Integrating, Structuring and Visualising Cancer Data

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Abstract

The primary purpose of this project is to determine what type of database functions better for integration of cancer data and investigate the added value of visualising cancer data. Data for this research were mostly collected from COSMIC and the Gene Ontology Consortium. This thesis first describes the set up of a relational database using MonetDB, followed by the set up of an RDF database, using D2RQ. Secondly the way of evaluating these databases and the visualisation is described. The visualisation was made using Gephi. It was concluded that the RDF database is more suitable for the integration of cancer data and the visualisation did give additional insight. In the future these databases and visualisation can help the mapping from genes to hallmarks.
Acknowledgements

Firstly, I am grateful to God for the insight and wellbeing He has given me during this project. I want to sincerely thank Katy Wolstencroft, my supervisor, for her continuous expertise and guidance during the project. I also want to thank Fons Verbeek, my second supervisor, for his additional guidance and the arrangements he made with regards to a workplace. Lastly, I want to thank Teddy Etoeharnowo, my partner during the first part of the project, for the pleasant collaboration and his sagacity.
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Chapter 1

Introduction

Cancer is a leading cause of death with 8.2 million cancer-related deaths in 2012 \[1\] and is therefore a focus for large-scale research efforts. A lot of the data from all this research is publicly available. Databases about cancer, like COSMIC (a curated set of gene mutations) \[2\], and general biology databases, like Reactome (a curated and peer reviewed pathway database) \[3\], KEGG (a pathway database focussing on molecular interactions, reactions and relations) \[4\] and Gene Ontology Consortium (gene product description database) \[5\], are a few examples of the databases storing this data used for this research. This data is not only interesting from a biological point of view, but also from a data science point. Cancer data can have many different forms. Functional descriptors, pathways and mutations are only a few examples. This heterogeneous data is also dynamic, since it is continuously updated. Integrating and cataloguing this data can lead to new insights into cancer genes. It can expose implicit relationships between the data from all the different sources. This is why it is important to create a system which can integrate new data and merge it with the data the system contains. The traditional way of doing this is to create a relational database. This is not always a suitable way, since an SQL Database schema can’t be easily changed when new data arrives and an SQL database can’t query other datasources without integrating that data or postprocessing. A Resource Description Framework (RDF) \[6\] database on the other hand is more dynamic since it can change a schema relatively easily and it is possible to query other datasources without integrating the data. We will compare these two databases to see which of the two is more suitable. The Gene Ontology terms are concepts or classes to describe gene functions. All these terms are organised in a hierarchical structure, since they have super– and subclass terms that are respectively less or more specific concepts or classes. When this hierarchy is visualised, it is easier understood and can also give more or new insights. Whereas the hierarchical structure can be hidden when it is shown in a relational representation.


1. Introduction

1.1 Cancer Data and the Hallmarks of Cancer

Cancer hallmarks are underlying principles covering all aspects and functions of cancer. The overall goal is to create a more concrete mapping from genes to these hallmarks using gene ontology term annotation. The hallmarks framework is a useful conceptual framework, but it is interpreted in different ways in different studies. When a more systematic mapping is created between data and hallmarks, there will be less ambiguity in the interpretation. To reach this goal we created a subgoal for this project, namely finding out what type of database is better in connecting the different datasources, relational or RDF, and visualising cancer genes with the related gene ontology terms in the gene hierarchy. This is done following the research question: 

*How does semantic modelling contribute to the data model and clustering of cancer data?*

This thesis describes two parts. The first part describes the creation of a relational database containing data from different sources. This is done in collaboration with Teddy Etoeharnowo, student at Leiden University. The second part describes creating an RDF database, linking it to other databases and visualising the data, which I did on my own. The clustering of the data mentioned in the research question is done by Teddy and described in his thesis. First we will take a look at the databases used in this project and how RDF works. Next we explain the hallmarks of cancer, the differences between RDF and relational databases and how the differences with RDF could be exploited when studying the hallmarks of cancer. Then we discuss the platform we set up to connect all the different sources. We evaluate our contributions and lastly we will draw our conclusion.
Chapter 2

Definitions

In this chapter we will elucidate the different sources and the Research Description Framework.

We retrieved data for our project from the following sources:

- The ‘Catalogue of somatic mutations in cancer’ (COSMIC) \(^2\) contains a curated set of gene mutations involved in cancer and is used as a gold standard data set for this project.

- Reactome “is a free, open-source, curated and peer reviewed pathway database.” \(^3\)

- Kyoto Encyclopedia of Genes and Genomes (KEGG) Pathways wires “diagrams of molecular interactions, reactions, and relations.” \(^4\)

- Gene Ontology (GO) \(^5\) contains descriptions for gene products across databases in terms of three different aspects.

The GO database classifies functions along three aspects:

- Molecular Function

- Cellular Component

- Biological Process

These three aspects mark the top of the GO hierarchy. An ontology is a definition of an entity and their properties and relations in a certain domain \(^7\). A gene ontology does this for genes in an hierarchical structure.

A Relational Database \(^8\) holds a lot of data organised in tables. This data can be accessed, defined, controlled and manipulated using Structured Query Language (SQL) \(^9\). A relational database is the standard database to store a lot of data.
MonetDB is a database management system used to set up relational databases [10].

Resource Description Framework (RDF) [6] is the W3C standard for the semantic web to interchange data on the web. RDF uses Uniform Resource Identifiers (URI’s), these are strings of characters to identify sources or relations, to denote a resource and uses them in triples (RDF statements) to link two URI’s together. A triple exists of a subject (a URI), a predicate (a relation/link/URI) and a object (a URI or a literal). When all this data is linked together it forms a graph, where the nodes are the URI’s and the edges the relations between them. When data is structured in this way, either on the web or on a local database, it can be queried using SPARQL [11]. SPARQL stands for SPARQL Protocol and RDF Query Language and it works similar to SQL. To query a data on the web, that database should have a SPARQL endpoint. This is the link used in a federated query.

Provenance [12], in the data science field, means where the data comes from and when it was retrieved. This allows more verification when checking the data, since it could have multiple sources or be verified at multiple times. It can also help with conflicting data to find the source of the conflict.
Chapter 3

Related Work

In this section we will describe the hallmarks of cancer and list the advantages RDF has over a relational database.

3.1 The Hallmarks of Cancer

The hallmarks of cancer are conceptual descriptions of the disruptive cellular processes that occur in the development of cancer. Cancer has eight hallmarks and two enabling characteristics as shown in figure 3.1. These hallmarks include sustaining proliferative signalling, evading growth suppressors, avoiding immune destruction, enabling replicative immortality, activating invasion and metastasis, inducing angiogenesis and resisting cell death. The enabling characteristics are genome instability and mutation, and tumor-promoting inflammation. Besides the cancer cells, tumours contain normal cells that also contribute to the hallmarks. Understanding and recognising these hallmarks will significantly help treat human cancer [13]. There have been many attempts to map cancer hallmarks to functional data, but no systematic method for identifying hallmarks has been established. This means the mappings are heterogeneous and incomparable.

3.2 Bio2RDF

Bio2RDF [14] is a mashup system to help the process of bioinformatics knowledge integration. More than twenty different public bioinformatics data sources are available in a normalised RDF format from the Bio2RDF.org server. With the use of three different rdfizer (converters to RDF) Bio2RDF locally stored multiple databases, related to specific topics, so these can be extracted in minutes rather than hours. The Bio2RDF framework provides access to normalised RDF documents from many different sources, and offers a method
for users to add knowledge sources by creating new rdfizers and also a way to keep privacy of private data by using built-in routing capability.

3.3 Relational database vs RDF

A relational database and an RDF database have many similarities, but also a vast amount of differences. Although the relational database is the standard for creating databases, RDF does have some significant advantages over it. RDF is great in data exchange interoperability; it can integrate structured data from other databases, semi-structured data like HTML and unstructured data like text. A relational database is bound to a schema when integrating data and has to change the schema before adding data different than before. RDF does not have this problem, it is not bound to a schema. It can add new connections without changing the whole structure or schema. Another advantage of RDF is being able to add data in multiple languages. This is ideal for data used internationally. The next advantage of RDF is that it is easier to find literals. When searching for a certain word or phrase in SQL, you have to know in what column it can be found. RDF on the other hand can search without this requirement. The next advantages are the most important with regards to this project. Using SPARQL it is possible to create federated queries. This means it is possible to query
external databases with our data, without having to download all the data on your system or server. RDF is also better at handling hierarchical structured data. This should make querying the GO database and other ontology data easier than it would be using SQL. The last advantage RDF has is the fact that it is a graph. This makes it easier to visualise the data. When visualising a relational database it will show tables, whereas visualising RDF can create a big graph, not only showing all the relations between URI’s, but also hierarchical structures using directed edges.

These last three advantages (federated querying, handling hierarchical structure and visualising the data) create great expectations for our project, since we use a lot of different sources, query hierarchical data and want to visualise it. To see if the results will live up to the expectations, we will test the RDF and relational database both using Jim Gray’s “20 questions” method \[15\]. The idea is to ask the 20 most important questions (queries in this case) to test your system. We used this method to compare the relational database with the RDF one.
Chapter 4

Methods and Development

In this chapter will be explained how the relational database was set up, what problems came up, the way provenance was recorded, how the RDF database was set up and finally how the data was visualised.

4.1 The Relational Database

To set up the relational database we created an ER-diagram and database using MonetDB [10]. MonetDB was the preferred choice since some of the developers were present at Leiden University, so when encountering problems we could ask them for help. Another advantage MonetDB has, is the embedded version for R. This is very useful for the data mining the collected data. We started off with getting the data from the COSMIC gene census [16]. This gene census is a curated list of all genes that have mutations proven to be associated with cancer and is a gold standard set. It contained the following data for all genes, the datatype is shown in parentheses:

- Gene Symbol (String)
- Name (String)
- Entrez ID (Integer)
- Genome Location (String)
- Chromosome band (String)
- Somatic Tumour Type (String)
- Germline Tumour type (String)
• Tissue Type (Character)
• Molecular Genetics (String)
• Mutation Types (String)
• Synonyms (String)

All this data was formatted as a Comma-separated Values file (CSV). We split all these columns and linked it all to the Entrez ID (a unique number bound to a single gene). This gave a lot of weak entities in the ER-diagram, meaning this data could not be uniquely identified by the attributes (i.e. multiple rows could have the same value), but only by its Entrez ID. This means all the data was split into multiple CSV files, where Entrez ID was almost always the first column (and therefore the key). After creating the diagram and adding all the data to the database, we did the same for KEGG, Gene Ontology and Reactome. Figure 4.1 shows the ER-diagram. It shows that the only attribute that did not need Entrez ID as a foreign key is the KEGG Human ID. This is because this ID also uniquely identifies to a gene.

In figure 4.1, the blue relations come from COSMIC, the red from the Gene Ontology, all yellow from Kegg and the green from Reactome. The purple relation is a combination between COSMIC and Gene Ontology since we got synonyms from both of these sources.
4.1.1 Data Cleaning

To add all the data to the database we created csv-files containing all the data. This type of files split the data into different columns depending on a chosen delimiter. This gave a minor setback when discovering that the preferred delimiters, comma, semicolon and colon, were also used in the data. This meant that the data would split into multiple columns when this was not supposed to. To solve this we replaced the semicolon in the data with a comma and chose the semicolon as the delimiter.

4.1.2 Provenance

After adding all this data in the different tables and creating different entities in the diagram, we did the same thing for the provenance of all the data. Provenance is important with dynamic data from multiple sources. When data from different sources or timestamps conflicts with each other, it is important to know which source and which update is the source of the conflict. It is furthermore good for the verification of the data. If the same data comes from multiple sources, consensus may show and will therefore be more reliable. We created a table specially for the provenance listing all the tables that got their data from a certain database. The exception to this was the synonyms table. Since the synonyms came from COSMIC and KEGG we added a column to this table listing whether it came from COSMIC or KEGG.

4.1.3 Evaluation

To evaluate the relational database, we queried the relational database using the top 18 questions identified by potential database users (in this case, bioinformaticians researching cancer data), using the method mentioned in section 3.3. We checked if not only we could create the queries and run them, but also if the answers to the queries were correct by sampling.

4.2 The RDF Database

To query our relational database with existing databases there should either be a local copy of the database or post-processing should be done. This takes up extra space and time for every new database we want to query, but not integrate in the existing database. A Resource Description Framework (RDF) database has the advantage of being able to query existing and online databases without having to get a local copy; the data is queried at its source. The RDF database could be set up in two ways. The first is setting it up from scratch like the relational database. The second one is converting the relational database. Since I had no knowledge of RDF at the start of the project and it would take significantly less time, I decided to go with the second
option. The D2RQ tool was seemingly ideal for this since “the D2RQ Platform is a system for accessing relational databases as virtual, read-only RDF graphs. It offers RDF-based access to the content of relational databases without having to replicate it into an RDF store.” Converting the database was relatively easy. After downloading a JDBC driver from the MonetDB site, the relational database could be mapped to an RDF one. We had to create a mapping using the generator D2RQ provided. This generator created the entire RDF graph mapped from the relational database. There was one issue with the mapping with regards to the level of the column names. The column names had the following format $\text{databasename.tablename.columnname}$. Unfortunately third level column names (names that exist out of three parts) were not supported. The solution to this was to create aliases for the database name and table name, so the format would change into $\text{databasename.tablename.columnname}$. With the renewed mapping we could run the RDF database. After the set-up we found out federated querying was not supported in this version of D2RQ (though it was the newest on their website). Since this is one of the main benefits from RDF over relational databases this was important to be fixed. Luckily it was mentioned as an issue on GitHub, where the solution could be found, namely a small change in the source code.

4.2.1 URI’s

One of the advantages of RDF was that it was possible to link the data from GO directly to URI’s from Bio2RDF. “Bio2RDF is an open-source project that uses Semantic Web technologies to build and provide the largest network of Linked Data for the Life Sciences.” It has a SPARQL endpoint to query the entire database. This was very useful, since the GO terms in our data were single terms, but did not have the hierarchical structure and data Bio2RDF does have. This meant that when changing the single GO terms in our database to the URI used by Bio2RDF, the data was part of the entire hierarchy and was automatically updated. It also meant that querying the data sources is easier. It is still necessary to make the query federated, but it needs one less sub-query this way. With the URI’s in place, it was possible to make efficient queries using SPARQL.

4.2.2 Evaluation

To evaluate the RDF database we used the same questions mentioned in subsection 4.1.3.

4.3 The Visualisation

When looking at data in a tabular or listed format it is very hard to uncover relationships between genes and/or GO terms. When the data is visualised, it is easier to uncover implicit relationships. Since RDF could
query multiple sources, it was relatively easy to translate the data from these sources with our data to a visual
graph. Using directed edges it was also possible to visualise the hierarchical structure from the GO database.

For the visualisation Gephi was a good choice. Gephi is an “interactive visualisation and exploration platform
for all kinds of networks and complex systems, dynamic and hierarchical graphs.” Gephi has multiple
plug-ins, algorithms and functions to manipulate the graph available.

To visualise the cancer genes with their related Gene Ontology terms (GO terms) I queried the RDF database
federated with the Bio2RDF Sparql Endpoint to get the list of all genes with the related GO terms and
superclasses of these terms. Next I used Gephi to visualise this list, making a big directed graph including all
the genes, their related gene ontology terms and the terms further up the hierarchy. One of the neat functions
of Gephi was the heat map, this marked a starting node as red and all the nodes connected to this node a
lighter red, depending on their distance. Figure shows a graph from all biological process genes where
the direction of the edges is from parent terms to subclass terms or genes. The marked node is the biological
regulation (a GO term far up the hierarchy), the one in the middle of the top right.

With the direction of the edges flipped, it shows when marking a gene all its related GO terms. This can be
used for example when trying to find a common parent for two genes.

Gephi also had a function to have the node size based on the degree. The degree of a node is the number of
edges coming in and going out of a node. The in-degree is the number of edges coming in, the out-degree
vice versa. Both the in-degree and the out-degree are useful for creating graphs that easily show either what
gene ontology term belongs to a big number of genes or have many subclass GO terms, or what genes are
related to a lot of different GO terms.

There are different algorithms Gephi has available to organise a graph. Some are very simple and have one
function, for example contraction, expansion, rotate and random layout. Fruchterman Reingold and isometric
layout organise the graph in a certain shape. The algorithm I used most is called ForceAtlas 2. “ForceAtlas2
is a force directed layout: it simulates a physical system in order to spatialize a network. Nodes repulse each
other like charged particles, while edges attract their nodes, like springs. These forces create a movement that
converges to a balanced state. This final configuration is expected to help the interpretation of the data.”

Figure shows the graph just after importing the data from the Molecular Function aspect class. Figure shows the same graph after executing the Force Atlas 2 algorithm.
4.3.1 Gephi

In figure 4.5 is a screenshot of the program shown. At the top left are three tabs shown, “Overview” is for editing the graph structure, “Data Laboratory” is for editing the data and “Preview” is for editing the graph in a visual manner. Below the tabs is a part for the appearance, I used this mainly to base the node size on the out-degree. Below the appearance is the algorithm part, where you can select, edit and run an algorithm to edit the graph. Just left of the graph is a toolbar with multiple functions, the orange sun like symbol (selected in the figure) is the heat map. On the right is a part for statistics, I used this mainly to calculate the degree for every node. When the “Average Degree” has run once, the Data Laboratory shows both the in-degree and the out-degree for every node.
Chapter 4. Methods and Development

Figure 4.3: Before executing the Force Atlas 2 algorithm

Figure 4.4: After executing the Force Atlas 2 algorithm
Figure 4.5: Screenshot of Gephi
Chapter 5

Results and Evaluation

In this chapter, we describe the evaluation of the relational and RDF database, and the visualisation.

5.1 Relational Database

As mentioned before, to evaluate the relational database the “20 questions” method from Jim Gray was used \[15\]. Instead of 20 questions we queried 18, because additional questions did not add value to the evaluation. The 18 questions we tested were the following:

SQL does not support federated querying. This made questions 8, 10 and 18 unable to be answered. Questions 6, 14 to 17 could not be fully answered; it only gave the GO terms we had in our database. All these questions could be answered with post-processing or downloading a local copy of the external database (GO in this case).

5.2 RDF

To evaluate the RDF database the same questions were used as in section 5.1. Using federated querying it was possible to also answer the questions using external data sources. These questions also showed a new problem. D2RQ did not support the combination of the aggregates HAVING and COUNT. This made 5 questions left unanswered, since it did need the combination of the two, namely 5, and 7 to 11. Note that these questions probably could be answered if the system was not made with D2RQ, but with another tool.
Table 5.1: Evaluation questions

<table>
<thead>
<tr>
<th>Question</th>
<th>Relational</th>
<th>RDF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Return all the pathways associated with gene X</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>2. What other genes from COSMIC are involved in these pathways?</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>3. Return all the cancer genes with recessive mutations</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>4. Which are oncogenes and which are tumour suppressor genes?</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>5. Return all the cancer genes that are associated with more than one cancer - which cancers, which tissue types?</td>
<td>✓</td>
<td>⏎</td>
</tr>
<tr>
<td>6. Which pathways and Gene Ontology terms are associated with breast cancer?</td>
<td>~</td>
<td>✓</td>
</tr>
<tr>
<td>7. Which Gene Ontology Biological Process terms are common to all melanomas - or are there none common to all?</td>
<td>✓</td>
<td>⏎</td>
</tr>
<tr>
<td>8. Are there any shared GO terms further up the hierarchy?</td>
<td>⏎</td>
<td>⏎</td>
</tr>
<tr>
<td>9. Which GO Molecular function terms are common to all melanomas?</td>
<td>✓</td>
<td>⏎</td>
</tr>
<tr>
<td>10. Are there any shared GO terms further up the hierarchy?</td>
<td>⏎</td>
<td>⏎</td>
</tr>
<tr>
<td>11. Which GO Cellular Component terms are common to all melanomas?</td>
<td>✓</td>
<td>⏎</td>
</tr>
<tr>
<td>12. Return all the genes that are not assigned to any pathways</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>13. Return all the genes that are only assigned to pathways from Reactome, but not from KEGG</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>14. Which GO biological process terms are associated with the cytokine-cytokine receptor interaction pathway?</td>
<td>~</td>
<td>✓</td>
</tr>
<tr>
<td>15. Which genes are associated with angiogenesis?</td>
<td>~</td>
<td>✓</td>
</tr>
<tr>
<td>16. Which genes are associated with apoptosis?</td>
<td>~</td>
<td>✓</td>
</tr>
<tr>
<td>17. Which genes are associated with signalling and binding?</td>
<td>~</td>
<td>✓</td>
</tr>
<tr>
<td>18. Which genes are in the same cellular components?</td>
<td>⏎</td>
<td>✓</td>
</tr>
</tbody>
</table>

5.3 Visualisation

The visualisation was evaluated by creating graphs for all three aspect classes (Cellular Component, Molecular Function and Biological Process) and examined for nodes or connections that stood out. It allowed us to map the flat gene mutation data onto the hierarchical structure of the gene ontology, revealing new ways of exploring the functional relationships between gene mutations.

5.3.1 Cellular Component

Figure 5.1 shows the genes and related GO terms of cellular component. The node size is based on the out-degree. The red node is the GO term furthest up the hierarchy, cellular component. The four biggest nodes (and therefore the GO terms with the most connected genes) are nucleus, nucleoplasm, cytoplasm and cytosol. These nodes and their neighbours are marked with pink, yellow, cyan and blue respectively. The genes that relate to more than one of these GO terms have the colours of its parents mixed.
5.3.2 Molecular Function

Figure 5.2 shows the genes and related GO terms of molecular function. The node size is based on the out-degree. The red node is the GO term furthest up the hierarchy, molecular function. The biggest node is protein binding and is marked with cyan.

5.3.3 Biological Process

Figure 5.3 shows the genes and related GO terms of biological process. The node size is based on the out-degree. The red node is the GO term furthest up the hierarchy, biological process. The biggest node is biological regulation and is marked with cyan. As cancer is about disrupting existing regulatory processes in the cell, this was not surprising. The graph additionally shows how clusters of genes were associated with particular forms of disruption and therefore provides cancer specialists with a new way of examining similarities and differences between these clusters.
Figure 5.2: All genes and GO terms classified under Molecular Function (out-degree)
Figure 5.3: All genes and GO terms classified under Biological Process (out-degree)
Chapter 6

Conclusions

The comparison between a relational database and an RDF one results in a reasonable preference for RDF. The flexibility RDF brings is a big advantage when dealing with multiple sources. The fact that it is possible to query different sparql endpoints and retrieving data that way costs less time and space as opposed to making a local copy of every database or post-process the result of the queries. It also gives an advantage for visualisation since it is easier to query hierarchical structures. The relational and RDF database do perform similarly well, apart from the hierarchical data and for federating with other resources.

The visualisation of the three aspects revealed multiple things that could be overlooked watching only the textual data. Gephi allows the visualisation of functional clusters in the data. The function to base the node size on the out-degree is also ideal to quickly notice the important GO terms.

6.1 Future work

The overall goal of this project is to link genes to hallmarks. The database and visualisation made in this project could help that research. The visualisations made in this project were focused on the Gene Ontology terms, not on the genes. After linking a lot of genes to Hallmarks, the focus will shift towards which genes play the most important role in cancer. When the node size in my visualisation is based on the in-degree it is easy to see which genes are related to the most GO terms and could therefore be important in cancer. The in-degree results can also be compared with the biological pathway data already in the database, to identify which pathways are key and pivotal for different clusters of cancer types. I created three examples of these visualisations, one for each aspect class.
6.1.1 Cellular Component

In figure 6.1 is the colouring done the same as in 5.1. The two biggest nodes (the genes with the most amount of related GO terms) are “ezrin” and “catenin (cadherin-associated protein), beta 1”, marked as red and green respectively.

![Diagram showing cellular component]

Figure 6.1: All genes and GO terms classified under Cellular Component (in-degree)

6.1.2 Molecular Function

In figure 6.2 is the heat mapped node “protein binding”. The two biggest nodes are “tumor protein p53” and “retinoic acid receptor, alpha”, marked as blue and green respectively.
6.1. Future work

6.1.3 Biological Process

In figure 6.2 is the heat mapped node (with a green palette) “biological regulation”. The two biggest nodes are “tumor protein p53” and “Notch homolog 1, translocation-associated (Drosophila) (TAN1)”, marked as blue and red respectively. p53 came our highest in both Biological Process and Molecular Function - this is very significant. P53 plays a key role in binding and regulation and has already been shown to be associated with many different cancers. This also suggests a role in multiple hallmark processes, which can be validated by combining the results of this work with the results of a related project by Atagun Isiktas, an Erasmus exchange student.
Figure 6.3: All genes and GO terms classified under Biological Process (in–degree)


