Enhancing Collaboration in Big Biomedical Data Settings
Knowledge Visualization, Data Mining and Decision Making Issues

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Keywords: Big Data, Data Mining, Decision Support Systems, Collaboration, Knowledge Visualization, Data and Information Quality, Situational Awareness, Biomedical Data.

Abstract: Biomedical researchers need to efficiently and effectively collaborate and make decisions by meaningfully assembling, mining and analyzing available large-scale volumes of complex multi-faceted data residing in different sources. Arguing that dealing with data-intensive and cognitively complex settings is not a technical problem alone, this paper reports on the development and practical use of an innovative web-based collaboration support service in a biomedical research context. The proposed service builds on the synergy between machine and human intelligence to facilitate and augment the underlying knowledge management, data mining and decision making processes. Evaluation results indicate that the service enables stakeholders to make more informed decisions, by displaying the aggregated information according to their needs.

1 INTRODUCTION

Collaboration support technologies and platforms are crucial in today’s biomedical research settings, where multidisciplinary communities ranging from biologists to bioinformaticians need to assimilate clinico-genomic research information and scientific findings and explore diverse associated issues (Ekins et al., 2011). At the same time, biomedical research is associated with large-scale amounts of multiple types of data, obtained from diverse and distributed sources. An ever-increasing volume of biomedical resources, including multiple types of data sets and analysis tools, are available on the web. For instance, recent technology advances in Next Generation Sequencing (NGS) platforms entail an exponential increase in the size and number of experimental data sets available (Quail et al., 2012). However, in most cases, the raw information is so overwhelming that researchers are often at a loss to even know where to begin to make sense of it.

This paper reports on a web-based collaboration support service that aims to fully cover the diversity of requirements in contemporary biomedical research settings by providing a series of innovative features. Firstly, the service provides advanced collaboration support functionalities through innovative virtual workspaces based on alternative data visualizations schemas. Secondly, it is able to meaningfully accommodate the outcomes of latent knowledge mining services in a collaboration session, thus offering added value concerning recognition of biomedical data patterns. Thirdly, by supporting emergent semantics and the incremental formalization of argumentative collaboration, it augments individual and collective decision making. By providing ease-of-use and expressiveness for users and advanced reasoning by the machine, the service also provides appropriate recommendation mechanisms that enable stakeholders to project their future actions in their dynamic working settings.

The proposed platform has been developed in the context of an FP7 EU research project, namely Dicode (http://dicode-project.eu/), which exploits and builds on prominent high-performance computing paradigms and large data processing technologies to facilitate and augment collaboration and decision making in data-intensive and cognitively-complex settings.

The remainder of this paper is structured as follows: Section 2 reports on related work and highlights existing problems and requirements; Section 3 sketches the overall approach followed in the Dicode project, putting emphasis on knowledge visualization, data mining and decision making issues; Section 4 provides an illustrative example to demonstrate the use of the proposed service in a
biomedical setting; finally, Section 5 concludes by discussing related remarks and outlining evaluation results.

2 RELATED WORK

Easy visualization and analysis of big biomedical data is a highly important requirement in the settings under consideration. Towards fulfilling it, a series of applications and web services that link together bioinformatic tools and databases have recently emerged. For instance, BioGRID (Stark et al., 2006), BNDB (Birkl and Yona, 2006) and BioMart (Guberman et al., 2011) are repositories which store readily combined data sets and provide platforms to easily visualize such data. Similarly, the GenePattern platform provides access to more than 180 tools for genomic analysis to enable reproducible in silico research (http://www.broadinstitute.org/cancer/software/genepattern/). In addition, many collaborative resource sharing networks have been established, e.g., the eagle-i consortium (https://www.eagle-i.net/), to address the researchers’ data sharing needs and accelerate the discovery of new knowledge. Integration of these separate systems and resources into a single flexible infrastructure that streamlines heterogeneous workloads is a challenging task.

At the same time, a number of projects and initiatives aim at addressing diverse collaboration requirements in a variety of biomedical contexts. For instance, GRANATUM (http://granatum.org) tries to bridge the information, knowledge and collaboration gap by providing integrated access to the globally available data resources needed to perform complex cancer chemoprevention experiments and conduct studies on large-scale datasets; Health-e-Child (http://www.health-e-child.org) gives clinicians a comprehensive view of a child’s health by integrating biomedical data, information and knowledge that spans the entire spectrum from imaging to genetic to clinical and epidemiological data; Virolab (http://www.virolab.org) offers a user friendly environment to facilitate tasks such as data archiving, data integration, data mining and simulation; finally, SIMBioMS (http://simbioms.org) is a multi-module solution for biomedical data management that is able to accommodate experiments requiring non-conventional data storage solutions.

While certainly helpful in addressing specific biomedical subjects, the above projects and initiatives do not deal with big data issues; moreover, they do not exploit the synergy between human and machine intelligence in order to meaningfully accommodate and interpret the results of the associated data mining services through an environment that facilitates and enhances collaboration among stakeholders.

As the number of related Web services is constantly increasing, their proper integration becomes a critical issue. A few approaches have been already launched to facilitate the collaboration, data sharing and decision making among scientists by providing them with a platform to share resources. A well known example of this category of related work is myExperiment (Goble et al., 2010), an online research environment that supports the social sharing of bioinformatics workflows, i.e., procedures consisting of a series of computational tasks, which can then be reused according to their specific requirements. Another representative example is BioCatalogue (http://www.biocatalogue.org/), which is a registry of web services that allows users to annotate and comment on the available services in order to assist them in identifying the more suitable ones (services are presented in terms of their functions, data types and resources). A third example is MethodBox (https://www.methodbox.org/), which enables researchers to browse and download data sets, share methods and scripts, find fellow researchers with similar interests and share knowledge. Instead of workflows, MethodBox users share statistical methods for epidemiology and public health research. Finally, the Galaxy Project (http://galaxy.psu.edu/) offers a web-based platform allowing researchers to perform and share their analyses. In any case, approaches of this category demonstrate a set of limitations, mainly concerning incorporation of collective intelligence and flexibility in the integration of services offered. Moreover, they lack mechanisms for a meaningful integration of data mining services to appropriately support tasks such as the discovery of patterns and dependencies within big data sets, which are very common in the biomedical research domain.

As results from the above, collaboration in the biomedical domain involves assembling and analyzing big volumes of complex multi-faceted data. In this context, a holistic approach integrating collaboration, new knowledge co-production, decision making and data mining services is required. Biomedical researchers need a highly flexible service that enables them to easily and meaningfully embed data mining in their collaborative data analysis and decision making.
process. This service should first of all be focused on improving efficiency; it has to improve current work practices that are often characterized by fragmentation of information and multiple disparate tools in use; it also has to improve the quality and speed of the current processes, paying much attention to data and decision provenance issues. Secondly, such a service should be focused on improving effectiveness, in that it enables stakeholders figuring out how to carry out their daily tasks better; for instance, how to improve their work methodologies when elaborating and interpreting big biomedical data residing in diverse sources. Finally, such a service should enable stakeholders transform their work, thus leading to new processes, innovative work methodologies, and new insights. The solution described in the next section is geared towards this direction.

3 COLLABORATION IN DICODE

Dicode provides a novel Web-based collaboration support service with advanced knowledge management, data mining and decision making functionalities. The service enables the seamless integration of these functionalities and allows their interoperation from both a technical and conceptual point of view. In this regard, semantics techniques have been exploited to define an ontological framework for capturing and representing the diverse stakeholder and associated data perspectives.

3.1 Knowledge Visualization Issues

Collaboration in Dicode brings together two paradigms: the Web 2.0 paradigm, which builds on flexible rules favouring ease-of-use and human interpretable semantics, and the traditional decision support paradigm, which requires rigid rules that reduce ease-of-use but render machine interpretable semantics. To achieve this, our approach builds on a conceptual framework, where formality and the level of knowledge structuring during collaboration is not considered as a predefined and rigid property, but rather as an adaptable aspect that can be modified to meet the needs of the tasks at hand. By the term formality, we refer to the rules enforced by the system, with which all user actions must comply. Allowing formality to vary within the collaboration space, incremental formalization, i.e. a stepwise and controlled evolution from a mere collection of individual ideas and resources to the production of highly contextualized and interrelated knowledge artifacts and finally decisions, can be achieved (Shipman and McCall, 1994).

Dicode offers alternative visualizations of the collaboration space (called ‘Dicode views’), which comply with the incremental formalization concept. Each Dicode view provides the necessary mechanisms to support a particular level of formality. The more informal a view is, the greater easiness-of-use is implied. At the same time, the actions that users may perform are intuitive and not time consuming; however, the overall context is human (and not system) interpretable. On the other hand, the more formal a view is, the smaller easiness-of-use is rendered; the actions permitted are less less and more time consuming. The overall context in this case is both human and system interpretable (Karacapilidis and Tzagarakis, 2012). The views that are particularly interesting in the context of this paper are:

- **Mind-map View**: a collaboration space is displayed as a mind map (Figure 1), where users can interact with the items uploaded so far. The map deploys a spatial metaphor permitting the easy movement and arrangement of items on the collaboration space. The aim of this view is to support information triage (Marshall and Shipman, 1997), i.e. the process of sorting and organizing through numerous relevant materials and organizing them to meet the task at hand.

- **Formal View**: this view enables the posting of predefined knowledge items, which adhere to a specific argumentation model (i.e., IBIS (Kunz and Rittel, 1970)). It invokes a set of dedicated scoring and reasoning mechanisms aiming to aid users conceive the outcome of a particular collaborative session and receive support towards reaching a decision (Figure 2).

In the ‘mind-map view’ of the collaboration space, stakeholders may organize their collaboration through dedicated item types such as ‘ideas’, ‘notes’, ‘comments’ and ‘services’. Ideas stand for items expressing one’s knowledge about the overall issue, an already asserted idea or note. Comments are items that usually express less strong statements and are uploaded to express some explanatory text or point to some potentially useful information. Multimedia resources can also be uploaded into the mind-map view (the content of which can be displayed upon request or can be
directly embedded in the workspace).

A detailed description of the knowledge visualization related technologies can be found in (Karacapilidis et al., 2011).

3.2 Data Mining Issues

In the ‘mind-map view’, service items enable users to configure, launch and monitor the execution of external data mining services from within the collaboration workspace, and allow the automatic upload of their results into the workspace when the execution of these services terminates.

As with any other item type, users may specify a title and a content, which gives the ability to attach a longer description to the item, when such an item type is uploaded into the collaboration workspace. Once uploaded, users may configure the item and specify which data mining service it corresponds to. The set of available data mining services with which the service item can be associated is stored centrally at a dedicated registry (the exploitation of a specific data mining service; namely Subgroup Discovery, is discussed in Section 4). Once service items on the collaboration workspace have been configured, they can be executed by supplying the required parameters to the data mining service. Visual cues indicate the status of service items: whether they have yet to be executed, are currently executing or have finished their execution.

Service items appearing on collaboration workspaces can be explicitly related with other items in the workspace via relationships or can be spatially arranged and grouped. When the execution of a service item terminates, the results – consisting of one or more files – are automatically uploaded into the collaboration workspace and explicitly connected to the service item whose execution produced them.

Once the results of service items are available (i.e., uploaded into the collaboration workspace), users can treat them as regular items. Furthermore, users may rate service items in order to indicate which service they consider as the most useful one in the context of the discourse.

More details on the data mining technologies exploited in our approach can be found in (Tsiliki et al., 2012).

3.3 Decision Making Issues

In the ‘formal view’ of the collaboration space, the available knowledge item types include ‘issues’, ‘alternatives’, ‘positions’, and ‘preferences’. Issues correspond to problems to be solved, decisions to be made, or goals to be achieved. For each issue, users may propose alternatives (i.e. solutions to the problem under consideration) that correspond to potential choices. Positions are asserted in order to support the selection of a specific course of action (alternative), or avert the users’ interest from it by expressing some objection. A position may also refer to another (previously asserted) position, thus arguing in favour or against it.

Finally, preferences provide individuals with a qualitative way to weigh reasons for and against the selection of a certain course of action. A preference is a tuple of the form [position, relation, position], where the relation can be “more important than” or “of equal importance to” or “less important than”. The use of preferences results in the assignment of various levels of importance to the alternatives in hand. Like the other discourse elements, they are subject to further argumentative discourse.

The above four semantic types of items enable users to contribute their knowledge on the particular problem or need (by entering issues, alternatives and positions); as well as to express their relevant values, interests and expectations (by entering positions and preferences). Moreover, this view continuously processes the elements entered by the users (by triggering its reasoning mechanisms each time a new element is entered), thus facilitating users to become aware of the elements for which there is (or there is not) sufficient (positive or negative) evidence, and accordingly conduct the discussion in order to reach consensus.

Alternatives, positions and preferences have an activation label indicating their current status (they can be active or inactive). This label is calculated according to the argumentation underneath and the type of evidence specified for them. Active elements are taken into account in a scoring mechanism that calculates the weight of each alternative expressed and indicates the one that prevails each time (for more details on the decision making algorithms used, see (Karacapilidis and Papadias, 2001)).

Dicode collaboration spaces can be transformed at any time from one view into another. During such transformations, the semantically enriched item types available in one view are transformed into the respective item types of the desired destination view. The transformation is rule-based; such rules can be defined by users participating in a collaboration session and reflect the evolution of a community’s collaboration needs. After a transformation into the desired view occurs, the collaboration may continue in this view, with the users being able to exploit the item types available in order to keep conducting the
discourse in the desired formality level and take advantage of the provided functionality.

4 AN EXAMPLE OF USE

To better illustrate the use of the proposed Web-based collaboration support service and in particular how the available functionalities can be used in the biomedical context, we present a scenario which is indicative of the way researchers collaborate in this field, where research is carried out by multidisciplinary teams consisting of biologists, medical doctors, clinical researchers and statisticians, each of which contributes from his/her perspective to the problem being discussed.

Figure 1 shows the collaboration workspace operated in the ‘mind-map view’, where a team of three researchers is discussing an issue related to breast cancer research. In particular, they are collaborating in order to determine how to augment existing datasets in order to study how Tamoxifen (Tam) resistant cells modulate global gene expression.

Tam is a widely used antagonist of the estrogen receptor, whereas its resistance is a well-known obstacle to successful breast cancer treatment (Huber-Keener et al., 2012). While adjuvant therapy with Tam has been shown to significantly decrease the rate of disease recurrence and mortality, recurrent disease occurs in one third of patients treated with Tam within 5 years of therapy. The team initially selected and analyzed gene-expression data from 300 patient samples. These data are derived from whole human genome expression arrays (Affy U133A Plus 2.0, see http://www.affymetrix.com). Although the sample is relatively large, they believe that augmenting the data with publicly available data will be a good idea for obtaining statistically significant results.

All participating researchers may upload into the collaboration workspace items to express their opinion on the issue being discussed. In the instance shown in Figure 1, they have uploaded items of type ‘idea’ to propose additional data sets (“Consider also Next Generation Sequencing (NGS) data” (Figure 1 - (a)) and “Work with gene-expression data (Figure 1 - (b))). Participants have responded to the proposed alternatives (ideas) by uploading items and connecting them via arrows to other items to which they refer. Participants may also change an arrow’s colour to indicate the semantics of the relationship: green-coloured arrows express arguments in favour, red-coloured arrows express arguments against,
while grey-coloured arrows indicate neutrality. Furthermore, they can aggregate items on the workspace by drawing coloured rectangles around them and give a title to the groupings. For example, the orange-coloured rectangle with title “Supplementary information” (Figure 1 - (c)) groups together bibliographic resources that the team has obtained from external repositories and are relevant to their research.

As the discussion evolves, the team thinks about exploiting the Subgroup Discovery (SD) data mining algorithm (Atzmueller et al., 2005) using both data sets as input. SD is the task of finding patterns that describe subsets of a data set that are highly correlated relative to a target attribute. This is a popular approach for identifying interesting patterns in the data, since it combines a sound statistical methodology with an understandable representation of patterns. For example, in a group of patients that did or did not respond to specific treatment, an interesting subgroup may be that patients who are older than 60 years and do not suffer from high blood pressure respond much better to the treatment than the average.

To invoke the SD algorithm on the NGS data, they upload the associated service item into the workspace (Figure 1 - (e)) and start configuring the service. Configuring the service includes the specification of the URI for the REST-based SD service and specification of parameters such as input file, number of rules to be used, service ontology, and minimum number of subgroups to be retrieved (more details can be found in (Tsiliki et al., 2012)). After configuring the service, they trigger its execution. As long as the SD service is executing, the icon representing the service appears with a green colour. Upon successful termination of the SD service, the icon changes its colour to orange and the results are automatically uploaded into the collaboration workspace (Figure 1 - (f)). To clearly indicate the execution of the SD service on the gene expression data and the results it returned, the team groups together the relevant items and supplies a descriptive title (“Apply data mining to NGS data”). The team can now assess the output of the SD execution by commenting on the results and connecting them to other items in the collaboration workspace (Figure 1 - (g)).

The team can follow the same procedure (invoking the SD service and collectively assessing its output) for the gene expression data. The three researchers are able to carefully examine the commonalities between the two SD runs (on gene expression and NGS data) and share their insights.

As the collaboration continues and more items are added to the collaboration space, the team decides to switch to a different view, in order to reach a decision. For this, they decide to transform the ‘mind-map view’ into the ‘formal view’, which provides elaborated scoring and reasoning mechanisms that further facilitate the decision making process. By transforming the ‘mind-map view’ into the ‘formal view’, they can assess the output of the SD service and connect it to other items in the collaboration workspace.

![Figure 2: The ‘formal view’ of the collaboration illustrated in Figure 1.](image-url)
view’ of the collaboration workspace, all available semantic types – including the service items - are transformed into the appropriate types of the ‘formal view’, based on well-specified rules.

Figure 2 shows the collaboration space in the ‘formal view’. As noted above, the team can continue the collaboration in this view by adding more items (each time a new item is added, the reasoning mechanism is triggered). Furthermore, it allows the team to see which is the best argumented alternative solution (or ‘winning’ solution) by highlighting it using visual cues. Based on the current state of the collaboration, the currently ‘winning’ solution is the alternative “Consider also NGS data” (item in blue underlined font colour in Figure 2).

5 DISCUSSION & CONCLUSIONS

5.1 Evaluation Issues

Dicode has been already introduced in three real-life settings (i.e. the biomedical research assimilator, decision making on clinical treatment effects, and opinion mining from unstructured Web 2.0 data) for a series of pilot experimentations. For the setting considered in this paper, 61 users from 4 European countries participated in a detailed evaluation of the proposed service. The above users had a varying level of hands-on experience in related technologies (ranging from ‘early adopters’ to semi-experienced and novice users); their background was on disciplines such as Bioinformatics, Biology and Computer Science. Feedback requested was of both quantitative and qualitative type. Answers to the quantitative questions of the questionnaires were given for ordinal data in a 1-5 scale (questions concerning the quality, acceptability and accessibility of the service), where 1 stands for ‘I strongly disagree’ and 5 for ‘I strongly agree’, and for continuous numerical data (scale data) in a 0-10 scale (questions concerning the services’ usability), where 0 stands for ‘none’ and 10 for ‘excellent’.

As far as the overall quality of the proposed collaboration support service is concerned (Table 1), the evaluators agreed that: the objectives of the service are met (median=4, mode=3), the service is novel to their knowledge (median=4, mode=4), they are satisfied with the performance of the service (median=4, mode=4), and they are overall satisfied with this service (median=4, mode=4). The evaluators seemed to be to some extent sceptical as to whether the service is able to address the data intensive decision making issues (median=3, mode=3).

With respect to the acceptability of the service, the evaluators overall agreed that the service has all the functionality they expected (median=4, mode=3), the interface of the service is pleasant (median=4, mode=4) and that they will recommend this service to their peers/community (median=4, mode=3).

The analysis of qualitative evaluation results showed that, overall, reviewers found the service “promising”, “easy and intuitive”, as well as “very useful for a complex use case”. However, a few technical and documentation issues were raised, such as: “A bit slow loading time both for the workspace list and the mind-map view”; “The arrows’ graphics were not very pleasant for me: they start from the middle of the icon and not from the beginning of the square ... the overall idea however, is quite good”; “I got a bit confused until I fully understand what I had to do”; “I often missed some system information”.

Such findings reveal the need for more detailed documentation of the service, as well as for provision of help files and system messages.
5.2 Final Remarks

The service described in this paper offers an innovative environment that allows users “immerse” in Web 2.0 interaction paradigms and exploit its enormous potential to collaborate through reviewing, commenting on and extending the shared content. The Dicode environment enables stakeholders maintain chains of views and opinions, accompanied by the supporting data, which may reflect, at any time, the current collective knowledge on the issue under consideration, and justify a particular decision made or action taken.

The proposed service may fully cover the needs of the three stages of situational awareness needed in the above settings (Haendel et al., 2012; Kahn, 2011), namely perception (i.e. perceive the status, attributes, and dynamics of relevant elements in the setting under consideration), comprehension (i.e. perform a synthesis of disjointed elements of the previous stage through the processes of pattern recognition, interpretation, and evaluation), and projection (i.e. extrapolate information from previous stages to find out how it will affect future instances of the operational setting) (Endsley, 1995). Moreover, the development of the proposed service has adopted an agile, analytic and adaptive approach that enables stakeholders to fully leverage and reap the benefits of the associated biomedical “big data”. Such an approach can improve the quality and effectiveness of decisions in the context under consideration.

The service described in this paper has been integrated in the Dicode workbench environment (de la Calle et al., 2012), which is a web-based application that integrates - at the level of the user interface - various data mining and collaboration support services. The objective is to provide users with a uniform and easy access to the available Dicode services. The type and number of services appearing on the Dicode workbench can be easily configured by end users according to the needs of the particular context and problem under consideration. In such a way, current work practices have been admittedly improved in terms of efficiency and effectiveness. The issue of information fragmentation as well as that of data and decision provenance are properly addressed. Moreover, by providing users with useful hints, our approach enables stakeholders figuring out how to carry out their daily tasks in a more effective way. Finally, the proposed service enables stakeholders to follow and adopt innovative work methodologies, which build on the synergy of human and machine reasoning.

Future work directions include investigation of additional services for data-intensive computing (e.g. services already developed in projects such as ADMIRE - http://www.admire-project.eu), considering whether they can be integrated in the Dicode environment. Also, a thorough investigation of the Dataspace concept and the related data management abstraction (Halevy et al., 2006), considering its suitability to the purposes of our approach.

ACKNOWLEDGEMENTS

This publication has been produced in the context of the EU Collaborative Project “DICODE - Mastering Data-Intensive Collaboration and Decision”, which is co-funded by the European Commission under the contract FP7-ICT-257184. This publication reflects only the authors’ views and the Community is not liable for any use that may be made of the information contained therein.

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