STATISTICAL ANALYSIS OF BIOMOLECULAR DATA USING UNICORE WORKFLOWS

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Keywords: UNICORE, Workflow, R environment, GridBean.

Abstract: Nowadays the role of e-Science is important, especially in the area of life sciences. Experiments and their analysis are carried out in collaboration of many scientific groups from institutes located all over the world. Moreover, they work with immense amount of data which usually needs to be processed statistically. Therefore, the need for computing power is increasing. It usually can not be supplied by a standard laboratory. That is why e-Science makes use of grid technology. UNICORE (Uniform Interface to Computing Resources) is a middleware enabling access to the Grid resources in a seamless and secure way.

In this paper we present UNICORE gridbean for statistical R environment which enables to process statistically data on the Grid. Being used as a part of more complex workflow task it can analyze results given by another applications and calculate needed statistics. By presenting example workflow constructed in UNICORE Rich Client application, authors show power of the Chemomentum workbench built on UNICORE Grid system.

1 INTRODUCTION

Growing need for computing power in many areas of scientific research has entailed interest in the grid technology. It has been successfully used in many projects within areas such as 3D graphics, quantum chemistry, molecular modeling or bioinformatics. Particularly, computing power plays an important role in biology research. Increasing number of known sequences, huge molecules systems and metabolic pathways demand a lot of computational time for processing. The grid middleware which offers an uniform access to the resources can be a very attractive solution. It enables the use of geographically distributed resources through the Internet. Running several tasks on the different computing systems can save time significantly. Grid environments like UNICORE (Uniform Interface to Computing Resources) provide access to the resources and applications in a seamless and secure way.

Applications such as BLAST (Basic Local Alignment Search Tool), Clustal and NAMD (Not Another Molecular Dynamics) are widely used by the molecular biology scientists. Authors successfully supported them on the UNICORE Grid (Borcz et al., 2007; Kluszczyński and Bała, 2008; Kluszczyński and Bała, 2009). However, there has been noticed the need for the statistical tools to analyze data. We have decided to develop a gridbean which integrates the statistical environment R with the grid. The purpose of this paper is to present plugin for the UNICORE Rich Client. Next, authors point out UNICORE ability to construct scientific workflows to create complex simulations to process and analyze biomolecular data.

2 MOLECULAR LIFE SCIENCES

The aim of Life sciences is to study living organisms to help explaining how they are related to each other and to the environment. Biology plays here key role along with the computer and information sciences. Bioinformatics is one of the disciplines which has become very popular nowadays. There exist many confusions about the definition of “bioinformatics”. According to the Bioinformatics Definition Committee of Biomedical Information Science and Technology

Borcz M., Kluszczyński R. and Bała P. (2010).
STATISTICAL ANALYSIS OF BIOMOLECULAR DATA USING UNICORE WORKFLOWS.
In *Proceedings of the First International Conference on Bioinformatics*, pages 217-220
DOI: 10.5220/0002742102170220

Initiative Consortium (Huerta et al., 2000) bioinformatics is related to the databases and focuses on computational tools to store, archive, analyze and visualize biology data. It is strongly related to the computational biology, which studies biological systems by developing methods for mathematical modeling and techniques for simulations.

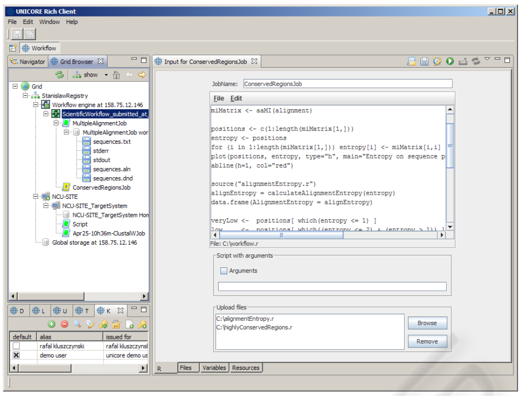
Biologists and programs they use have to handle huge amount of data. As an example can serve NAMD, an application for molecular dynamics, which simulates the behavior of a molecular system of many thousands of atoms. BLAST is used to find regions of similarity between the DNA sequences. It searches through huge sequence databases and compares very long strands. Clustal allows for enacting pairwise alignment and can create a phylogenetic tree and use it to align multiple sequences. Typical experiments consist of many steps and sequence alignment is usually one of them. Therefore programs widely used by biologists require computing power that can not be provided by a standard computer facilities available at research lab or department.

High throughput experiments and large simulations produce output which has to be statistically processed. It can be done using various programs like R, SPSS or Statistica. Authors focus on the first of them. R is a free software environment and a high level programming language for statistical calculations and data analysis. It enables scientists like mathematicians, physicians and biologists to make calculations and to visualize the data. Besides basic commands and functions there are available more than 1700 technical packages providing more advanced tools.

3 SCIENTIFIC WORKFLOW SYSTEMS

Workflows play central role in the computationally intensive science (e-Science). They can be used as analysis pipelines in many disciplines such as biology, chemistry, geosciences or physics. In the 2004 the definition of a workflow in the grid systems has been postulated by the Global Grid Forum (Fox and Gannon, 2006). In the Grid context workflow is automation of the processes which involves the orchestration of a set of grid services or agents that must be combined together to solve a problem or to define a new service. The advantages of the scientific workflows are numerous (Yu and Buyya, 2005). Below we present most important ones:

- an ability to build dynamic applications which use distributed resources,
- dynamic utilization of resources in order to increase throughput and reduce execution costs,
- promotion of a collaborations between scientific groups involved in a different parts of the experiment.



Grid
StanislawRegistry
Workflow engine at 158.75.12.146
ScientificWorkflow_submitted_at_
MultipleAlignmentJob
MultipleAlignmentJob wor
sequences.txt
stderr
stdout
sequences.aln
sequences.dnd
ConservedRegionsJob
NCU-SITE
NCU-SITE_TargetSystem
NCU-SITE_TargetSystem Hom
Script
Apr25-10h36m-ClustalWJob
Global storage at 158.75.12.146

default	alias	issued for
□	rafal kluszczynski	rafal kluszczynsl
☒	demo user	unicore demo us

JobName: ConservedRegionsJob

```
miMatrix <- aaMI(alignment)

positions <- c(1:length(miMatrix[1,]))
entropy <- positions
for (i in 1:length(miMatrix[1,])) entropy[i] <- miMatrix[i,i]
plot(positions, entropy, type="h", main="Entropy on sequence p
abline(h=1, col="red")

source("alignmentEntropy.r")
alignEntropy = calculateAlignmentEntropy(entropy)
data.frame(AlignmentEntropy = alignEntropy)

veryLow <-  positions[ which(entropy <= 1) ]
low     <-  positions[ which((entropy <= 2) & (entropy > 1)) ]
```

File: C:\workflow.r

Script with arguments

□ Arguments

Upload files

C:\alignmentEntropy.r
C:\highlyConservedRegions.r

Figure 1: UNICORE Rich Client application with loaded gridbean for R Environment.

Workflow systems are being developed as a part of grid middlewares and as a standalone applications.

The UNICORE middleware has an ability to build and run workflows on the grid. The UNICORE workflows allow the use of loops and if-else statements to create sophisticated tasks run on the remote systems.

4 UNICORE GRID MIDDLEWARE

Standards used in grid middlewares have been changing over the time and new application areas have been discovered. UNICORE project has been established in 1997 in order to enable an easy and secure access to supercomputers in Germany (Streit, 2009). During the last decade it has become international and has been successfully used in many scientific projects. Its popularity is still growing and today UNICORE is widely utilized in Europe along with other widely known grid environments like gLite, Globus and ARC.

Version 6 of the UNICORE middleware is being developed based on the web-service technology and adopts grid services standards. UNICORE provides a flexible and user-friendly client framework. UNICORE Rich Client (URC) targets a wide range of users with varying grid experience. It provides a graphical view of the grid and can be run on most of the platforms. URC offers to the users a full set of functionalities in a graphical representation. The user may see his previous and currently running jobs and download the results or specific resources from the grid (Fig. 1).

Applications are integrated with the UNICORE infrastructure through gridbeans. Gridbeans separate the layer of application specific user interface from the actual implementation of grid middleware. This idea emerges from the experience of UNICORE 5 (Ratering, 2005) and is considered as one of the highest advantages of UNICORE.

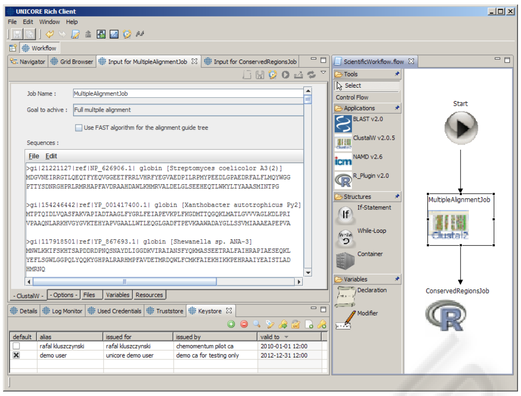
5 APPLICATION GRIDBEANS

Gridbeans are plugins which provide a graphical interface to the application. Grid environments supply clients with special services enabling to download plug-ins by simply selecting them from the list. Once gridbean is loaded into the client, a user can run tasks without any specific knowledge about the environment or the way of executing the program on the host. He just has to fill in particular fields and options in the interface and than press submit button. Moreover, UNICORE clients have an ability to check the existence of application on the grid. User can see available programs on particular target systems and decide which one to use.

In the last years, authors have developed gridbeans for bioinformatics tools like BLAST, NAMD or Clustal (Borcz et al., 2007; Kluszczyński and Bała, 2008; Kluszczyński and Bała, 2009). All mentioned gridbeans provide a graphical interface which makes possible to run the applications in an easy way. They contain special fields and components to input data and to set up options. Moreover, BLAST and Clustal interfaces are designed in a way similar to the existing web interfaces, to which biologists are used to.

Recently, we have designed and implemented `RGridBean`. It integrates statistical R environment (R Development Core Team, 2005) with the grid and it can be used as a part of workflow. The R has been already integrated with the ACGT grid environment based on Globus Toolkit 4 (Wegenera et al., 2009), however it cannot be reused in the UNICORE workflows. Grid solutions proposed in (Grose et al., 2006; Wegenera et al., 2009) demand knowledge about new R packages from the users. UNICORE Rich Client allows to run R scripts on the grid without execution of additional commands. With the help of `RGridBean` users just select the script and submit it to the remote system. The script remains in the same form in which it was executed locally on the PC.

In the example presented in the section 6 the R plugin processes the results given by other biology applications. The main panel (Fig. 1), besides a field for a job name, contains a text area to write commands and open or save scripts. Moreover, there have been prepared special components, which allow to input script arguments and attach additional files. After job is finished, user can see its results shown in two different output panels. In the first one, there are visible results of calculations presented as text. In the second there are displayed generated plots which can be saved in a PNG format.



Job Name : MultipleAlignmentJob

Goal to achive : Full multpile alignment

☐ Use FAST algorithm for the alignment guide tree

Sequences :

```
>gi|21221127|ref|NP_626906.1| globin [Streptomyces coelicolor A3(2)]
MDGVNEIRRGTLQEQTFYEQVGGEETFRRLVHRFYEGVAEDPILRPMYPEEDLGPAEDRFALFLMQYWGG
PTTYSDNRGHPRLRMRHAPFAVDRAAHDAWLKHMRVALDELGLSEEHEQTLWKYLTYAAASMINTPG

>gi|154246442|ref|YP_001417400.1| globin [Xanthobacter autotrophicus Py2]
MTPTQIDLVQASFAKVAPIADTAAGLFYGRLFEIAPEVKPLFKGDMTTQGQKLMATLGVVVAGLKDLPRI
VPAAQNLARKHVGYGVKTEHYAPVGAALLWTLEQGLGADFTPEVKAAWADAYGLLSSVMIAAAEAPEPVA

>gi|117918501|ref|YP_867693.1| globin [Shewanella sp. ANA-3]
MNWLKKIFSKHTSAPDDRDPNQSNAYDLIGGDKVIRAIANSFYQKMASSEETRALFAIHRAPIAESEQKL
YEFLSGWLGGPQLYQQKYGHPALRARHMPFAVDETMRDQWLFCMKFAIEKHIKKPEHRAAIYEAISTLAD
HMRNQ
```

default	alias	issued for	issued by	valid to
☐	rafal kluszczynski	rafal kluszczynski	chemomentum pilot ca	2010-01-01 12:00
☒	demo user	unicore demo user	demo ca for testing only	2012-12-31 12:00

Figure 2: An example of a scientific workflow involving Clustal and R gridbeans. The workflow is presented in the dedicated editor of the UNICORE Rich Client.

6 WORKFLOW EXAMPLE

UNICORE Rich Client has an ability to design workflow tasks combining several applications. This functionality is provided by a workflow editor. It enables a graphical construction of tasks together with programming blocks realizing loops and if-else statements. Workflows consist of tasks or processes. Workflow elements are related by dependencies corresponding to the data flow between them. As blocks of such workflows there are used gridbeans, which are downloaded to the client. Of course some tasks can be independent and not related to other workflow components. With every sub-job, user can assign the site where it should be run or leave decision to the workflow service. Dedicated editor enables very user-friendly and intuitive construction of workflows. URC supports drag-and-drop technique, which makes it easy to design workflow structure and dependencies between elements.

In Fig. 2 there is presented an example workflow which uses Clustal and R gridbeans. Designed experiment at the first stage aligns a family of globin proteins. Next, the multiple alignment obtained by Clustal is statistically processed. The results are presented in the text and graphical form. It is important to mention, that once designed workflow can be used in the future. To execute simulations for another family of proteins the user should just change the sequences data in the gridbean for Clustal and resubmit the workflow.

During the protein sequence analysis scientists usually look for motifs. These are small conserved regions which have functional and structural significance. However, regions with a high number of changes are responsible for the specificity of molecules. Shannon entropy as the measure of uncertainty in a data set is a good indicator of variability (Bui et al., 2007). Entropy can be calculated in the R environment in an easy way using aaMI package (Wollenberg, 2005).

The article (Bui et al., 2007) provides an example of such an application. Its authors analyze the arenavirus protein sequence variability to identify conserved regions that could be targeted for development of a universal renaviral vaccine. They looked also for high variable regions which could be helpful in diagnosis. To do this they performed multiple sequence alignments of chosen proteins using ClustalW program and calculated Shannon entropy. Fig. 2 presents an example of a workflow performing similar tasks.

Of course workflows can be much more complicated. The UNICORE can handle workflows with thousands of elements and dependencies. With the help of an editor it is very easy to create even so complex simulations.

7 CONCLUSIONS

In this paper authors presented plugin designed for statistical R environment. It makes it possible to analyze and process data from many scientific applications, not only limited for molecular ones like BLAST, Clustal or NAMD. Being used as a part of workflow, it plays crucial role in experiment conclusions. The workflow systems can be very useful for scientists. With the help of special editors, like the one in UNICORE middleware, workflow construction is intuitive and user-friendly. An additional advantage is the reduction of frequency of human errors. Once designed workflow can by used for different data. This automates the process of experiment enabling the scientists to focus only on results and conclusions.

ACKNOWLEDGEMENTS

This work was supported by European Commission under IST grant Chemomentum (No. 033437) and the European Social Fund with the National Budget of the Republic of Poland under the Integrated Regional Development Operational Programme, Objective 2.6 „Regional Innovation Strategies and transfer of knowledge“ project of Kujawsko-Pomorskie Province „Scholarships for PhD Students 2008/2009 - ZPORR“.

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