GenomeAssist
An Online Sequence Aligner Comparison Tool

Mansi Arora and Roger Que

2013–12–16

Abstract

We present GenomeAssist, a Web-based tool for the comparison of sequence aligners. GenomeAssist provides genomicists with a graphical interface to run existing alignment tools on a backend cluster, without needing any command line knowledge or provisioning of local shell accounts. Results are aggregated into user-friendly visualizations that allow at-a-glance views of accuracy and runtime performance.

1 Background

Sequence alignment is, perhaps more than any other class of algorithms, fundamental to genomic data processing. A wide variety of approaches to the problem have emerged, variously motivated by the increasingly parallel nature of scientific computing, the discovery of new algorithms and data structures such as the FM-index, and changes in how sequencers themselves extract and present sequence data. In particular, the shift towards next-generation sequencers, which trade an overall higher throughput and lower cost for shorter individual reads, has given rise to many different alignment algorithms and tools geared towards their output [6]. With the large number of available alignment tools, questions arise about which one of them is most suitable for any particular data set.

Unfortunately, alignment tools have a relatively high barrier to entry. The first problem is one of resources: The amounts of data and computational power required to evaluate a set of sequence aligners against any given scenario are often too cost-prohibitive for a single user. This problem may be ameliorated in institutional environments with the availability of a computing cluster specifically geared towards research use, shared by a group or a department. However, this does nothing to address the second problem, which is one of general user accessibility. As many aligners are designed to be run on “headless” servers with no direct display output, they are generally instead invoked by logging in remotely to a command-line interface, and then specifying the preferred parameters by text strings. This process carries a high cognitive overhead for users unaccustomed to such software, overhead that is unrelated to the immediate problem of sequence alignment. In addition, there may be network security questions involved in the provisioning of accounts; for example, administrators may be reluctant to provide full shell access to a cluster when users should only be able to run alignment tools.

For this reason, some sequence alignment and search tools are available through Web-based interfaces, which can be launched through a browser. The most well-known of these tools is almost certainly BLAST, which is available through the Web site of the National Center for Biotechnology Information [1]. Other frontends have been developed for other aligners. Of particular note is Crossbow [3], which is designed for whole-genome resequencing analysis. The Crossbow pipeline combines the Bowtie aligner with the SoapSNP genotyper, and allows for the immediate spawning of jobs on Amazon EC2. Additional tools exist for aligners such as LALIGN/PLALIGN, the CLUSTAL toolkit, and MAFFT.

One major limitation of many of these Web frontends is that they do not make any attempt to make the aligners more accessible to a wider audience, but simply make them available for non-local usage. For example, Crossbow simply provides a text entry field for "Bowtie options" that are passed directly on the Bowtie command line, requiring the user to read the manual and arrive at the appropriate argument string on his or her own. Output, too, is frequently presented as raw text, instead of in a format that can be immediately understood at a glance.

A more fundamental problem, however, lies in the fact that no existing Web-based tool allows the user to directly compare different alignment algorithms, meaning that a genomicist who wishes to investigate the performance of various aligners receives no help in efficient decision making. As different aligners have significantly different performance profiles, whether specified in terms of accuracy and error reporting, or in terms of computing resources such as memory and CPU time, it is important for genomicists to understand these differences. However, configuring, installing, and running a large collection of tools can be a tedious task, made more troublesome by the accessibility issues mentioned previously.

In order to fill this unmet need, we have created GenomeAssist, an online tool specifically geared towards the comparison of sequence aligners. GenomeAssist provides a common, consistent frontend to various alignment tools, allowing genomicists to easily simultaneously run several aligner instances against a single common set of read and reference data. Results are presented through a graphical frontend that normalizes the differing output formats into charts and graphs that allow for quick visual comparisons, while still allowing the user to delve further into each aligner's particular output should the need arise. New tasks can be easily created based on the parameters used for previous runs, allowing users to iteratively arrive at the optimal settings for their specific scenario.

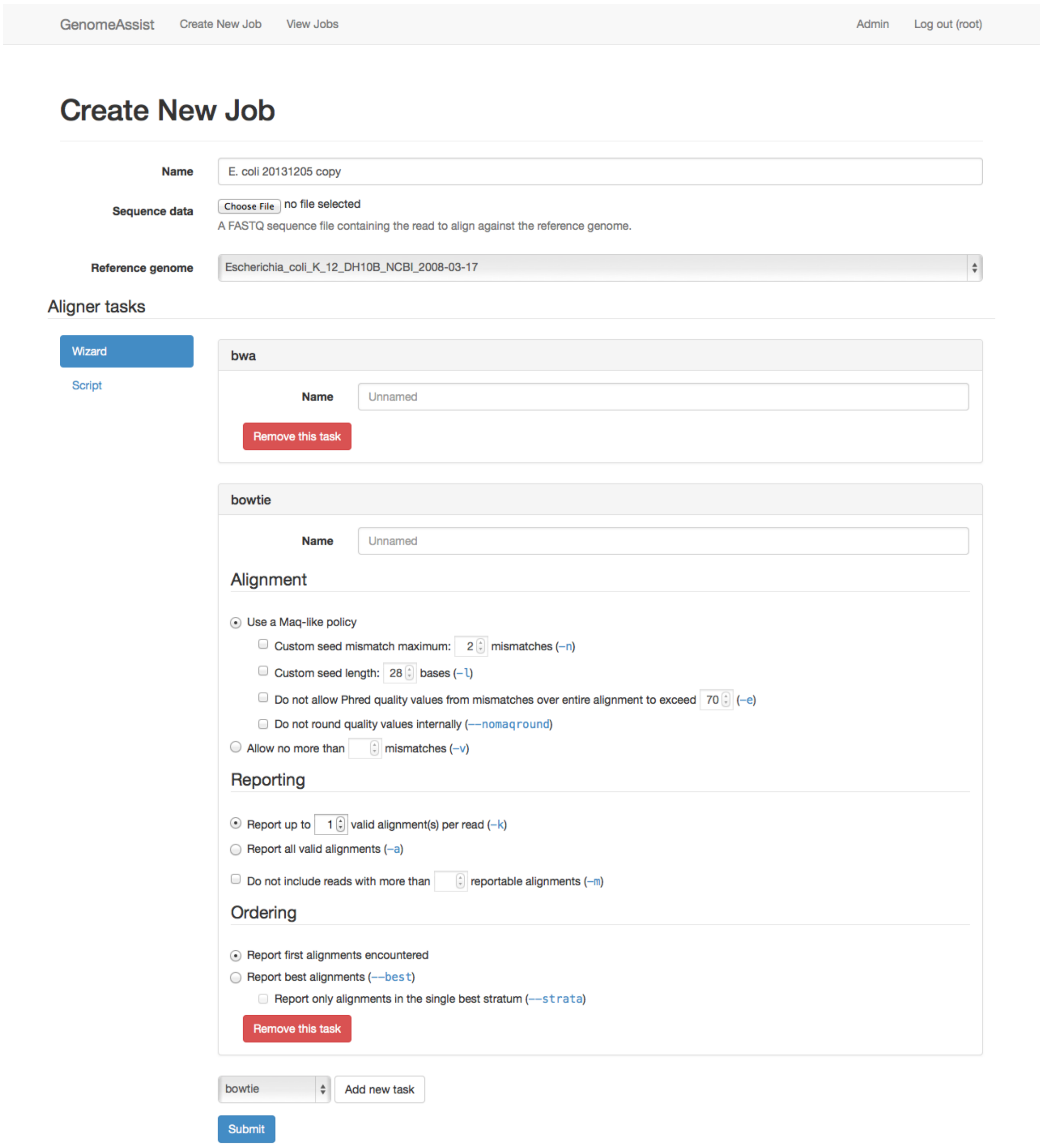
2 Feature overview

The GenomeAssist interface is centered on the creation of *jobs*, which are collections of aligner runs operating on a shared read file and reference genome. Each run contained within a job is referred to as an *aligner task*, or simply a *task*. GenomeAssist requires that all tasks be part of a job, although a job may contain only a single task. As detailed in Section 2.2, a job's results can be viewed in aggregate, or broken down by each component task. Currently, GenomeAssist implements a minimal user account system, which restricts the viewing of job results to the creating user.

2.1 Creating jobs

An overview of GenomeAssist's job creation interface is shown in Figure 1. At the top of the provided form are basic fields for setting an optional job name that will be used in the rest of GenomeAssist, uploading a read file, and specifying a reference genome. This read file and reference genome will be used for all of the tasks belonging to this job.

The majority of the page is dedicated to the aligner task creation form. By default, a wizard-like interface is provided, through which the user can graphically add new tasks and specify their respective options. For users already familiar with the command-line operation of a specific aligner, CLI option names such as `-k` or `--best` are also indicated, with links to the aligner's manual page if available. Multiple tasks using the same aligner may be specified, allowing users to run a single aligner with different options. This may be useful, for example, if the user wishes to compare different seed sizes for a hash table–based aligner, and select a value with an acceptable tradeoff between accuracy and speed.



Create New Job

Name: E. coli 20131205 copy

Sequence data: Choose File no file selected

A FASTQ sequence file containing the read to align against the reference genome.

Reference genome: Escherichia_coli_K_12_DH10B_NCBI_2008-03-17

Aligner tasks

bwa

Name: Unnamed

bowtie

Name: Unnamed

Alignment

- [✓] Use a Maq-like policy
  - ☐ Custom seed mismatch maximum: 2 mismatches (−n)
  - ☐ Custom seed length: 28 bases (−l)
  - ☐ Do not allow Phred quality values from mismatches over entire alignment to exceed 70 (−e)
  - ☐ Do not round quality values internally (−−nomaqround)
- ○ Allow no more than mismatches (−v)

Reporting

- [✓] Report up to 1 valid alignment(s) per read (−k)
- ○ Report all valid alignments (−a)
- ☐ Do not include reads with more than reportable alignments (−m)

Ordering

- [✓] Report first alignments encountered
- ○ Report best alignments (−−best)
  - ☐ Report only alignments in the single best stratum (−−strata)

Figure 1: GenomeAssist’s job creation interface, showing options available for Bowtie.

More advanced users may directly edit a job's *task script* by selecting the script view. The script defines the list of tasks and their respective options in a serialized JSON format, and is what is actually processed by the job scheduling backend. For example:

```
[{
    "aligner": "bwa",
    "name": "BWA task 1",
    "options": "[omitted]"
}, {
    "aligner": "bowtie",
    "name": "Bowtie task 2",
    "options": "[omitted]"
}]
```

This feature allows for a more compact specification of the parameters passed to a job, useful in cases where job information is being sent by some external textual medium such as e-mail. (Note that users do not need to use task scripts to create a new job based on the specifications of a job that they have already created; instead, they may create copies of existing jobs from the job output page, as outlined in Section 2.2.) The user is not required to use the wizard to individually specify each option, but can instead simply paste the job script into the appropriate text entry field. Once entered, the graphical wizard's fields are resynchronized with the options given in the script, so that the user may switch back to the wizard view and make further changes to task options without needing to modify the serialized script.

2.2 Viewing job output

After submitting a job to GenomeAssist, the user can view its current status and any eventual output on the job detail page. Upon a job's successful completion, a summary visualization is shown, as in Figure 2, composed of a *hit map* and resource usage statistics.

The hit map gives a linear view of all loci to which a read successfully aligned in at least one of the aligner tasks. Alignments are indicated by vertical lines, colored by their average quality value over all tasks. Darker lines indicate higher quality values. Individual alignments may be hovered over with the mouse to display their exact position and quality value information.

Below the hit map is a chart displaying the comparative resource usage of each aligner task. Currently, the amount of userland and system CPU time consumed, as well as peak memory utilization, are displayed on the chart. This allows the user to quickly gauge the relative efficiency of each aligner task, in comparison to its alignment accuracy.

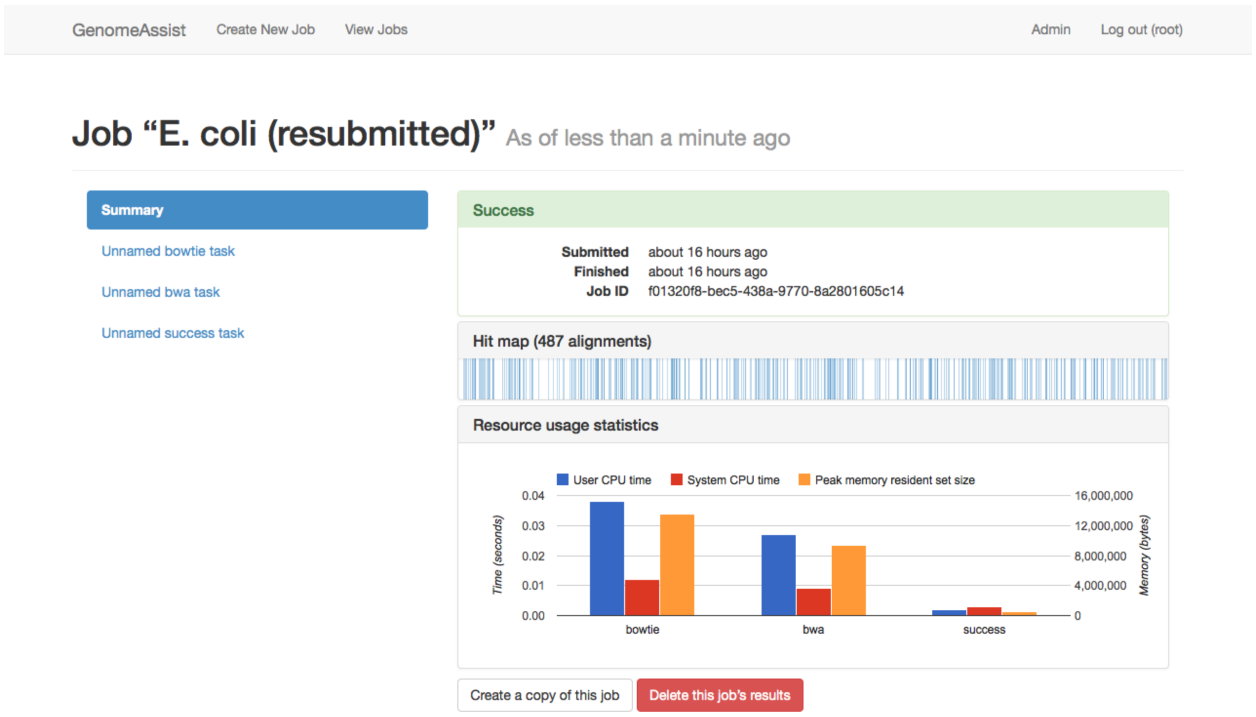
At the bottom of the summary view are buttons allowing the user to create a copy of this job, which pre-fills the job creation form with the reference genome and aligner options that were used in the job currently being viewed, or delete the job's results, hiding them from the default job listing. Job result deletion may be undone at any time, assuming that the deleted job's information has not been pruned from the database.

Status information, hit maps, and resource usage statistics are also available for individual tasks within a job, assuming that they have completed successfully. In addition, the raw textual output of each aligner is displayed, allowing further analysis to be performed with external tools.

3 Implementation

GenomeAssist is implemented as a Python application, using the Django Web application framework [2] and the Celery distributed task library [7]. In our testing, we used an on-disk SQLite database to store job and task information, along with a RabbitMQ message broker for coordinating task execution, although any combination supported by the above libraries should be sufficient. Currently, the resource usage tracking functionality requires that GenomeAssist be run on a Unix-like platform; it has been tested to work on Mac OS X and Ubuntu Linux.

Jobs are handled using a MapReduce-like



Job “E. coli (resubmitted)” As of less than a minute ago

Success

Submitted about 16 hours ago
Finished about 16 hours ago
Job ID f01320f8-bec5-438a-9770-8a2801605c14

Figure 2: GenomeAssist's job detail page, showing a sample alignment of 1,000 reads against the *Escherischia coli* genome.

paradigm, with individual aligner tasks being spun off to individual worker processes, and their results collated by a final aggregation task before being presented to the user. Aligner tasks are implemented as Celery task classes with two bespoke methods. The first, `parse_options`, is used to transform the URL-encoded options string passed in by the GenomeAssist frontend, along with the read and reference genome paths, into a list of command-line arguments. These arguments are then used to spawn a subprocess on the same machine as the Celery worker process. If the aligner does not encounter any errors, its output is passed to the the second custom method, `parse_output`, which transforms it into a format usable by the GenomeAssist frontend. A standard function for converting SAM output to this format is provided with GenomeAssist. Finally, when all aligner tasks have completed, the collected results are passed to the aggregator, which outputs data suitable for use by the visualizations on a job's summary page.

In its current incarnation, GenomeAssist shares data among the frontend and worker processes, such as reference genome indexes and uploaded read files, by means of mounted network shares on each host.

The frontend user interface is largely built on Twitter Bootstrap and jQuery, with some charting functionality provided by Google Charts. The use of these standard UI frameworks minimizes browser compatibility issues, allowing GenomeAssist to be used more easily in heterogeneous computing environments.

The GenomeAssist source code, including basic setup instructions, is available at `https://github.com/query/genomeassist`.

4 Future work

Currently, GenomeAssist supports BWA [5] and version 1.0 of the Bowtie aligner [4], with the graphical wizard interface only available for Bowtie. Some features of these aligners are also not yet available; for instance, GenomeAssist does not support the alignment of paired-end reads. GenomeAssist can easily be extended to support additional command-line aligners, however, by providing an HTML wizard form and implementing a Celery task class with appropriate methods for parsing options and text output, as outlined in Section 3.

GenomeAssist implements data sharing by means of locally mounted network file shares. Although Unix filesystem drivers are generally available for distributed file systems such as HDFS and Amazon S3, more direct support of these storage backends would be useful in situations where GenomeAssist is being installed by users in restricted computing environments who cannot or do not wish to install and configure these drivers.

References

[1] BLAST: Basic local alignment search tool. National Center for Biotechnology Information. http://blast.ncbi.nlm.nih.gov/.

[2] Django: The Web framework for perfectionists with deadlines. Django Software Foundation. https://www.djangoproject.com/.

[3] Ben Langmead, Michael Schatz, Jimmy Lin, Mihai Pop, and Steven Salzberg. Searching for SNPs with cloud computing. *Genome Biology*, 10(11):R134, 2009.

[4] Ben Langmead, Cole Trapnell, Mihai Pop, and Steven Salzberg. Ultrafast and memory-efficient alignment of short DNA sequences to the human genome. *Genome Biology*, 10(3):R25, 2009.

[5] Heng Li and Richard Durbin. Fast and accurate short read alignment with Burrows–Wheeler transform. *Bioinformatics*, 25(14):1754–1760, Jul 2009.

[6] Heng Li and Nils Homer. A survey of sequence alignment algorithms for next-generation sequencing. *Briefings in Bioinformatics*, 11(5):473–483, 2010.

[7] Ask Solem and contributors. Celery: Distributed task queue. http://www.celeryproject.org/.