here we assume that the private tier compute core is the same (Ghz, processor model, etc) as public tier compute core in our evaluation.

B. Evaluation Results

We ran a number of simulation sessions, varying the parameters shown in Table I. Table II gives the fixed a_i, b_i and c_i parameters that determine the scalability of each pipeline stage. Finally, Table III gives miscellaneous fixed parameters (recall that the various R parameters influence the reward given for completing a pipeline run in a given time, as described in Section III-A2). The scalability factors were derived from profiling of the real GATK with a variety of thread counts and input data sizes; the other parameters were selected by trial and error in order to exhibit a cross-section of the system's behaviour. In particular the arrival batch size and job size parameters were chosen to produce significant short-term workload variation, such that the scaling and resource allocation algorithms would experience a wide range of cluster utilisation during a given simulation run.

All our experiments measure how performance varies with changing system workload by varying the mean job inter-arrival interval. For context, a mean interval of 2.0 time units represents a very busy system where much public resource hiring is necessary to keep the task queue from growing out of control, whilst a mean interval of 3.0 time units corresponds to a quiet system where the private resource tier is rarely if ever fully occupied. All measurements were repeated 10 times, and all error bars represent a single standard deviation either side of the mean.

We found that SCAN Scheduler can achieves a sound compromise between the behaviour of the always-scale and never-scale baselines when running with a constant resource allocation policy (i.e. when every run uses the same execution plan). Figure 4 shows an example of this behaviour, where the predictive algorithm mimics the never-scale baseline with a light workload and the always-scale baseline with a heavy load. At intermediate loads it performs

Parameter	Values
Resource allocation algorithm	Greedy, long-term, long-term adaptive, best constant
Horizontal scaling algorithm	Always-scale, never-scale, predictive scaling
Mean job inter-arrival interval	2.0, 2.1 ... 3.0 TUs
Task completion reward function	Time-based, throughput-based
Public tier core cost (CUs / TU)	20, 50, 80, 110

Table I
VARIABLE SIMULATION PARAMETERS

Pipeline stage	a_i	b_i	c_i
1	0.35	5.38	0.89
2	2.70	-0.53	0.02
3	1.74	3.93	0.69
4	3.35	0.53	0.79
5	1.03	17.86	0.91
6	0.02	0.39	0.25
7	0.01	5.10	0.02

Table II
PER-PIPELINE-STAGE SCALABILITY FACTORS

Parameter	Values
Simulation time (TUs)	10,000
Private tier core cost (CUs / TU)	5
R_{max} (CUs)	400
$R_{penalty}$ (CUs)	15
R_{scale} (CUs / TU)	15,000
Possible instance sizes (cores)	1, 2, 4, 8, 16
Mean jobs per arrival event	3
Jobs per arrival variance	2
Mean job size (arbitrary units)	5
Job size variance	1

Table III
MISCELLANEOUS SIMULATION ATTRIBUTES FIXED ACROSS ALL RUNS

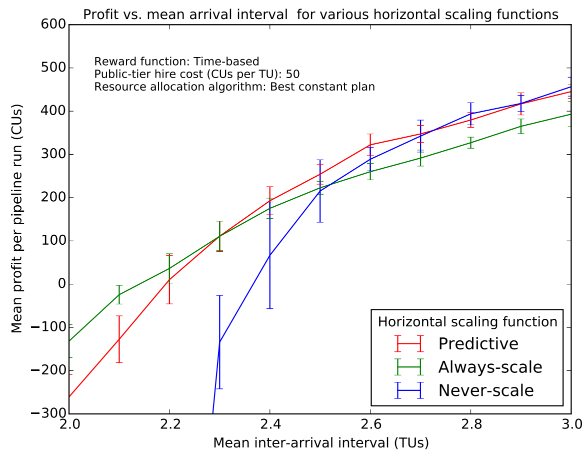


Figure 4. Reward-to-time vs. cores for various horizontally-scaled, heterogeneous simulation.

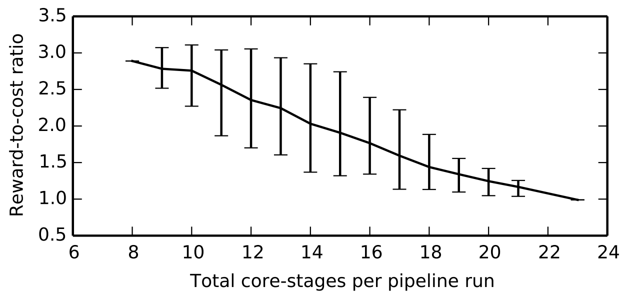


Figure 5. Reward-to-cost ratio vs. cores for horizontally-scaled, heterogeneous simulation.

marginally better than either baseline, although it remains within a standard deviation of either.

Also we combined both dynamic horizontal scaling and heterogeneous workers, again permitting different stages to use different degrees of multithreading, but allowing (simulated) CELAR to resize each of these pools as required. We now pay the 30 second startup penalty whenever a worker was previously assigned to a pool that uses a different number of threads, as CELAR would need to shut it down, adjust the number of VCPUs, and restart it for its new role. Figure 5 shows the relationship between the number of cores employed per pipeline run and the reward-to-cost ratio achieved. This configuration achieves a ratio of 3.11, the best of all configurations, thanks to its ability to support multithreaded pipeline stages without the rigidity of statically assigning workers to phases.

We explored all permutations of resource allocation algorithm, horizontal scaling algorithm, reward scheme and workload, and found that our proposed algorithms are often able to improve performance above their respective baselines, demonstrating that real-world workloads using the GATK and similar analysis tools may benefit from intelligent cluster scaling and pipeline stage sizing. We found that the SCAN outperforms the best-constant baseline algorithm in many circumstances, and that the SCAN's predictive horizontal scaling represents a useful compromise between the two baseline schemes that always or never scale when private resources are fully occupied.

V. RELATED WORK

In the life sciences area there are many systems available that process genome data, primarily those are done through various workflow systems. Some examples include Galaxy, TransMart, Taverna, BioMart, and InforSense KDE [19]–[23]. To the best of our knowledge, they all can hire public cloud resources to satisfy their resource requirements, but follow a simple hire-on-demand policy when doing so. None of these systems have smart mechanisms to improve the application performance and reduce the cost of big genome analysis.

Galaxy is a web-based platform with many built-in genome analytic workflows [19]. In particular, the Galaxy CloudMan was developed as a software package to provide a common interface to different cloud infrastructures. It depends on the cloud infrastructure to improve performance and cost effective for particular applications. TransMart is a translational platform allowing the management and exploration of clinical and omics data [20]. It supports complicated data queries crossing domains by using multiple relational databases, but does not provide any mechanism to address the performance and cost-effective issues. Cloud computing is simply employed to provide elastic computing resource for back-end database systems.

String and Cytoscape are application platform for searching and visualizing molecular function and/or interaction networks and biological pathways and integrating these networks with annotations, gene expression profiles and other state data [24], [25]. Similarly, BRISK and the cBio Cancer Genomics Portal focus mainly on the exploration of omics data, and iDASH provides biomedical and behavioural researchers with access to data, software and a high-performance computing environment [26]–[28]. None of them address performance issues or reduce the cost of required resources for genomic data analysis in clouds.

There are some works on scheduling strategies for cloud environments [29]–[31]. In [29], authors proposed an optimized scheduling algorithm to achieve the optimization or sub-optimization for cloud scheduling. In this algorithm an Improved Genetic Algorithm (IGA) is used for the automated scheduling policy. It is used to increase the utilization rate of resources and speed. However, the majority of these scheduling strategies are static in nature. They produce a good schedule given the current state of resources in Clouds or Grids and do not take into account changes in resource availability. SCAN enables dynamic scheduling that is done on-the-fly considering the current state of the system and adaptive in application nature.

VI. Conclusion

Genome analysis needs to process large amounts of omic data. An application platform must be smart enough to handle those data requirements and facilitate the corresponding processes. In this paper, we present the SCAN, a smart application platform for big genomic data analysis in clouds. We discuss the smart mechanisms of the SCAN, as well as its key components. We conduct a simulation study which shows that SCAN scheduler is able to outperform simple baseline schemes in a wide variety of circumstances.

In the future, we intend to investigate how the SCAN can better work with proteome analysis and drug discovery applications. We also plan to adopt learning algorithms to guide the Scheduler, and enhance the interaction between the SCAN and Cloud middleware.

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