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Blanquer I, Brasche G, Cala J, Gagliardi F, Gannon D, Hiden H, Soncu H, Takeda K, Tomas A, Woodman S. [Supporting NGS pipelines in the cloud.](#)

*EMBnet.journal* 2013, 19, 14-16.

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DOI link to article: <http://dx.doi.org/10.14806/ej.19.A.625>

**Date deposited:** 19th May 2014



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## Supporting NGS Pipelines in the cloud

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### Motivation and Objectives

The availability of workflow management systems (Romano, 2007, Smedley *et al.*, 2008) and public cloud computing infrastructures (Schatz *et al.*, 2010) have become a major breakthrough in the usage of computing resources for scientists / the science community. However, the combination of both approaches has shortcomings (Magellan Final Report, 2011, Blanquer *et al.*, 2012), such as the need to reduce administration effort to user, or the need for simple programming models for the transition from previous more conventional computing approaches and the support of legacy software. Although projects such as GATK, galaxy, 1000genomes (<http://www.1000genomes.org/>) use cloud, end users must have sophisticated knowledge of IT to deploy and use such resources. With this in mind, Microsoft Research (Microsoft Research– Cloud Research Engagement, 2013) has started several initiatives to improve the use of clouds in science. The “cloud4science” initiative, see <http://www.cloud4science.eu/>, considers next generation sequencing (NGS) as an excellence reference use case. This initiative builds on the results of the VENUS-C and e-Science Central projects, see <http://www.venus-c.eu/> and <http://www.es-sciencecentral.co.uk/>, in which two different scientific workflow engines, namely the *Generic Worker* and *e-Science Central* were applied to solve specific bioinformatics problems requiring intensive computing. We propose an integration and enhancement of these two workflow engines with a set of selected bioinformatics tools to provide an easy-to-use framework for a cloud-enabled NGS pipeline for mutation analysis.

The resulting framework and components will simplify the deployment of processing services, the access to data and the sharing of the results.

### Methods

The development of the framework focuses on three different categories: Computing resources;

workload management and orchestration software; and bioinformatics legacy software.

As public cloud computing resources we selected Microsoft’s Windows Azure, see <http://www.windowsazure.com>. Windows Azure provides both users and application developers with different abstraction levels (PaaS and IaaS), including the support of Windows or Linux Virtual Machines (which is a requirement for many Bioinformatics tools). This makes Windows Azure an attractive platform to build upon.

The workload management and orchestration software need to deal with the two main types of NGS workflows: Coarse-grained data flows and fine-grained complex workflows. To tackle the first problem, the Generic Worker has been selected as it has been proven to be efficient in large-scale alignment problems (Carrión *et al.*, 2012). To deal with finer-grain complex workflows, eScience Central is used. E-science Central can scale very well in drug discovery problems (Cala *et al.*, 2012). Reference data for alignment is obtained from the UCSC Genome Bioinformatics repository (<http://hgdownload.cse.ucsc.edu>), and it is replicated in the Azure storage for convenience.

Finally, for the implementation of the pipeline, several tools have been selected for the initial prototype, covering sequence conversion (seqtk – <https://github.com/lh3/seqtk> and samtools – <http://samtools.sourceforge.net/>), Quality Control Analysis (fastqc – <http://www.bioinformatics.babraham.ac.uk/projects/fastqc/>), alignment (bowtie2 – <http://bowtie-bio.sourceforge.net/bowtie2> and HPG aligner – <http://docs.bioinfo.cipf.es/projects/hpg-aligner>), Variant call file generation (GATK – <http://www.broadinstitute.org/gatk/>) and visualization (GenomeMaps – <http://www.genomemaps.org/> and JBrowse – <http://jbrowse.org/>).

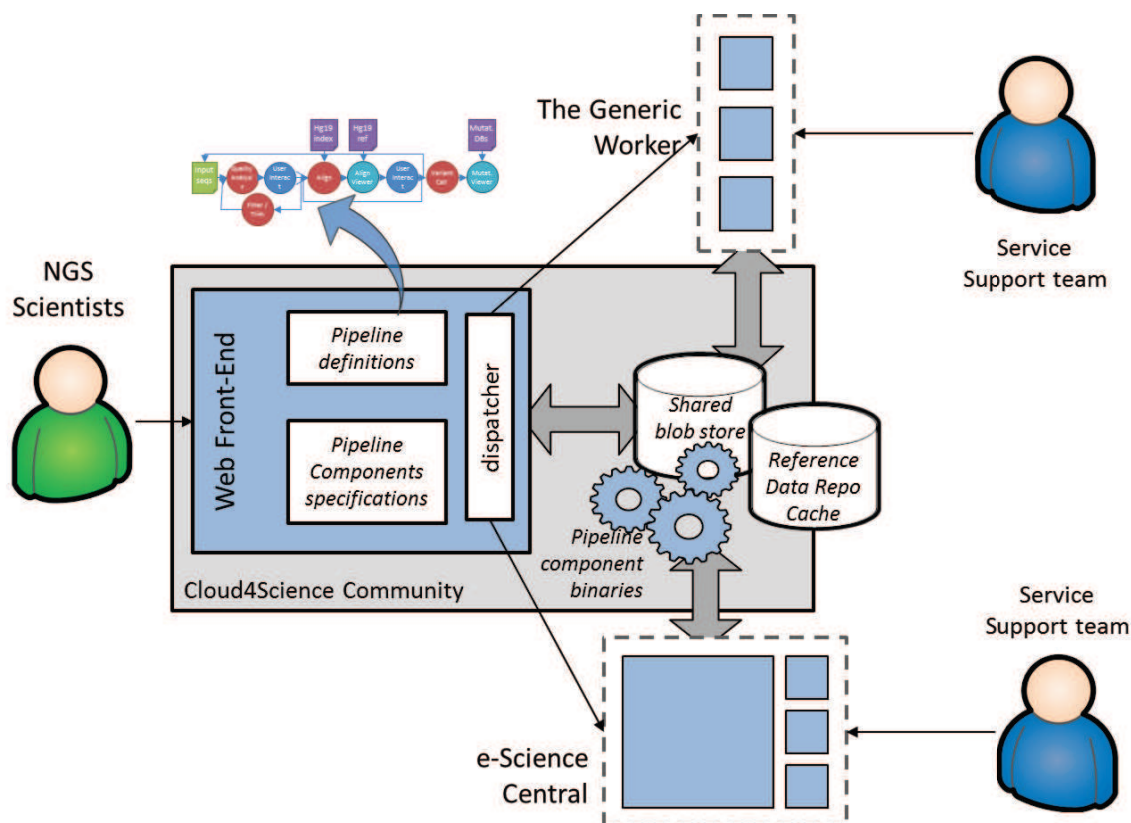


Figure 1. Simplified Architecture of the C4S platform-NGS framework

## Results and discussion

The components are integrated through a shared blob store that hosts user-specific and shared data. As shown in Figure 1, the two different deployments of the enactment services are orchestrated through a web front-end, which exposes the interface to the users. The user interface is customized to guide the user through the different steps: uploading, conversion, quality control, trimming and filtering (repeatedly), alignment, visualization, quality control, variant call and final visualization. Interaction is managed through the use of server-based visualization tools, such as GenomeMaps. Early results of the performance achieved by the individual components demonstrated speed-up factors in the order of 63 times faster with 100 Azure cores (efficiency of 63%) using Generic Worker (Carrión *et al.*, 2012) and 176 times faster with 200 Windows Azure cores (efficiency of 88.2%) using e-Science Central (Cala *et al.*, 2012). Improved results will be obtained by optimizing the data transfer among the processing nodes.

This first prototype will be improved in the first half of 2013 providing the users with more flexibility to alter the workflow, repeating or skipping individual or grouped steps and enhanced management of data to foster sharing and collaboration.

Eventually, it is important to note that the software in development in this project aims to becoming self-supported in the future by the establishment of an open end-user community, by the adoption of an open source software license scheme. Generic Worker and e-Science Central are released through Open Source licenses and the entire Cloud4Science environment will be released in the form of an open and collaborative project.

## Acknowledgements

The authors want to thank Microsoft and the cloud4Science project for funding this research activity.

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