A NEW LATENT SEMANTIC ANALYSIS BASED METHODOLOGY FOR KNOWLEDGE EXTRACTION FROM BIOMEDICAL LITERATURE AND BIOLOGICAL PATHWAYS DATABASES

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Abstract: Nowadays, a considerable amount of genetic and biomedical studies are mostly diffused on the Web and freely available. This exciting capability, if from one side opens the way to new scenarios of cooperating research, on the other side makes the knowledge retrieval and extraction an extremely time consuming operation. In this context, the development of new tools and algorithms to automatically support the scientist activity to achieve a reliable interpretation of the complex interactions among biological entities is mandatory.
In this paper we present a new methodology aimed at quantifying the biological degree of correlation among biomedical terms present in literature. The proposed method overcomes the limitation of current tools based on public literature information only, by exploiting the trustworthy information provided by biological pathways databases. We demonstrate how to integrate trusted pathway information in a semantic correlation extraction chain based on UMLS Metathesaurus and relying on PubMed as literature database. The effectiveness of the obtained results remarks the importance of automatically quantifying the degree of correlation among biomedical terms in order to helpfully support the scientist research activity.

1 INTRODUCTION

The pace of genetical and biological research has surprisingly spread in the last few years. The devepement of new technologies (DNA/RNA next generation sequencing) and the improvement of the old one (microarray for gene expression at lower costs) have being supporting the activity of scientists and researchers. Hundred of experimental results supported by the biotechnologic enhancement have highlighted the mechanisms behind the complex interactions among biological entities as well as brought to light new unknown phenomena. Nevertheless, if on one side this rising technological development opens the way to amazing scenarios in the biomedical research, the problem of handling the great amount of new information calls for the need of developing new computational infrastructures. Specifically, the capability of extracting relevant knowledge from genetical and biomedical studies has become one of the major thrusts in bioinformatic research. Nowadays, the main sources of information about the biomedical research are mainly biomedical literature databases and classification systems such as ontologies and thesaurus. Most of these systems are distributed on the Web and thus they are extremely easy to access and opened to the entire scientific community. However, in this scenario, the scientist have to face the twofold drawback of 1) *retrieving* the documents containing the information that he/she is looking for and 2) *correlating* the concepts in order to better extract the knowledge they provide. Both the operation are extremely time-consuming and the degree of correlation among biological concepts strongly depends on the scientist knowledge background. Therefore, an automated tool for the computation of a quantified score between biological terms according to literature information is strongly necessary in order to support the analysis of experimental results occurring during the research activity and to refine the design of the experiments by focusing on the most relevant features. The correlation score must be the result of a statistical co-occurrences analysis of biological terms both in the same article and in the related ones. Moreover, the tool must be able to integrate as many as possible sources of information, distributed on the Web and collected in different formats and structures, in order to guarantee the best accuracy and reliability for

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the computed biological correlation score. Section 2 overviews the state of the art where the proposed tool is contextualized. Section 3 shows the methodology used to both retrieve the biological pathway information and extract the knowledge by the overall information base. Section 4 demonstrates the effectiveness of the proposed approach in computing the biological correlation score among biomedical terms. In Section 5 the conclusions and the opening of the future work are faced.

2 BACKGROUND

To improve the quality of the search over public literature databases, many search engines have been developed to classify and correlate the huge amount of paper that a search may return. Most of this tools improves the search engine capability adopting ontologies and thesaurus as information base. *GoPubMed* (Doms, A. and Schroeder, M., 2005) is a search engine tools that make the search on *PubMed* (PubMed) repository categorized and ranked. In details, it applies text-mining algorithm in order to classify abstracts retrieved from PubMed according to terms coming from GO and *Medical Subject Headings* (MeSH) vocabulary (MeSH, 2005). A further extension to GoPubMed is *GoGene* (Plake, C. et al., 2009). The scope of this tool is to rank a list of genes, occurring in a document set after a PubMed search, according to terms of GO and MeSH. After performing a document search by means of GoPubMed, a text mining algorithm looks for gene names, GO and MeSH terms over the collection of paper abstracts. Finally, it returns a list of genes associated with concepts of GO and MeSH. Even if the association is performed computing a correlation score between a single gene and a term, the scope of the score is not to express a measure of biologic relationship between either two terms, or two gene, or a gene and a term, but it is an a posteriori statistical analysis that allows to map a gene into a ontology term. Furthermore, the problem of computing a quantified semantic correlation score among biological concepts according to the information coming from ontologies has been addressed in (Wang, J. Z. et al., 2007). In this work authors developed a tool for measuring the semantic similarity of two Gene Ontology terms (The Gene Ontology Consortium, 2000). The algorithm exploits the graph-based hierarchical topology of GO and it aggregates the semantic contribute of the ancestors providing a numeric value that reflects the distance among GO terms from the biological meaning point of view. Nevertheless, this tools is limited in foreclosing a set of biological topics related to the genetical and biological field and the base of information is strongly limited to the GO vocabulary. For instance, the medical term "*Parkinson* is not present in GO, therefore the correlation between this disease and a certain gene is uncomputable.

A different approach for providing a quantified measure among biological terms, based on the *Vector Space Model* theory is proposed in (Abate, F. et al., 2010). In this work, the authors apply the *Latent Semantic Indexing* (LSI) algorithm (Gliozzo, A. M. and Strapparava, C., 2005) to a set of document abstracts automatically retrieved through PubMed web services. The LSI algorithm is strongly based on the decomposition, by means of *Singular Value Decomposition* (SVD) algorithm, of a term-by-document occurrences matrix X in three sub-matrix U, Σ and V where U and V contain the left and right singular vectors of X and the matrix Σ is a diagonal matrix containing the singular values. The correlation score about two terms in the X matrix is calculated by applying the *cosine product* of the vector of U-*by*-Σ matrix corresponding to the correlating terms. Transforming the X matrix into the U-*by*-Σ matrix allows to consider not only the occurrences of terms but also the co-occurrences, exploiting the conceptual links among terms occurring in the different documents, but belonging to the same context. The analysis performed by the LSI algorithm is further coupled with a pre-processing phase based on the *Metamap* program, provided by NIH (Aronson, A. R., 2001). The algorithm behind Metamap allows to extract biomedical concepts from document text so that each abstract is translated into a list of biomedical concepts, namely a list of UMLS Concept Unique Identifiers (CUI) (Bodenreider, O., 2004). Moreover, the authors emphasize that the resulting correlation scores, namely *Semantic Correlation Score, SRS* allow the comparison among biological concepts belonging to the same retrieved document abstract set but it looses accuracy when comparing terms and concepts belonging to different experimental run and document set. Therefore, the SRSs go out of the scope of calculating an universal correlation score as the validity of the comparison is limited to a specific experimental run. In order to overcome this limitation, authors analyze the density function of the statistical distribution of the correlation scores within a single experimental run and divide the density function in percentiles. Consequently, the evaluation through percentiles allow to evaluate the correlation between genes and biological concepts independently of the experimental run, because it provides an information on the frequency distribution of the SRSs in the overall CUI set occurring

in an experimental run.

Nevertheless, the effectiveness of the methodology introduced in (Abate, F. et al., 2010) strongly depends on the reliance of the information in the retrieved abstract documents. Scientific papers, and specifically those from PubMed as far as the biomedical field is concerned, are certainly the most consulted source of information by scientist and biologist because they contain the more updated state of the art in science and medicine. However, the nature itself of biomedical literature is characterized by a significant level of uncertainty. In fact, the scientific publications, reporting the state of the art on scientific topics, are continually evolving and, as a consequence, the addicted argumentations might be often contradicting. Therefore, a biological correlation score computed by considering documents coming exclusively from the biomedical literature is affected by a certain level of uncertainty. For this reason, integrating the set of documents coming from literature with *trusted* information is a mandatory step in order to enhance the computational accuracy of the biological correlation among biological concepts. In order to get the scope, a twofold question must be answered: firstly, what are the *trusted* source of informations and to what extend a source of information can be considered as *trusted*; secondly, once the *trusted* information have been collected, what is the more effective way to integrate this information in the Latent Semantic Analysis algorithmic infrastructure?

2.1 *Trusted* Information Sources

It is worth underlining that several sources of biomedical information, mainly ontologies and thesaurus, are universally accepted as *trusted* source of information. GO, for instance, correlates gene and gene products by means of annotations. GO curators coordinate the development of the ontology rooted in the experimental literature through an annotation-driven process and, moreover, the accuracy of the relations and terms definitions are continually checked (Hill, D. P. et al., 2008). Moreover, genetic and metabolic pathways are a graph-based representation of the interaction of genes and proteins in a biological process.

The annotations related to new discovered pathways are collected in several pathway databases. These databases play a key role in the genetic and biologic research field. Examples of pathways databases that have been developed in the last years are the Kyoto Encyclopedia of Genes and Genomes (KEGG) (Kanehisa, M. and Goto, S., 1999), BioGRID (Stark, C. et al., 2006), HumanCyc (Romero, P. et al., 2004). On the base of pathways information, a number of knowledge based tools have been developed. In particular, *Pathway Commons* is a projects that aims at integrating all the distributed databases and the pathway information under a common web interface (Pathway Commons, 2007), providing a single access point to multiple pathway data sources. *Pathway Commons* runs on *cPath* software engine (Cerami, E. G. et al., 2006), an open source framework that makes the aggregation of custom pathway data sets easy. The key feature of cPath is mainly the ability to support standard pathways exchange format as PSI-MI (Hermjakob, H. et al., 2004) and BioPax (BioPAX, 2007), as well as providing all the information content in XML format through web service API. Moreover, cPath stores external link records matching the biological entity with Gene Ontology terms if the references are present in the PSI-MI file.

2.2 Integration of *Trusted* Information in the LSI Algorithm

LSI is particularly effective for text clustering applications because it exploits co-occurrences among terms in order to gather *latent* associations (Gliozzo, A. M. and Strapparava, C., 2005). This feature makes the LSI particularly successful in handling synonyms and polysemys. However, LSI considers all the words in the documents set as a *bag of words*, where all the terms are equally weighted. In (Chakraborti, S. et al., 2006), authors introduce the "*sprinkling*", an efficient technique that enhances text classification accuracy taking into account document class labels. Labeling the documents helps LSI promoting inferred latent associations between words conceptually belonging to the same class. Considering the LSI algorithm, the documents labeling results in creating a new occurrences matrix where new terms are added. Fig-

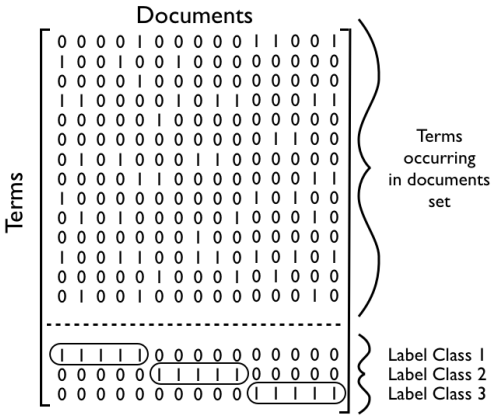


Figure 1: Modified Occurrences Matrix with *sprinkling* label classes.

ure 1 shows how *sprinkling* technique influences the occurrence matrix content during the LSI algorithm computation. The class-labelled terms corresponds to extra rows with non-zero value only in the labelled documents, and all-zeros otherwise. The term rows added by the *sprinkling* artificially create new co-occurrences among terms belonging to the same document class making explicit the implicit associations. Therefore, the efficiency in promoting implicit associations makes the *sprinkling* process a good candidate to integrate *trusted* information in the LSI algorithm in order to promote implicit associations among terms embedded in the document set. Starting from LSI and the *sprinkling* idea we developed a new customized methodology in order to integrate the associations coming from the *trusted* biological pathway with the information included in a set of documents retrieved from PubMed web services.

3 METHODOLOGY

The complete flow of the propose method is mainly composed by three phases depicted in Figure 2: *Document Abstract Analysis*, *Semantic Analysis and Trusted Info Integration*, *Results Presentation*. The following sub-sections describe the methodologies behind each phases in more details.

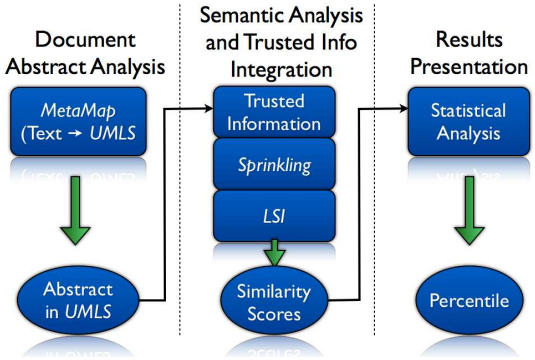


Figure 2: Complete Semantic Analysis Flow.

3.1 The *Document Abstract Analysis* Phase

The initial set of documents is composed by abstract retrieved through PubMed web services. In particular, we consider the case the scientist is interest in quantify the biological correlation score among a biological process and a specified gene. The set of keyword used to query the PubMed webservice is composed by the biological process and the gene name (initial keyword set), and a list of synonyms and terms correlated to both the gene and the biological process (expanded keyword set), resulting from querying the UMLS database(Bodenreider, O., 2004). In detail, in order to get the more complete set of synonyms and correlated terms, we exploit the fact that ULMS database store the relations among concepts belonging to almost 37 different biomedical database and ontologies (Bodenreider, O., 2004). Hereafter, we select the relevant relations in order to download the more related abstract set, exploiting the methodology introduced in (Abate, F. et al., 2010). It is worth noting that the more the retrieved abstracts relate both the biological process and the gene, the more the resulting biological score is accurate. In fact, the presence of unrelated with the specified terms increases the noising information that in turn alter the result accuracy.

Moreover, in the *Document Abstract Analysis* phase, the retrieved set of document abstracts from PubMed written in *Natural Language* are translated in a *Concept Language* exploiting Metamap capability. In fact, Metamap allows to map natural language text in *Concept Unique Identifiers* (CUI). Pre-processing the abstracts by means of Metamap makes the semantic analysis more accurate in that it reduces the ambiguities among terms that express the same concept with different sentences and words, and it allows to reduce non-relevant terms filtered by *Semantic Type* (Abate, F. et al., 2010). Therefore, at the end of *Document Abstract Analysis* phase, the set of abstract documents from PubMed translated in Concept Language is returned forming the set of documents on whom the semantic analysis is performed.

3.2 The *Semantic Analysis and Trusted Info Integration* Phase

This phase is the main core of the proposed flow and it consists of 1) retrieving the *Trusted Information*, 2) applying the *sprinkling* technique in order to integrate the information from the document abstract, 3) performing the latent semantic analysis in order to get the most accurate *SRS list* .

3.2.1 Trusted Information

The proposed tool considers genetical pathways as *trusted* source information. In fact, genetical pathways are a graphical-based representation of the gene involved in a specific biological pathways. Thus, they provide a direct link between a gene and the corresponding biological process and in this sense they are good candidate as additional source of information

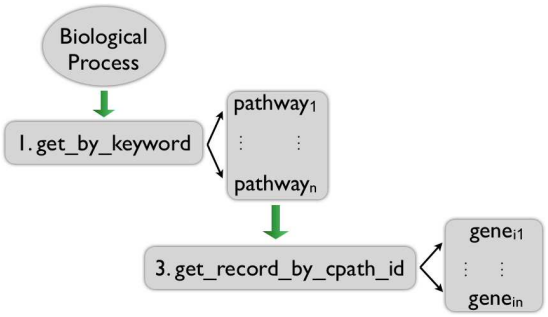


Figure 3: *GetPathwayInformationByBiologicalProcess* procedure to get *trusted* information.

to the biomedical abstracts set. Moreover, genetical pathways are constantly subjected to a review process and consequently they can be considered as *trusted*. In order to automatically access genetical pathways information, a software client for querying *Pathway Commons* web-service has been developed. In details, pathways information are extracted through the *GetPathwayInformationByBiologicalProcess* procedure shown in Figure 3. *GetPathwayInformationByBiologicalProcess* returns from Pathway Commons the list of pathways where the biological process specified as input occurs in the pathway description or in the labeling title. Hereafter, for each pathway in the list, the *cpath_id* (i.e. the unique pathway identifier according to cPath framework (Cerami, E. G. et al., 2006), is extracted from the pathway description and it is used to access the complete set of genes involved in the pathway.

It is worth noting that the presented method achieves a twofold scope: firstly, the link between the specified gene and biological process is confirmed consulting a *trusted* source of information; secondly, a list of gene *trustly* involved in the specified biological process are collected. The latter information is particularly tailored in enhancing the co-occurrences of genes correlated with the specified gene and biological process, increasing the overall accuracy during the semantic analysis.

3.2.2 Applying *Sprinkling* to Semantic Analysis

In this phase, the information extracted from pathway database are integrated in the semantic analysis process of PubMed abstracts. The term-by-document occurrence matrix is the main data structure processed by the LSI algorithm and, consequently, it is the main access point to integrate additional information. The term-by-document occurrence matrix is a two-dimensional occurrence matrix in which the columns represent the dimensional space of a corpus of documents and the rows represent the dimensional space of

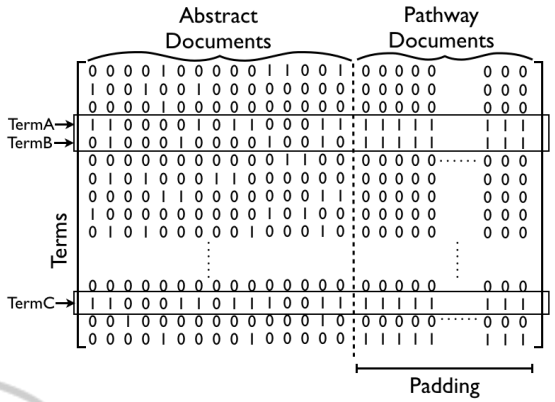


Figure 4: Occurrences Matrix adding pathway information. The dashed line separate the abstract document set by document pathways.

the terms occurring into the documents. However, the abstract set and the retrieved pathways present a different structure of the informational content. The abstract set is composed by documents already suitable for the latent semantic analysis algorithm, whereas the pathways are represented as a connected graph. Therefore, in order to integrate pathways content in the semantic analysis flow, the information coming from pathways are firstly extracted and translated into a new document containing the *trusted* information. In detail, the created *trusted document* contains the list of gene names involved in the retrieved pathways as well as the list of retrieved biological pathways. Nevertheless, adding a single document to the overall document set weakly affects the semantic analysis in terms of accuracy because poorly relevant from the statistical point of view. Thus, the *trusted document*, containing the extracted pathway information, is replicated. We refer at this procedure as *document padding*. Figure 4 shows a trivial term-by-document occurrences matrix sprinkled with additional document padding. The number of instances of the padded document, namely *NPD*, is obtained according the following equation:

$$NPD = \lceil p \cdot NAD \rceil \quad (1)$$

where *NAD* is the total number of PubMed abstract document and p is a padding factor spanning from 0 to 1. Consistently with this equation, the number of padded document spans from zero to the same number of document abstracts. Padding the overall document set with *trusted* information affects the singular values of the occurrence matrix. In fact, the singular values reflect on the distribution of the prevalent concepts occurring in the document set. The higher the singular value score, the greater is the *presence*

of the concept in the overall document corpus. It is worth noting that increasing the *p* factor makes the *trusted concepts* included in the *trusted documents* predominant with respect to the overall concepts.

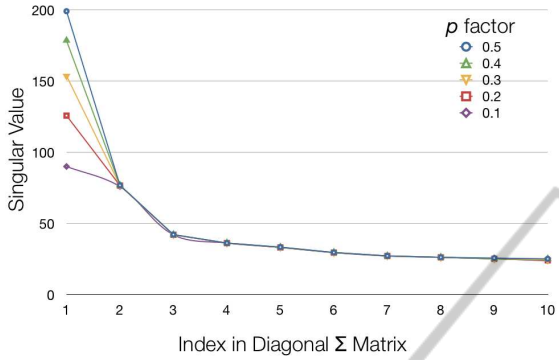


Figure 5: Singular values obtained launching the latent semantic analysis for computing the biological correlation score between AKT1 gene and Angiogenesis biological process. The ordinate reports the singular value score and the abscissa represents the index in the diagonal singular value matrix.

The analysis of the singular values is fundamental to evaluate how the *trusted document* padding affects on the overall document corpus by coherently tuning the *p* factor value. In the LSI algorithm, the singular values, obtained after applying the *SVD*, represent the attendance of the concepts in the analyzed documents set. The more a concept is relevant and frequent in the document set the higher is the singular value corresponding to it. Moreover, during the latent semantic analysis the singular values computed by SVD are set in the diagonal Σ matrix in ascending order, and consequently the first singular values represent the more relevant concepts in the analyzed corpus. Figure 5 plots the first ten singular values resulting from the analysis of abstract document set for the computation of the correlation score among the *Angiogenesis* biological process and *AKT1* gene term. The singular values are obtained with five different *p* factor values. When the document padding is increased by tuning the *p* factor, the concepts in the *trusted* documents become more relevant respect to the concepts in the abstract document set. When the *p* factor increases even more the concepts in the *trusted document* set become so relevant that the concepts in the abstract document set are overcome. As a consequence, the singular values corresponding to the *trusted document* set are boosted up and they occupy the first positions in the diagonal Σ matrix. This is the reason why, as shown in Figure 5, the greater the *p* factor value, the higher the first singular value score. Therefore, with greater *p* factor values the most relevant concepts in the overall document set correspond mainly to the concepts in the *trusted document* set.

The alteration on the singular values of the occurrence matrix by the trusted document padding consequently reflects on the correlation score between the biological terms. Consider the scenario depicted in Figure 4: *TermA* and *TermB* present a weak correlation in the document abstract set because quite linearly independent, whereas they are strongly correlated in the *trusted document* set. The document padding increases the parallelism of the two terms vector, consequently enhancing the correlation score. Furthermore, both *TermA* and *TermB* are correlated with *TermC* creating an indirect correlation due to co-occurrence. If the *TermC* occurs even in the *trusted document* set the resulting correlation score between *TermA* and *TermB* is further enhanced. Moreover, when a term occurs both in the document abstract set and in the *trusted documents* set, the term conceptually belongs to the *trusted concepts* as well. If two biological terms belong to the *trusted concepts* their correlation score is higher because conceptually linked to the predominant concepts in the overall documents content. Specifically, the biological correlation score between the biological process and the gene term is influenced by trusted information by a twofold effect: in the case the terms corresponding to biological process and gene term occur both in the document abstract set and in the *trusted documents* the score is directly affected; moreover, the correlation score is further enhanced by the presence of terms correlated with both the biological process and gene terms because occurring both in the document abstract set and in the *trusted document* set. Table 1 shows the correlation scores between *Angiogenesis* and *AKT1* gene, both in SRSs and in Percentile. The reported results show that increasing the *p* factor value implies a corresponding increase in the correlation score. Therefore, it is possible to assert that the proposed methodology, provides an effective correlation score combining the information extracted in the document abstract set with the *trusted* information extracted from pathways databases. Moreover, the influence of the *trusted* information on the semantic text analysis is tuned by the *p* factor parameter that directly affects the correlation results.

Table 1: SRS and Percentile values corresponding to *p* factor.

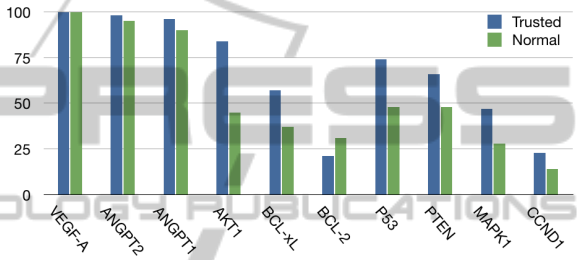
***p* Factor**	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**
SRS	15.7	17	18.1	18.8	19.5
Percentile	76	78	82	83	84

3.3 The *Results Presentation* Phase

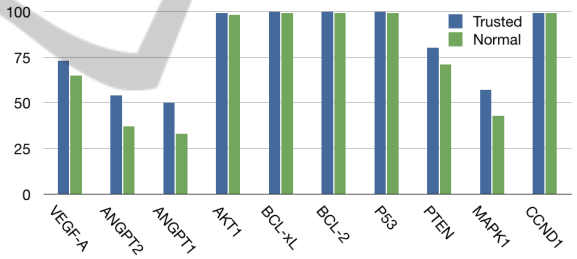
An evaluation criterion allowing the comparison among each gene in the genes set and each biological process is fundamental in order to focus the attention only on those genes correlated with the biological processes of interest behind a certain degree of correlation. Therefore, the correlation measurement between genes and biological processes must express an universally valid score allowing the comparison among different correlation analysis. Actually, SRS provides a percentage measurement to compare genes and biological process corresponding to terms belonging to the same occurrence matrix and thus it quantifies the semantic relationship of biological terms during the same semantic text analysis (i.e. a single execution of the tool). Different analyses are characterized by different sets of documents and concepts. Consequently, SRSs values computed on different occurrences matrices are not directly comparable. In order to define an evaluation criterion that allows to compare SRSs resulting from different semantic analysis, and therefore different occurrences matrices, we analyzed the SRS distribution on different occurrences matrix. The SRS Distribution (SRSD) is defined as the density function that reports the percentage of occurrences, or frequencies, of a certain score for the possible SRSs corresponding to all the CUIs occurring within the correlation analysis. Furthermore, the SRSD has been divided into hundred percentile intervals of equivalent area depending on the frequency percentage of the SRS in the density function. We define each interval as Biological Correlation Index (BCI) expressing that the higher the BCI, the greater the degree of biological correlation between the biological process and the genes. The evaluation through BCI allows to evaluate the correlation between genes and biological process independently of the experimental run, because it provides an information on the frequency distribution of the SRSs in the overall terms occurring in an experimental run.

4 EXPERIMENTAL RESULTS

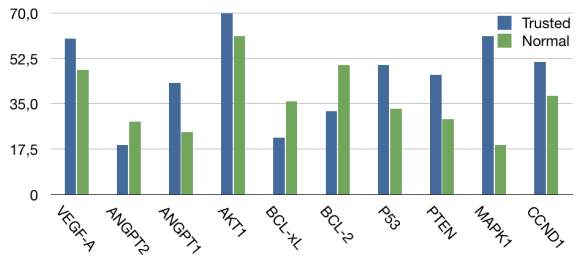
The following section reports the correlation scores among a set of three biological processes (*Angiogenesis*, *Apoptosis*, and *Signal Transduction*) and ten gene terms (*VEGFA*, *ANGPT2*, *ANGPT1*, *AKT1*, *BCL-xL*, *BCL-2*, *P53*, *PTEN*, *MAPK1*, *CCND1*) applying the proposed flow. Figure 6 resumes the results and demonstrate the effectiveness of integrating the information coming from the PubMed document abstract set with the information from pathway database. The biological correlation scores obtained integrating trusted information (*Trusted INFO*) are compared with the scores obtained without integrating any *trusted* information (*Normal INFO*). Moreover, *p* factor has been set to *0.5*. This choice implies that the *trusted document* set has been padded in order to equal almost the half of the number of abstract document set and to emphasize the effect of the integration of *trusted* information on the overall document set. Furthermore, the biological correlation score is reported in the *BCI* format in order to allow the comparison among the scores of same set of genes computed in different biological process (Abate, F. et al., 2010).



(a) Angiogenesis.



(b) Apoptosis.



(c) Signal Transduction.

Figure 6: Experimental Results Expressed in BCI score.

In order to have a better understanding of the resulting biological correlation scores, the functional definition of the gene set according to NCI Thesaurus is listed below:

- *VEGFA*: This gene is involved in the regulation of blood vessel growth.

- *ANGPT2*: This gene encodes angiopoietin-2 protein and it plays a role in both angiogenesis and neovascularization.
- *ANGPT1*: This gene plays a role in both vascular development and angiogenesis.
- *AKT1*: This gene is involved in signal transduction and negative regulation of apoptosis.
- *BCL-xL*: This protein plays a role in the modulation of apoptosis.
- *BCL2*: This gene is involved in apoptotic regulation. Overexpression of this gene promotes the pathogenesis of B-Cell lymphomas, due to anti-apoptotic activity.
- *P53*: This protein plays a role in the regulation of both the cell cycle and apoptosis.
- *PTEN*: This gene plays a role in signal transduction and apoptosis. It is also involved in the regulation of cell cycle progression.
- *MAPK1*: This gene plays a role in signal transduction and positive regulation of the cell cycle.
- *CCND1*: This gene plays a role in the regulation of mitotic events.

From the same *NCI Thesaurus* source, Angiogenesis is defined as the "*blood vessel formation*" and, specifically for the case of tumor angiogenesis, it is "*the growth of blood vessels from surrounding tissue to a solid tumor*". It is worth noting that the results concerning the biological correlation scores between angiogenesis and the gene set coherently reflect the NCI Thesaurus definitions. In fact, *VEGFA*, *ANGPT1* and *ANGPT2* present the almost same correlation scores with the *Angiogenesis* biological process both in the case of *Trusted INFO* and in the case of *Normal INFO*. The small difference in the results depends on the fact that in both the cases the biological correlation scores presents highest BCI, therefore the *Trusted INFO* poorly affect the accuracy of the computation. Moreover, the correlation score of *AKT1* gene term with *Angiogenesis* process is highly enhanced by the integration of *Trusted INFO*. This gene is specifically involved in the *Signal Transduction* and in the *Apoptosis* process, whereas it is less typical of *Angiogenesis* biological process respect to *VEGFA*, *ANGPT1*, and *ANGPT2* genes even if correlated with it. Our results reflects this assertion because *AKT1* gene directly appears in the *Angiogenesis* pathway and it is directly correlated with this biological process according to the *trusted information* set, but its correlation according to the information coming from the document abstract set is minor compared with *VEGFA*, *ANGPT1*, and *ANGPT2* genes. Coherently, this gene presents a lower biological correlation score compared with *VEGFA*, *ANGPT1*, and *ANGPT2* genes even if, correctly, its score has been significantly boosted by adding *Trusted INFO*.

Moreover, the integration of *Trusted INFO* enhances the biological correlation score of *P53*, *PTEN*, *MAPK1* and *CCND1*. These genes are generally involved in *Apoptosis*, *Signal Transduction* and *Cell Cycle* biological processes that are indirectly related with *Angiogenesis* process as well. The *AKT1* gene, that is mainly involved in *Signal Transduction* and *Apoptosis*, also occurs in the *Angiogenesis* pathway. The biological correlation of the AKT1 gene with *P53*, *PTEN*, *MAPK1* and *CCND1* genes and, on the other side, the occurrence of this gene in the *trusted* document concerning *Angiogenesis* process creates an indirect link between *P53*, *PTEN*, *MAPK1* and *CCND1* genes and the same *Angiogenesis* process. It accordingly results in a biological correlation score enhancement.

Furthermore, the introduction of *Trusted* information positively increases *ANGPT1*, *ANGPT2* and *MAPK1* genes scores. These genes are generally typical of *Angiogenesis* and *Signal Transduction* but these processes are sometime related to *Apoptosis* and thus they co-occur in the document abstact set. Therefore, even if the *Apoptosis* pathway do not include this gene set, the indirect biological correlation between terms in the *Trusted* information and terms occurring in the document abstract set, belonging to the *Apoptosis* semantic area, increases the resulting value of the biological correlation score. However, all of them present a score significatively lower than the one of *Apoptosis* genes *AKT1*, *BCL-xL*, *BCL2*, and *P53*.

According to the results concerning *Signal Transduction* process, the biological correlation score of *MAPK1* gene is particularly interesting. This gene is strongly related to *Signal Transduction*, but this biological processes is quite generic and it interact with many biological phenomena typical of the cell cycle. Considering only the document abstract set as information base, the occurrence of *MAPK1* gene is not always frequently guaranteed, thus resulting in a low correlation score. However, integrating the *Trusted* information the score is almost triplicated. The introduction of *Trusted* information creates the missing conceptual links of the *MAPK1* gene with terms semantically correlated with the biological process of interest, resulting in an increase of the final biological correlation score. This result remarks the effectiveness of the proposed approach in enhancing accuracy of measuring the biological degree of correlation.

Furthermore, integrating *Trusted* information in the document abstract set makes the results more accurate also reducing the biological correlation score. *BCL2* gene, for instance, is functionally specific of *Apoptosis* biological process. On the wave of this assertion, this gene further decreases the correlation score in the case of both *Angiogenesis* and *Signal Transduction* when applying *Trusted* information. The expected behavior would be at most of unaltered result because the *Trusted* information do not addict any further information concerning the correlation score between *BCL2* and the two biological processes. However, integrating *Trusted* information increases the correlation score of those terms related to the biological processes and their correlation scores overcomes the *BCL2* one, that in turn becomes lower. Similar consideration are also valid about the biological correlation score between *BCL-xL* gene and *ANGPT2* gene and *Signal Transduction* biological process.

5 CONCLUSIONS

The proposed semantic analysis tool provides a framework for measuring the biological correlation score among biomedical terms. The score is the results of a text mining analysis performed on the abstracts of the most relevant scientific publications with the support of the completeness of the UMLS Metathesaurus. The knowledge extracted by biomedical literature is further integrated with the information coming from sources generally known as trustworthy. In order to satisfy this requirement, public biological pathways databases have been chosen and the embedded information are first retrieved and then correlated in the overall semantic analysis flow. Moreover, in order to integrate the knowledge coming from an heterogeneous base of information, a new version of the latent semantic analysis, based on the sprinkling technique, has been developed. The results remark the efficiency of the proposed approach in enhancing the accuracy of the biological correlation score computation by combining the knowledge extracted by scientific document abstract set with the pathways information.

As future step the complete automation of the tool will allow to retrieve the document abstract set in an automated and accurate manner. Moreover, the integration of information coming from other trusted sources will be tailored and developed in order to better improve the overall accuracy and robustness of the proposed semantic analysis method.

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