The *GOSim* package

Holger Fröhlich

October 13, 2014

1 Introduction

The Gene Ontology (GO) has become one of the most widespread systems for systematically annotating gene products within the bioinformatics community and is developed by the Gene Ontology Consortium (The Gene Ontology Consortium, 2004). It is specifically intended for describing gene products with a controlled and structured vocabulary. GO terms are part of a Directed Acyclic Graph (DAG), covering three orthogonal taxonomies or "aspects": *molecular function, biological process* and *cellular component*. Two different kinds of relationship between GO terms exist: the "is-a" relationship and the "part-of" relationship. Providing a standard vocabulary across any biological resources, the GO enables researchers to use this information for automated data analysis.

The *GOSim* package (Fröhlich et al., 2007) provides the researcher with various information theoretic similarity concepts for GO terms (Resnik, 1995, 1999; Lin, 1998; Jiang and Conrath, 1998; Lord et al., 2003; Couto et al., 2003, 2005). Moreover, since version 1.1.5 *GOSim* contains several new similarity concepts, which are based on so-called diffusion kernel techniques (Lerman and Shakhnovich, 2007). Additionally *GOSim* implements different methods for computing functional similarities between gene products based on the similarties between the associated GO terms (Speer et al., 2005; Fröhlich et al., 2006; Schlicker et al., 2006; Lerman and Shakhnovich, 2007; del Pozo et al., 2008). This can, for instances, be used for clustering genes according to their biological function (Speer et al., 2005; Fröhlich et al., 2006) and thus may help to get a better understanding of the biological aspects covered by a set of genes.

Since version 1.1 *GOSim* additionally offers the possibility of a GO enrichment analysis using the topGO package (Alexa et al., 2006). Hence, *GOSim* acts now as an umbrella for different analysis methods employing the GO structure.

2 Usage of *GOSim*

To elucidate the usage of *GOSim* we show an example workflow and explain the employed similarity concepts. We create a character vector of Entrez gene IDs, which we assume to be from human:

```
> library(GOSim)
> genes=c("207","208","596","901","780","3169","9518","2852","26353","8614","7494")
```

Next we investigate the GO annotation within the current ontology (which is *biological process* by default):

```
> getGOInfo(genes)
```

	207	208	596	901	780
go_id	Character,106	Character,29	Character,116	Character,3	Character,17
Term	Character,106	Character,29	Character,116	Character,3	Character,17
Definition	Character,106	Character,29	Character,116	Character,3	Character,17
IC	Numeric,106	Numeric,29	Numeric,116	Numeric,3	Numeric,17
	3169	9518	2852	26353	8614
go_id	Character,24	Character,3	Character,50	Character,3	Character,12
Term	Character,24	Character,3	Character,50	Character,3	Character,12
Definition	Character,24	Character,3	Character,50	Character,3	Character,12
IC	Numeric,24	Numeric,3	Numeric,50	Numeric,3	Numeric,12
	7494				
go_id	Character,15				
Term	Character,15				
Definition	Character,15				
IC	Numeric,15				

2.1 Term Similarities

Let us examine the similarity of the GO terms for genes "8614" and "2852" in greater detail:

```
> getTermSim(c("GO:0007166","GO:0007267","GO:0007584","GO:0007165","GO:0007186"),me
```

	GO:0007166	GO:0007267	GO:0007584	GO:0007165	GO:0007186
GO:0007166	0.2628131	0.1806383	0.1266641	0.1945233	0.2628131
GO:0007267	0.1806383	0.3551639	0.0000000	0.1806383	0.1806383
GO:0007584	0.1266641	0.0000000	0.5128961	0.1266641	0.1266641
GO:0007165	0.1945233	0.1806383	0.1266641	0.1945233	0.1945233
GO:0007186	0.2628131	0.1806383	0.1266641	0.1945233	0.4016432

This calculates Resnik's pairwise similarity between GO terms (Resnik, 1995, 1999):

$$sim(t, t') = IC_{ms}(t, t') := \max_{\hat{t} \in Pa(t,t')} IC(\hat{t}) \tag{1}$$

Here $Pa(t, t')$ denotes the set of all common ancestors of GO terms t and t', while $IC(t)$ denotes the information content of term t. It is defined as (e.g. Lord et al. (2003))

$$IC(\hat{t}) = -\log P(\hat{t}) \tag{2}$$

i.e. as the negative logarithm of the probability of observing $\hat{t}$. The information content of each GO term is already precomputed for each ontology based on the empirical observation, how many times a specific GO term or any of its direct or indirect offsprings appear in the annotation of the GO with gene products. GOSim provides a normalized version of Resnik's similarity measure, which divides the information content of the minimum subsumer by the maximum information content of all GO terms, hence obtaining a number between 0 and 1.

```
> data("ICsBPhumanall")
> IC[c("GO:0007166","GO:0007267","GO:0007584","GO:0007165","GO:0007186")]

GO:0007166 GO:0007267 GO:0007584 GO:0007165 GO:0007186
  3.006413   4.062846   5.867200   2.225221   4.594539
```

This loads the information contents of all GO terms within "biological process". Likewise, the data files `ICsMFhumanall` and `ICsCChumanall` contain the information contents of all GO terms within "molecular function" and "cellular component" for human. Since GOSim version 1.1.4.0 the information content of GO terms relies on the mapping of primary gene IDs (mainly Entrez) to GO terms provided by the libraries org.Dm.eg.db (fly), org.Hs.eg.db (human), org.Mm.eg.db (mouse), etc. Additionally, it is possible to pass a user provided mapping via the function `setEvidenceLevel`. Please refer to the manual pages for details. If only GO terms having certain evidence codes should be considered, one must explicitly calculate the corresponding information contents in the function `calcICs`. Again, more information on this function can be found in the manual pages.

To continue our example from above, let us also calculate Jiang and Conrath's pairwise similarity between GO terms, which is the default, for compairson reasons (Jiang and Conrath, 1998):

```
> getTermSim(c("GO:0007166","GO:0007267","GO:0007584","GO:0007165","GO:0007186"),ve
```

```
           GO:0007166 GO:0007267 GO:0007584 GO:0007165 GO:0007186
GO:0007166  0.9505312  0.5105747  0.2498911  0.7587689  0.7519293
GO:0007267  0.5105747  0.9828000  0.0000000  0.5740054  0.4169139
GO:0007584  0.2498911  0.0000000  0.9971692  0.2740140  0.2119568
GO:0007165  0.7587689  0.5740054  0.2740140  0.8919565  0.5820734
GO:0007186  0.7519293  0.4169139  0.2119568  0.5820734  0.9898931
```

Jiang and Conrath's similarity measure is defined as

$$sim(t, t') = 1 - \min(1, IC(t) - 2IC_{ms}(t, t') + IC(t')) \tag{3}$$

i.e. the similarity between t and t' is 0, if their normalized distance is at least 1.

Likewise, we can also compute Lin's pairwise similarity between GO terms (Lin, 1998):

3

```
> getTermSim(c("GO:0007166","GO:0007267","GO:0007584","GO:0007165","GO:0007186"),me
```

```
          GO:0007166 GO:0007267 GO:0007584 GO:0007165 GO:0007186
GO:0007166  1.0000000  0.5846115  0.3265762  0.8506792  0.7910622
GO:0007267  0.5846115  1.0000000  0.0000000  0.6572401  0.4773693
GO:0007584  0.3265762  0.0000000  1.0000000  0.3581018  0.2770009
GO:0007165  0.8506792  0.6572401  0.3581018  1.0000000  0.6525805
GO:0007186  0.7910622  0.4773693  0.2770009  0.6525805  1.0000000
```

It is defined as:

$$sim(t, t') = \frac{2IC_{ms}(t, t')}{IC(t) + IC(t')} \qquad (4)$$

Resnik's, Jiang-Conraths's and Lin's term similarities all refer to $IC_{ms}(t, t')$, the information content of the minimum subsumer of t and t', i.e. of the lowest common ancestor in the hierarchy. For illustration let us plot the GO graph with leaves GO:0007166 and GO:0007267 and let us compute their minimum subsumer (see Fig. **??**):

```
> library(igraph)
> G = getGOGraph(c("GO:0007166","GO:0007267"))
> G2 = igraph.from.graphNEL(G)
> plot(G2, vertex.label=V(G2)$name)
```
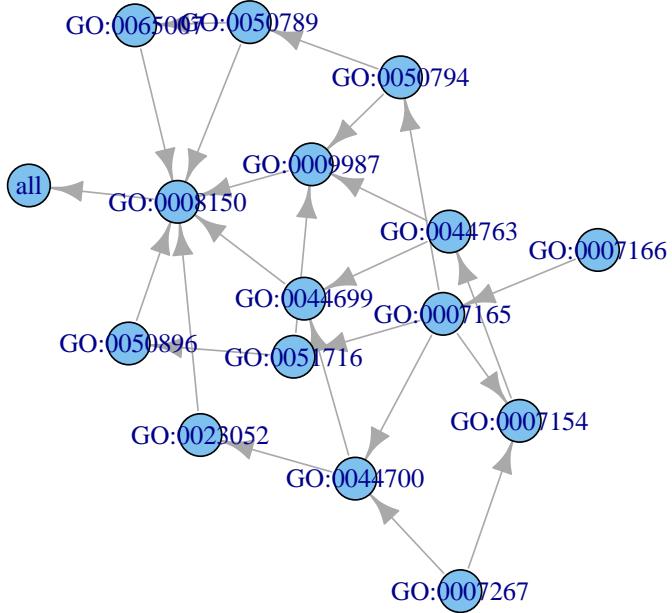
> getMinimumSubsumer("GO:0007166","GO:0007267")

[1] "GO:0023052"

In contrast to the above defined similarity measures Couto et al. (Couto et al., 2005) introduced a concept, which is not based on the minimum subsumer, but on the set of all disjunctive common ancestors. Roughly speaking, the idea is not to consider the common ancestor having the highest information content only, but also others, if they are somehow "separate" from each other, i.e. there exists a path to t or to t' not passing any other of the disjunctive common ancestors.

> getDisjCommAnc("GO:0007166","GO:0007267")

[1] "GO:0007154" "GO:0009987" "GO:0023052" "GO:0044699" "GO:0044700"
[6] "GO:0044763"

In this case the set of disjunctive common ancestors consists of the minimum subsumer, GO:0007154, and its parent, GO:0009987, because from both there exists a path to GO:0007166 not passing any other disjunctive common ancestor(see Fig. ??).

Based on the notion of disjunctive common ancestors Resnik's similarity concept can be extended by defining:

$$sim(t, t') = IC_{share}(t, t') = \frac{1}{|DisjCommAnc|} \sum_{t \in DisjCommAnc} IC(t) \qquad (5)$$

Likewise, Jiang-Conraths's and Lin's measures can be extended as well by replacing $IC_{ms}(t, t')$ by $IC_{share}(t, t')$.

```
> getTermSim(c("GO:0007166","GO:0007267","GO:0007584","GO:0007165","GO:0007186"),me

           GO:0007166 GO:0007267 GO:0007584 GO:0007165 GO:0007186
GO:0007166   3.006413   1.507568   1.448955   1.545332   2.225221
GO:0007267   1.507568   4.062846   0.000000   1.507568   1.507568
GO:0007584   1.448955   0.000000   5.867200   1.448955   1.448955
GO:0007165   1.545332   1.507568   1.448955   2.225221   1.545332
GO:0007186   2.225221   1.507568   1.448955   1.545332   4.594539
```

Finally, it should be mentioned that also the depth and density enriched term similarity by Couto et al. (Couto et al., 2003) has been integrated into *GOSim*:

```
> setEnrichmentFactors(alpha=0.5,beta=0.3)
> getTermSim(c("GO:0007166","GO:0007267","GO:0007584","GO:0007165","GO:0007186"),me

           GO:0007166 GO:0007267 GO:0007584 GO:0007165 GO:0007186
GO:0007166   9.038517    0.00000    0.00000   4.460424   3.879088
GO:0007267   0.000000   16.50672    0.00000   0.000000   0.000000
GO:0007584   0.000000    0.00000   34.42404   0.000000   0.000000
GO:0007165   4.460424    0.00000    0.00000   4.951609   0.000000
GO:0007186   3.879088    0.00000    0.00000   0.000000  21.109787
```

Since version 1.1.5 *GOSim* contains several new similarity concepts, which are based on so-called diffusion kernel techniques (Lerman and Shakhnovich, 2007) rather than on the information theoretic ideas presented before. For using these similarity measures it is necessary to pre-compute a diffusion kernel on the Gene Ontology graph via `calc.diffusion.kernel`. This will take some time and result in a kernel/similarity matrix that is stored in a file called e.g. 'diffKernelpowerBPhumanall.rda' (meaning matrix power diffusion kernel for ontology BP in human using all evidence codes) in the current working directory. Once the kernel is created, it has to be loaded into the environment first `load.diffusion.kernel`. Afterwards GO term similarities can be computed via function `getTermSim`. Please check the manual pages for details.

Since version 1.2 *GOSim* also contains Schlicker et al.'s GO term similarity measure (Schlicker et al., 2006), which is an adaption of Lin's similarity measure. Moreover, the graph information content similarity by Pesquita et al. has been implemented (Pesquita et al., 2007).

```
> getTermSim(c("GO:0007166","GO:0007267","GO:0007584","GO:0007165","GO:0007186"),me

          GO:0007166 GO:0007267 GO:0007584 GO:0007165 GO:0007186
GO:0007166  0.9505312  0.5105747  0.2498911  0.7587689  0.7519293
GO:0007267  0.5105747  0.9828000  0.0000000  0.5740054  0.4169139
GO:0007584  0.2498911  0.0000000  0.9971692  0.2740140  0.2119568
GO:0007165  0.7587689  0.5740054  0.2740140  0.8919565  0.5820734
GO:0007186  0.7519293  0.4169139  0.2119568  0.5820734  0.9898931
```

2.2 Functional Gene Similarities

The special strength of *GOSim* lies in the possibility not only to calculate similarities for individual GO terms, but also for genes based on their complete GO anntation. Since *GOSim* version 1.1.5 for this purpose the following ideas have been implemented:

1. Maximum (Couto et al., 2003) and average pairwise GO term similarity

2. Average of best matching GO term similarities (Schlicker et al., 2006).

3. Computation of a so-called *optimal assignment* of terms from one gene to those of another one (Fröhlich et al., 2006).

4. Similarity derived from Hausdorff distances between sets (del Pozo et al., 2008).

5. Embedding of each gene into a feature space: (Speer et al., 2005; Fröhlich et al., 2006) proposed to define feature vectors by a gene's maximum GO term similarity to certain prototype genes. More simple (but probably also less accurate), (Mistry and Pavlidis, 2008) recently proposed to represent each gene by a feature vector describing the presence/absence of all GO terms. The absence of each GO term is additionally weighted by its information content. Within a feature space gene functional similarities naturally arise as dot products between feature vectors. These dot products can be understood as so-called *kernel functions* (Schölkopf and Smola, 2002), as used in e.g. Support Vector Machines (Cortes and Vapnik, 1995). Depending on the choice of later normalization (see below) one can arrive at the cosine similarity (Eq. 6), at the Tanimoto coefficient (Eq. 7) or at a measure similiar to Lin's one (Eq. 8, Eq. 4).

2.2.1 Normalization of Similarities

Often, people want to normalize similarities, e.g. on the interval $[0, 1]$, for better interpretation. To do so, we can perform the transformation

$$sim_{gene}(g, g') \leftarrow \frac{sim_{gene}(g, g')}{\sqrt{sim_{gene}(g, g)sim_{gene}(g', g')}} \tag{6}$$

Provided $sim_{gene} \geq 0$, the consequence will be a similarity of 1 for g with itself and between 0 and 1 for g with any other gene. In case of a feature space embedding this transformation is equivalent to computing the cosine similarity between two feature vectors.

Another possibility is to use Lin's normalization (see Eq. 4):

$$sim_{gene}(g, g') \leftarrow \frac{2sim_{gene}(g, g')}{sim_{gene}(g, g) + sim_{gene}(g', g')} \tag{7}$$

Furthermore, one can use a normalization in the spirit of the Tanimoto coefficient:

$$sim_{gene}(g, g') \leftarrow \frac{sim_{gene}(g, g')}{sim_{gene}(g, g) + sim_{gene}(g', g') - sim_{gene}(g, g')} \tag{8}$$

In case of a feature space embedding the transformation corresponds exactly to the Tanimoto coefficient betweem two feature vectors.

We now give a more detailed overview over the different similarity concepts mentioned above.

2.2.2 Maximum and Average Pairwise GO Term Similarity

The idea of the maximum pairwise GO term similarity is straight forward. Given two genes g and g' annotated with GO terms $t_1, ..., t_n$ and $t'_1, ..., t'_m$ we define the functional similarity between between g and g' as

$$sim_{gene}(g, g') = \max_{\substack{i = 1,,...,n \\ j = 1,...,m}} sim(t_i, t'_j) \tag{9}$$

where sim is some similarity measure to compare GO terms t_i and t'_j. This idea is, for instance, realized in FuSSiMeg (Couto et al., 2003). Instead of computing the maximum pairwise GO term similarity one may also take the average here.

2.2.3 Average of Best Matching GO Term Similarities

The idea of this approach (Schlicker et al., 2006) is to assign each GO term t_i occuring in gene g to its best matching partner $t'_{\pi i}$ in gene g'. Hence multiple GO terms from gene g can be assigned to one GO term from gene g'. A similarity score is computed by taking the average similarity of assigned GO terms. Since, however, genes can have an unequal number of GO terms the result depends on whether GO terms of gene g are assigned to those of gene g' or vice versa. Hence, in Schlicker et al. (2006) it was proposed to either take the maximum or the average of both similarity scores. Both strategies are implemented in *GOSim*.

2.2.4 Optimal Assignment Gene Similarities

To elucidate the idea of the optimal assignment (Fröhlich et al., 2006), consider the GO terms associated with gene "8614" on one hand and gene "2852" on the other hand:

```
> getGOInfo(c("8614","2852"))

            8614          2852
go_id       Character,12 Character,50
Term        Character,12 Character,50
Definition  Character,12 Character,50
IC          Numeric,12   Numeric,50
```

Given a similarity concept sim to compare individual GO terms, the idea is now to assign each term of the gene having fewer annotation to exactly one term of the other gene such that the overall similarity is maximized. More formally the optimal assignment problem can be stated as follows: Let π be some permutation of either an n-subset of natural numbers $\{1, ..., m\}$ or an m-subset of natural numbers $\{1, ..., n\}$ (this will be clear from context). Then we are looking for the quantity

$$sim_{gene}(g, g') = \begin{cases} \max_\pi \sum_{i=1}^n sim(t_i, t'_{\pi(i)}) & \text{if } m > n \\ \max_\pi \sum_{j=1}^m sim(t_{\pi(j)}, t'_j) & \text{otherwise} \end{cases} \tag{10}$$

The computation of (10) corresponds to the solution of the classical maximum weighted bipartite matching (optimal assignment) problem in graph theory and can be carried out in $O(\max(n, m)^3)$ time (Mehlhorn and Näher, 1999). To prevent that larger lists of terms automatically achieve a higher similarity we may further sim_{gene} divide 10 by $\max(m, n)$.

In our example, using Lin's GO term similarity measure the following assignments yielding a corresponding similarity matrix are found:

```
> getGeneSim(c("8614","2852"),similarity="OA",similarityTerm="Lin",avg=FALSE, verb

filtering out genes not mapping to the currently set GO category ... ===> list of  2
term similarity matrix:
            GO:0010629 GO:0046885 GO:0006874 GO:0006979 GO:0007566 GO:0030968
GO:0010629   1.0000000 0.35490465 0.19542277  0.0000000  0.0000000  0.2007658
GO:0046885   0.3549046 1.00000000 0.43030745  0.0000000  0.0000000  0.1698320
GO:0006874   0.1954228 0.43030745 1.00000000  0.0000000  0.0000000  0.1637637
GO:0006979   0.0000000 0.00000000 0.00000000  1.0000000  0.0000000  0.4414432
GO:0007566   0.0000000 0.00000000 0.00000000  0.0000000  1.0000000  0.0000000
GO:0030968   0.2007658 0.16983198 0.16376373  0.4414432  0.0000000  1.0000000
GO:0033280   0.0000000 0.00000000 0.00000000  0.2092914  0.0000000  0.4483505
GO:0040015   0.3721151 0.12218460 0.13039013  0.0000000  0.1860972  0.1368560
```

```
GO:0043434  0.0000000 0.00000000 0.00000000  0.2605260  0.0000000  0.5528910
GO:0046697  0.0000000 0.00000000 0.00000000  0.0000000  0.7783503  0.0000000
GO:0071456  0.0000000 0.05201503 0.06225648  0.4052713  0.0000000  0.5447404
GO:2001256  0.1432364 0.11414955 0.12046150  0.0000000  0.0000000  0.1268545
            GO:0033280 GO:0040015 GO:0043434 GO:0046697 GO:0071456 GO:2001256
GO:0010629  0.0000000  0.3721151  0.0000000  0.0000000 0.00000000  0.1432364
GO:0046885  0.0000000  0.1221846  0.0000000  0.0000000 0.05201503  0.1141495
GO:0006874  0.0000000  0.1303901  0.0000000  0.0000000 0.06225648  0.1204615
GO:0006979  0.2092914  0.0000000  0.2605260  0.0000000 0.40527132  0.0000000
GO:0007566  0.0000000  0.1860972  0.0000000  0.7783503 0.00000000  0.0000000
GO:0030968  0.4483505  0.1368560  0.5528910  0.0000000 0.54474045  0.1268545
GO:0033280  1.0000000  0.0000000  0.4859237  0.0000000 0.35097269  0.0000000
GO:0040015  0.0000000  1.0000000  0.0000000  0.1781009 0.00000000  0.1074404
GO:0043434  0.4859237  0.0000000  1.0000000  0.0000000 0.42580898  0.0000000
GO:0046697  0.0000000  0.1781009  0.0000000  1.0000000 0.00000000  0.0000000
GO:0071456  0.3509727  0.0000000  0.4258090  0.0000000 1.00000000  0.0000000
GO:2001256  0.0000000  0.1074404  0.0000000  0.0000000 0.00000000  1.0000000
optimal assignment:
            GO:0010629 GO:0046885 GO:0006874 GO:0006979 GO:0007566 GO:0030968
GO:0010629        1         0          0          0          0          0
GO:0046885        0         1          0          0          0          0
GO:0006874        0         0          1          0          0          0
GO:0006979        0         0          0          1          0          0
GO:0007566        0         0          0          0          1          0
GO:0030968        0         0          0          0          0          1
GO:0033280        0         0          0          0          0          0
GO:0040015        0         0          0          0          0          0
GO:0043434        0         0          0          0          0          0
GO:0046697        0         0          0          0          0          0
GO:0071456        0         0          0          0          0          0
GO:2001256        0         0          0          0          0          0
            GO:0033280 GO:0040015 GO:0043434 GO:0046697 GO:0071456 GO:2001256
GO:0010629        0         0          0          0          0          0
GO:0046885        0         0          0          0          0          0
GO:0006874        0         0          0          0          0          0
GO:0006979        0         0          0          0          0          0
GO:0007566        0         0          0          0          0          0
GO:0030968        0         0          0          0          0          0
GO:0033280        1         0          0          0          0          0
GO:0040015        0         1          0          0          0          0
GO:0043434        0         0          1          0          0          0
GO:0046697        0         0          0          1          0          0
```

10

```
GO:0071456              0          0          0          0          1          0
GO:2001256              0          0          0          0          0          1
=====================
term similarity matrix:
          GO:0001934 GO:0001956 GO:0007204 GO:0008285 GO:0045909 GO:0010628
GO:0001934 1.00000000 0.31884336 0.18199644 0.25414486 0.3280870  0.9065684
GO:0001956 0.31884336 1.00000000 0.35698855 0.15779813 0.3124381  0.2918790
GO:0007204 0.18199644 0.35698855 1.00000000 0.17670495 0.4103843  0.1916341
GO:0008285 0.25414486 0.15779813 0.17670495 1.00000000 0.1596170  0.2344419
GO:0045909 0.32808696 0.31243812 0.41038426 0.15961704 1.0000000  0.3421795
GO:0010628 0.90656841 0.29187902 0.19163405 0.23444188 0.3421795  1.0000000
GO:0010629 0.88341800 0.14323644 0.18738474 0.54501949 0.1674750  0.9394387
GO:0019228 0.16972322 0.34108370 0.46126769 0.16511230 0.4431377  0.1780750
GO:0030263 0.53768169 0.03895394 0.04983805 0.05328585 0.0000000  0.5579314
GO:0030264 0.05301288 0.03821905 0.04864143 0.05192021 0.0000000  0.0000000
GO:0032024 0.39756345 0.63730945 0.43624498 0.19576113 0.3715106  0.3672641
GO:0043065 0.51862086 0.31824798 0.18151326 0.25339710 0.3273733  0.4859168
GO:0043280 0.71521907 0.14396173 0.15560831 0.21392831 0.1435905  0.7515003
GO:0043410 0.86908627 0.43346798 0.16175121 0.22317862 0.2975851  0.6463208
GO:0045599 0.19524196 0.13290279 0.13977234 0.42198544 0.1310989  0.1776742
GO:0045944 0.84089759 0.31576096 0.17950313 0.25029088 0.3243970  0.9232019
GO:0050769 0.43429381 0.28436546 0.15521828 0.21334324 0.4216132  0.4029113
GO:0051053 0.67953459 0.13918075 0.14865546 0.45113618 0.1381562  0.7122031
GO:0051055 0.65039476 0.11772184 0.14292096 0.40491955 0.1336152  0.6802600
GO:0051480 0.18368059 0.35911179 0.99180402 0.17829216 0.4131927  0.1935022
GO:0070374 0.80596426 0.41264819 0.15125169 0.20740823 0.2812671  0.5970753
GO:0071157 0.17844030 0.12489755 0.12883298 0.38649836 0.1222271  0.1617614
GO:0071333 0.15791354 0.32502484 0.68149839 0.15391441 0.3687019  0.1651188
GO:0090200 0.37850501 0.38358220 0.13720133 0.18660546 0.2588723  0.3488871
GO:2000353 0.33377457 0.23752704 0.12238158 0.16502841 0.2345299  0.3060727
GO:2001238 0.36826583 0.37641153 0.13383884 0.18167726 0.2534153  0.3390474
GO:0007186 0.26720333 0.26939824 0.18460669 0.25819191 0.1654470  0.2472380
GO:0002695 0.22007801 0.14396173 0.15560831 0.47416475 0.1435905  0.2014220
GO:0010579 0.60758037 0.22986660 0.11735835 0.15779813 0.2261048  0.5427966
GO:0014068 0.39446408 0.39451824 0.14240737 0.19427372 0.2672462  0.3642700
GO:0030518 0.22184371 0.23956576 0.15671929 0.21559634 0.1444517  0.2031207
GO:0030819 0.78464087 0.27452845 0.14800225 0.20256677 0.2761455  0.7085433
GO:0032962 0.62390673 0.23428654 0.12024546 0.16194864 0.2309581  0.5579314
GO:0043401 0.18520240 0.21218162 0.13325805 0.18082797 0.1258403  0.1681510
GO:0045742 0.37722034 0.38268923 0.13678042 0.18598749 0.2581913  0.3476513
GO:0045745 0.36650265 0.37516430 0.13325805 0.18082797 0.2524689  0.3373554
GO:0050728 0.18169213 0.12103696 0.14833294 0.42158261 0.1379022  0.1904048
```

GO:0051281	0.36463635	0.51408245	0.82201990	0.37356134	0.3474814	0.3355652
GO:0070474	0.30304961	0.21392453	0.12552444	0.14770597	0.5371171	0.3150341
GO:0071356	0.06965070	0.04617023	0.06229511	0.06777665	0.0000000	0.0000000
GO:0071375	0.07934080	0.05023743	0.06993437	0.07691810	0.0000000	0.0000000
GO:0071392	0.05871209	0.04109495	0.05339731	0.05737480	0.0000000	0.0000000
GO:0090004	0.31837899	0.48644738	0.13128821	0.17795176	0.2492503	0.3316331
GO:0008284	0.52148479	0.31932412	0.18238716	0.83460599	0.3286635	0.4887648
GO:0030335	0.47047325	0.45733181	0.16663498	0.23058080	0.3050573	0.4383232
GO:0006954	0.00000000	0.00000000	0.00000000	0.00000000	0.0000000	0.0000000
GO:0007049	0.10125241	0.05821424	0.08641867	0.09733977	0.0000000	0.0000000
GO:0045087	0.00000000	0.00000000	0.00000000	0.00000000	0.0000000	0.0000000

	GO:0010629	GO:0019228	GO:0030263	GO:0030264	GO:0032024	GO:0043065
GO:0001934	0.8834180	0.16972322	0.53768169	0.05301288	0.39756345	0.51862086
GO:0001956	0.1432364	0.34108370	0.03895394	0.03821905	0.63730945	0.31824798
GO:0007204	0.1873847	0.46126769	0.04983805	0.04864143	0.43624498	0.18151326
GO:0008285	0.5450195	0.16511230	0.05328585	0.05192021	0.19576113	0.25339710
GO:0045909	0.1674750	0.44313769	0.00000000	0.00000000	0.37151057	0.32737331
GO:0010628	0.9394387	0.17807498	0.55793145	0.00000000	0.36726410	0.48591680
GO:0010629	1.0000000	0.17439994	0.54907611	0.00000000	0.17951462	0.23603440
GO:0019228	0.1743999	1.00000000	0.04756549	0.04647432	0.41272661	0.16930293
GO:0030263	0.5490761	0.04756549	1.00000000	0.76892582	0.04558657	0.46346781
GO:0030264	0.0000000	0.04647432	0.76892582	1.00000000	0.04458335	0.45136246
GO:0032024	0.1795146	0.41272661	0.04558657	0.04458335	1.00000000	0.39663822
GO:0043065	0.2360344	0.16930293	0.46346781	0.45136246	0.39663822	1.00000000
GO:0043280	0.7355225	0.14654752	0.47905404	0.40405208	0.17490633	0.70063704
GO:0043410	0.4286789	0.31693087	0.15798112	0.04872672	0.52991020	0.45370543
GO:0045599	0.4155298	0.13241834	0.04469363	0.04372891	0.15884735	0.19480035
GO:0045944	0.8691041	0.16755285	0.71394167	0.05250039	0.39278254	0.51051478
GO:0050769	0.1965692	0.23780115	0.04841018	0.04728037	0.34535312	0.43318996
GO:0051053	0.6978366	0.14036472	0.62064129	0.04579454	0.16789912	0.20859120
GO:0051055	0.6671415	0.13524100	0.44907452	0.00000000	0.14116889	0.17391886
GO:0051480	0.1891706	0.46481870	0.05014181	0.04893073	0.43941984	0.18318844
GO:0070374	0.3966884	0.29752466	0.15021535	0.04638634	0.49912439	0.42083403
GO:0071157	0.3789525	0.12255922	0.04194583	0.04109495	0.14754447	0.17807135
GO:0071333	0.1619543	0.40926308	0.04527597	0.04428622	0.38944335	0.15754964
GO:0090200	0.1706975	0.27131524	0.37580949	0.36781069	0.45721814	0.60911953
GO:2000353	0.1500891	0.11670658	0.34357588	0.33687814	0.27862662	0.64427772
GO:2001238	0.1659695	0.26500167	0.36863425	0.36093485	0.44706654	0.59267736
GO:0007186	0.2408168	0.35865295	0.05499861	0.05354497	0.33674516	0.26637688
GO:0002695	0.4698884	0.14654752	0.04850166	0.04736763	0.17490633	0.21951705
GO:0010579	0.5344116	0.23382403	0.51599856	0.03821905	0.26814434	0.31824798
GO:0014068	0.1780793	0.28105884	0.04534089	0.04434833	0.47284146	0.39355320

```
GO:0030518   0.1987664 0.30764941 0.04876162 0.04761553 0.29138827 0.22127373
GO:0030819   0.6943227 0.13978220 0.61856523 0.04564481 0.33095101 0.41076798
GO:0032962   0.5490761 0.11476240 0.39229369 0.03895394 0.27417819 0.32678326
GO:0043401   0.1651560 0.26390952 0.04306930 0.04217273 0.25185292 0.18480499
GO:0045742   0.1701040 0.27052578 0.04395192 0.04301861 0.45594997 0.37638727
GO:0045745   0.1651560 0.26390952 0.04306930 0.04217273 0.44530823 0.36571620
GO:0050728   0.4447040 0.14007714 0.00000000 0.00000000 0.14596298 0.18125313
GO:0051281   0.3916027 0.38328136 0.04291406 0.04202387 0.60979728 0.36385788
GO:0070474   0.1544103 0.41376788 0.00000000 0.00000000 0.25180640 0.30244062
GO:0071356   0.0000000 0.05878453 0.04724700 0.04617023 0.05579138 0.06947992
GO:0071375   0.0000000 0.06554035 0.05151490 0.05023743 0.06184133 0.07911928
GO:0071392   0.0000000 0.05079703 0.04194583 0.04109495 0.04854645 0.05859069
GO:0090004   0.1624036 0.12477909 0.26105619 1.02058130 0.57617755 0.31770691
GO:0008284   0.2373824 0.17006297 0.05452169 0.05309282 0.39831119 0.51989403
GO:0030335   0.2134480 0.15628727 0.05104167 0.04978728 0.56180407 0.46917809
GO:0006954   0.0000000 0.00000000 0.00000000 0.00000000 0.00000000 0.00000000
GO:0007049   0.0000000 0.07980700 0.05993654 0.05821424 0.07438889 0.10089191
GO:0045087   0.0000000 0.00000000 0.00000000 0.00000000 0.00000000 0.00000000
             GO:0043280 GO:0043410 GO:0045599 GO:0045944 GO:0050769 GO:0051053
GO:0001934 0.71521907 0.86908627 0.19524196 0.84089759 0.43429381 0.67953459
GO:0001956 0.14396173 0.43346798 0.13290279 0.31576096 0.28436546 0.13918075
GO:0007204 0.15560831 0.16175121 0.13977234 0.17950313 0.15521828 0.14865546
GO:0008285 0.21392831 0.22317862 0.42198544 0.25029088 0.21334324 0.45113618
GO:0045909 0.14359053 0.29758509 0.13109895 0.32439701 0.42161318 0.13815619
GO:0010628 0.75150029 0.64632075 0.17767416 0.92320189 0.40291129 0.71220309
GO:0010629 0.73552249 0.42867890 0.41552981 0.86910408 0.19656919 0.69783664
GO:0019228 0.14654752 0.31693087 0.13241834 0.16755285 0.23780115 0.14036472
GO:0030263 0.47905404 0.15798112 0.04469363 0.71394167 0.04841018 0.62064129
GO:0030264 0.40405208 0.04872672 0.04372891 0.05250039 0.04728037 0.04579454
GO:0032024 0.17490633 0.52991020 0.15884735 0.39278254 0.34535312 0.16789912
GO:0043065 0.70063704 0.45370543 0.19480035 0.51051478 0.43318996 0.20859120
GO:0043280 1.00000000 0.35581504 0.17060336 0.70580784 0.18880885 0.58851010
GO:0043410 0.35581504 1.00000000 0.17643524 0.62095697 0.38782674 0.36528020
GO:0045599 0.17060336 0.17643524 1.00000000 0.19295940 0.56398485 0.36334547
GO:0045944 0.70580784 0.62095697 0.19295940 1.00000000 0.42859502 0.89993969
GO:0050769 0.18880885 0.38782674 0.56398485 0.42859502 1.00000000 0.18066935
GO:0051053 0.58851010 0.36528020 0.36334547 0.89993969 0.18066935 1.00000000
GO:0051055 0.56652778 0.32674210 0.32879640 0.64260292 0.15150587 0.54390365
GO:0051480 0.15683783 0.16308014 0.14076355 0.18114125 0.15644163 0.14977717
GO:0070374 0.33349222 0.93494170 0.16643102 0.57643178 0.36355289 0.34332811
GO:0071157 0.15763386 0.16259985 0.32021425 0.17653177 0.15731597 0.33672475
GO:0071333 0.13765840 0.28112917 0.12511796 0.15603302 0.13735308 0.13218892
```

```
GO:0090200 0.53480750 0.50690915 0.15276537 0.37416899 0.33088061 0.16111904
GO:2000353 0.47861622 0.30563127 0.13799483 0.33039825 0.29618227 0.14477534
GO:2001238 0.52209060 0.60771187 0.14944663 0.36415995 0.32302924 0.15743179
GO:0007186 0.22310634 0.41569542 0.19762166 0.26294644 0.22247007 0.21182945
GO:0002695 0.18926695 0.19647155 0.37813650 0.21718211 0.18880885 0.40137701
GO:0010579 0.49791837 0.55845669 0.13290279 0.95475829 0.28436546 0.60661177
GO:0014068 0.17371799 0.64670116 0.15786659 0.38975697 0.34301195 0.16680380
GO:0030518 0.19057139 0.35275172 0.17166251 0.21890146 0.19010697 0.18228255
GO:0030819 0.58600894 0.70460010 0.16329917 1.22952914 0.35601605 0.75349131
GO:0032962 0.47905404 0.57221986 0.13583481 0.53234541 0.29116065 0.46277665
GO:0043401 0.16288774 0.29983881 0.14887147 0.18314731 0.16254833 0.15679366
GO:0045742 0.16706246 0.62109575 0.15235096 0.37291353 0.32989845 0.16065814
GO:0045745 0.16288774 0.60506945 0.14887147 0.36243577 0.32167182 0.15679366
GO:0050728 0.15740531 0.44032289 0.33969886 0.17942456 0.15704152 0.35967194
GO:0051281 0.16215778 0.33130786 0.30781487 0.36061057 0.32023328 0.32412456
GO:0070474 0.13387850 0.27683954 0.12295528 0.29989865 0.39315259 0.12914229
GO:0071356 0.06022107 0.29730203 0.05445975 0.06876871 0.06008011 0.05770114
GO:0071375 0.06733108 0.33385218 0.06020947 0.07819834 0.06715492 0.06419648
GO:0071392 0.05186616 0.25475572 0.04753508 0.05808412 0.05176156 0.04998602
GO:0090004 0.16055023 0.28957626 0.14691652 0.31490302 0.27999240 0.15462663
GO:0008284 0.22053153 0.45589577 0.19559881 0.51328965 0.43518626 0.20950699
GO:0030335 0.20218546 0.41642345 0.18102954 0.46379271 0.39907660 0.19288020
GO:0006954 0.00000000 0.25898413 0.00000000 0.00000000 0.00000000 0.00000000
GO:0007049 0.08247807 0.08668825 0.07204021 0.09939915 0.08221389 0.07782324
GO:0045087 0.00000000 0.27943082 0.00000000 0.00000000 0.00000000 0.00000000
           GO:0051055 GO:0051480 GO:0070374 GO:0071157 GO:0071333 GO:0090200
GO:0001934  0.6503948 0.18368059 0.80596426 0.17844030 0.15791354 0.37850501
GO:0001956  0.1177218 0.35911179 0.41264819 0.12489755 0.32502484 0.38358220
GO:0007204  0.1429210 0.99180402 0.15125169 0.12883298 0.68149839 0.13720133
GO:0008285  0.4049195 0.17829216 0.20740823 0.38649836 0.15391441 0.18660546
GO:0045909  0.1336152 0.41319265 0.28126713 0.12222713 0.36870189 0.25887232
GO:0010628  0.6802600 0.19350221 0.59707526 0.16176141 0.16511880 0.34888709
GO:0010629  0.6671415 0.18917058 0.39668841 0.37895249 0.16195433 0.17069751
GO:0019228  0.1352410 0.46481870 0.29752466 0.12255922 0.40926308 0.27131524
GO:0030263  0.4490745 0.05014181 0.15021535 0.04194583 0.04527597 0.37580949
GO:0030264  0.0000000 0.04893073 0.04638634 0.04109495 0.04428622 0.36781069
GO:0032024  0.1411689 0.43941984 0.49912439 0.14754447 0.38944335 0.45721814
GO:0043065  0.1739189 0.18318844 0.42083403 0.17807135 0.15754964 0.60911953
GO:0043280  0.5665278 0.15683783 0.33349222 0.15763386 0.13765840 0.53480750
GO:0043410  0.3267421 0.16308014 0.93494170 0.16259985 0.28112917 0.50690915
GO:0045599  0.3287964 0.14076355 0.16643102 0.32021425 0.12511796 0.15276537
GO:0045944  0.6426029 0.18114125 0.57643178 0.17653177 0.15603302 0.37416899
```

```
GO:0050769   0.1515059 0.15644163 0.36355289 0.15731597 0.13735308 0.33088061
GO:0051053   0.5439037 0.14977717 0.34332811 0.33672475 0.13218892 0.16111904
GO:0051055   1.0000000 0.14395750 0.30782116 0.30546637 0.12763502 0.13565846
GO:0051480   0.1439575 1.00000000 0.15241308 0.12967464 0.68641384 0.13815629
GO:0070374   0.3078212 0.15241308 1.00000000 0.15406515 0.26493336 0.47866667
GO:0071157   0.3054664 0.12967464 0.15406515 1.00000000 0.11627969 0.14228290
GO:0071333   0.1276350 0.68641384 0.26493336 0.11627969 1.00000000 0.24286041
GO:0090200   0.1356585 0.13815629 0.47866667 0.14228290 0.24286041 1.00000000
GO:2000353   0.1223115 0.12314081 0.29035356 0.12938428 0.11099850 0.43406582
GO:2001238   0.1326552 0.13474741 0.57463937 0.13939968 0.23750866 0.89191211
GO:0007186   0.1765016 0.18633973 0.38510107 0.18042597 0.31553102 0.34503835
GO:0002695   0.3619262 0.15683783 0.18414548 0.34939005 0.13765840 0.16756089
GO:0010579   0.4392172 0.11805636 0.53163360 0.12489755 0.21088121 0.25933705
GO:0014068   0.1402797 0.14343645 0.60937914 0.14669795 0.25109319 0.45444183
GO:0030518   0.1528078 0.15796651 0.33047271 0.15853767 0.27339872 0.30052807
GO:0030819   0.5417666 0.14911409 0.66243137 0.15137765 0.13167215 0.31763715
GO:0032962   0.4490745 0.12097834 0.54409166 0.12748357 0.10923842 0.26497687
GO:0043401   0.1321350 0.13415872 0.28358829 0.13889913 0.46301278 0.26125033
GO:0045742   0.1352833 0.13772950 0.58659183 0.14192334 0.24219195 0.43881764
GO:0045745   0.1321350 0.13415872 0.57227618 0.13889913 0.23658152 0.42895194
GO:0050728   0.3467988 0.14944977 0.41391508 0.31485445 0.19291606 0.37813697
GO:0051281   0.3136332 0.81409510 0.31343039 0.28727435 0.57233839 0.28884138
GO:0070474   0.1251660 0.12632329 0.26266324 0.11511849 0.11357774 0.24302958
GO:0071356   0.0000000 0.06277042 0.27924902 0.05043397 0.51560532 0.25483610
GO:0071375   0.0000000 0.07053395 0.31125615 0.05532686 0.57100148 0.28122706
GO:0071392   0.0000000 0.05374615 0.24138385 0.04443888 0.44913575 0.22292384
GO:0090004   0.1303673 0.13216236 0.27410197 0.13719582 0.11827606 0.58609898
GO:0008284   0.1746496 0.18407858 0.42271783 0.17873833 0.15820761 0.37918272
GO:0030335   0.1613393 0.16804573 0.38856648 0.16649391 0.14621792 0.35147299
GO:0006954   0.0000000 0.00000000 0.24068887 0.00000000 0.22499621 0.21655431
GO:0007049   0.0000000 0.08733608 0.07954792 0.53371824 0.07356535 0.07039971
GO:0045087   0.0000000 0.00000000 0.25825085 0.00000000 0.24027013 0.23066763
             GO:2000353 GO:2001238 GO:0007186 GO:0002695 GO:0010579 GO:0014068
GO:0001934 0.33377457 0.36826583 0.26720333 0.22007801 0.60758037 0.39446408
GO:0001956 0.23752704 0.37641153 0.26939824 0.14396173 0.22986660 0.39451824
GO:0007204 0.12238158 0.13383884 0.18460669 0.15560831 0.11735835 0.14240737
GO:0008285 0.16502841 0.18167726 0.25819191 0.47416475 0.15779813 0.19427372
GO:0045909 0.23452986 0.25341533 0.16544703 0.14359053 0.22610477 0.26724622
GO:0010628 0.30607267 0.33904743 0.24723804 0.20142197 0.54279659 0.36427001
GO:0010629 0.15008907 0.16596950 0.24081684 0.46988842 0.53441156 0.17807925
GO:0019228 0.11670658 0.26500167 0.35865295 0.14654752 0.23382403 0.28105884
GO:0030263 0.34357588 0.36863425 0.05499861 0.04850166 0.51599856 0.04534089
```

```
GO:0030264 0.33687814 0.36093485 0.05354497 0.04736763 0.03821905 0.04434833
GO:0032024 0.27862662 0.44706654 0.33674516 0.17490633 0.26814434 0.47284146
GO:0043065 0.64427772 0.59267736 0.26637688 0.21951705 0.31824798 0.39355320
GO:0043280 0.47861622 0.52209060 0.22310634 0.18926695 0.49791837 0.17371799
GO:0043410 0.30563127 0.60771187 0.41569542 0.19647155 0.55845669 0.64670116
GO:0045599 0.13799483 0.14944663 0.19762166 0.37813650 0.13290279 0.15786659
GO:0045944 0.33039825 0.36415995 0.26294644 0.21718211 0.95475829 0.38975697
GO:0050769 0.29618227 0.32302924 0.22247007 0.18880885 0.28436546 0.34301195
GO:0051053 0.14477534 0.15743179 0.21182945 0.40137701 0.60661177 0.16680380
GO:0051055 0.12231148 0.13265519 0.17650161 0.36192617 0.43921721 0.14027972
GO:0051480 0.12314081 0.13474741 0.18633973 0.15683783 0.11805636 0.14343645
GO:0070374 0.29035356 0.57463937 0.38510107 0.18414548 0.53163360 0.60937914
GO:0071157 0.12938428 0.13939968 0.18042597 0.34939005 0.12489755 0.14669795
GO:0071333 0.11099850 0.23750866 0.31553102 0.13765840 0.21088121 0.25109319
GO:0090200 0.43406582 0.89191211 0.34503835 0.16756089 0.25933705 0.45444183
GO:2000353 1.00000000 0.42565095 0.17043710 0.14995556 0.23752704 0.27710074
GO:2001238 0.42565095 1.00000000 0.45341130 0.16357655 0.30973233 0.54619932
GO:0007186 0.17043710 0.45341130 1.00000000 0.22310634 0.59899810 0.35976742
GO:0002695 0.14995556 0.16357655 0.22310634 1.00000000 0.14396173 0.17371799
GO:0010579 0.23752704 0.30973233 0.59899810 0.14396173 1.00000000 0.26673083
GO:0014068 0.27710074 0.54619932 0.35976742 0.17371799 0.26673083 1.00000000
GO:0030518 0.15077324 0.29333945 0.40096172 0.19057139 0.25798039 0.31164093
GO:0030819 0.28552603 0.31039482 0.21077711 0.18031913 0.80570540 0.32880043
GO:0032962 0.24224950 0.25991773 0.16715416 0.14740834 0.51185417 0.27270051
GO:0043401 0.13290279 0.25580092 0.33397079 0.16288774 0.22849132 0.26960781
GO:0045742 0.26847935 0.52782094 0.46456731 0.16706246 0.31489797 0.55698685
GO:0045745 0.26300535 0.51620176 0.68956821 0.16288774 0.47177884 0.54406382
GO:0050728 0.12589407 0.36949901 0.24528662 0.37518069 0.16129923 0.39145296
GO:0051281 0.26204290 0.28284025 0.18637737 0.33666581 0.25275048 0.29804305
GO:0070474 0.22145124 0.23821386 0.15268474 0.13387850 0.21392453 0.25039531
GO:0071356 0.04804196 0.24894993 0.33604865 0.06022107 0.21985244 0.26391601
GO:0071375 0.05246140 0.27407573 0.38350699 0.06733108 0.23921956 0.29232594
GO:0071392 0.04257122 0.21840651 0.28268505 0.05186616 0.19568509 0.22984118
GO:0090004 0.22952691 0.24758423 0.18425690 0.16055023 0.22145124 0.26076939
GO:0008284 0.33430145 0.36890733 0.26787217 0.22053153 0.31932412 0.39520019
GO:0030335 0.31257520 0.34262700 0.24127903 0.20218546 0.29944313 0.36519261
GO:0006954 0.00000000 0.21083661 0.29960026 0.00000000 0.18313090 0.22545089
GO:0007049 0.06122166 0.06827613 0.10321131 0.08247807 0.05821424 0.07373689
GO:0045087 0.00000000 0.22419151 0.32730614 0.53979486 0.19312334 0.24078871
           GO:0030518 GO:0030819 GO:0032962 GO:0043401 GO:0045742 GO:0045745
GO:0001934 0.22184371 0.78464087 0.62390673 0.18520240 0.37722034 0.36650265
GO:0001956 0.23956576 0.27452845 0.23428654 0.21218162 0.38268923 0.37516430
```

```
GO:0007204 0.15671929 0.14800225 0.12024546 0.13325805 0.13678042 0.13325805
GO:0008285 0.21559634 0.20256677 0.16194864 0.18082797 0.18598749 0.18082797
GO:0045909 0.14445173 0.27614547 0.23095808 0.12584030 0.25819131 0.25246887
GO:0010628 0.20312066 0.70854332 0.55793145 0.16815105 0.34765126 0.33735540
GO:0010629 0.19876643 0.69432266 0.54907611 0.16515597 0.17010395 0.16515597
GO:0019228 0.30764941 0.13978220 0.11476240 0.26390952 0.27052578 0.26390952
GO:0030263 0.04876162 0.61856523 0.39229369 0.04306930 0.04395192 0.04306930
GO:0030264 0.04761553 0.04564481 0.03895394 0.04217273 0.04301861 0.04217273
GO:0032024 0.29138827 0.33095101 0.27417819 0.25185292 0.45594997 0.44530823
GO:0043065 0.22127373 0.41076798 0.32678326 0.18480499 0.37638727 0.36571620
GO:0043280 0.19057139 0.58600894 0.47905404 0.16288774 0.16706246 0.16288774
GO:0043410 0.35275172 0.70460010 0.57221986 0.29983881 0.62109575 0.60506945
GO:0045599 0.17166251 0.16329917 0.13583481 0.14887147 0.15235096 0.14887147
GO:0045944 0.21890146 1.22952914 0.53234541 0.18314731 0.37291353 0.36243577
GO:0050769 0.19010697 0.35601605 0.29116065 0.16254833 0.32989845 0.32167182
GO:0051053 0.18228255 0.75349131 0.46277665 0.15679366 0.16065814 0.15679366
GO:0051055 0.15280782 0.54176659 0.44907452 0.13213497 0.13528330 0.13213497
GO:0051480 0.15796651 0.14911409 0.12097834 0.13415872 0.13772950 0.13415872
GO:0070374 0.33047271 0.66243137 0.54409166 0.28358829 0.58659183 0.57227618
GO:0071157 0.15853767 0.15137765 0.12748357 0.13889913 0.14192334 0.13889913
GO:0071333 0.27339872 0.13167215 0.10923842 0.46301278 0.24219195 0.23658152
GO:0090200 0.30052807 0.31763715 0.26497687 0.26125033 0.43881764 0.42895194
GO:2000353 0.15077324 0.28552603 0.24224950 0.13290279 0.26847935 0.26300535
GO:2001238 0.29333945 0.31039482 0.25991773 0.25580092 0.52782094 0.51620176
GO:0007186 0.40096172 0.21077711 0.16715416 0.33397079 0.46456731 0.68956821
GO:0002695 0.19057139 0.18031913 0.14740834 0.16288774 0.16706246 0.16288774
GO:0010579 0.25798039 0.80570540 0.51185417 0.22849132 0.31489797 0.47177884
GO:0014068 0.31164093 0.32880043 0.27270051 0.26960781 0.55698685 0.54406382
GO:0030518 1.00000000 0.18150277 0.14819840 0.29209690 0.29962867 0.29209690
GO:0030819 0.18150277 1.00000000 0.61359704 0.15621637 0.31673193 0.30914130
GO:0032962 0.14819840 0.61359704 1.00000000 0.13089808 0.26434662 0.25903819
GO:0043401 0.29209690 0.15621637 0.13089808 1.00000000 0.26057039 0.25485553
GO:0045742 0.29962867 0.31673193 0.26434662 0.26057039 1.00000000 0.52582647
GO:0045745 0.29209690 0.30914130 0.25903819 0.25485553 0.52582647 1.00000000
GO:0050728 0.21114524 0.15028506 0.12383164 0.18167408 0.37705728 0.36800401
GO:0051281 0.16311437 0.30781242 0.25810450 0.14239968 0.28809266 0.28179904
GO:0070474 0.13462683 0.25819131 0.21826401 0.11831811 0.24242927 0.23737736
GO:0071356 0.28867021 0.05746362 0.04724700 0.48522580 0.25410019 0.24793151
GO:0071375 0.32300623 0.06390262 0.05151490 0.72478273 0.28033111 0.27284186
GO:0071392 0.24839124 0.04980768 0.04194583 0.88052109 0.22236050 0.21762227
GO:0090004 0.16148789 0.26923567 0.22610477 0.14115851 0.25214097 0.24668075
GO:0008284 0.22230455 0.41256254 0.32791800 0.18552347 0.37789345 0.36713802
```

	GO:0050728	GO:0051281	GO:0070474	GO:0071356	GO:0071375	GO:0071392
GO:0030335	0.20367476	0.37996912	0.30698758	0.17236599	0.35036498	0.34110028
GO:0006954	0.25018801	0.00000000	0.00000000	0.20985126	0.21583735	0.20985126
GO:0007049	0.08323263	0.07739180	0.05993654	0.06791182	0.07013252	0.06791182
GO:0045087	0.26921835	0.00000000	0.00000000	0.22307771	0.22985434	0.22307771
GO:0001934	0.1816921	0.36463635	0.3030496	0.06965070	0.07934080	0.05871209
GO:0001956	0.1210370	0.51408245	0.2139245	0.04617023	0.05023743	0.04109495
GO:0007204	0.1483329	0.82201990	0.1255244	0.06229511	0.06993437	0.05339731
GO:0008285	0.4215826	0.37356134	0.1477060	0.06777665	0.07691810	0.05737480
GO:0045909	0.1379022	0.34748145	0.5371171	0.00000000	0.00000000	0.00000000
GO:0010628	0.1904048	0.33556516	0.3150341	0.00000000	0.00000000	0.00000000
GO:0010629	0.4447040	0.39160266	0.1544103	0.00000000	0.00000000	0.00000000
GO:0019228	0.1400771	0.38328136	0.4137679	0.05878453	0.06554035	0.05079703
GO:0030263	0.0000000	0.04291406	0.0000000	0.04724700	0.05151490	0.04194583
GO:0030264	0.0000000	0.04202387	0.0000000	0.04617023	0.05023743	0.04109495
GO:0032024	0.1459630	0.60979728	0.2518064	0.05579138	0.06184133	0.04854645
GO:0043065	0.1812531	0.36385788	0.3024406	0.06947992	0.07911928	0.05859069
GO:0043280	0.1574053	0.16215778	0.1338785	0.06022107	0.06733108	0.05186616
GO:0043410	0.4403229	0.33130786	0.2768395	0.29730203	0.33385218	0.25475572
GO:0045599	0.3396989	0.30781487	0.1229553	0.05445975	0.06020947	0.04753508
GO:0045944	0.1794246	0.36061057	0.2998986	0.06876871	0.07819834	0.05808412
GO:0050769	0.1570415	0.32023328	0.3931526	0.06008011	0.06715492	0.05176156
GO:0051053	0.3596719	0.32412456	0.1291423	0.05770114	0.06419648	0.04998602
GO:0051055	0.3467988	0.31363316	0.1251660	0.00000000	0.00000000	0.00000000
GO:0051480	0.1494498	0.81409510	0.1263233	0.06277042	0.07053395	0.05374615
GO:0070374	0.4139151	0.31343039	0.2626632	0.27924902	0.31125615	0.24138385
GO:0071157	0.3148544	0.28727435	0.1151185	0.05043397	0.05532686	0.04443888
GO:0071333	0.1929161	0.57233839	0.1135777	0.51560532	0.57100148	0.44913575
GO:0090200	0.3781370	0.28884138	0.2430296	0.25483610	0.28122706	0.22292384
GO:2000353	0.1258941	0.26204290	0.2214512	0.04804196	0.05246140	0.04257122
GO:2001238	0.3694990	0.28284025	0.2382139	0.24894993	0.27407573	0.21840651
GO:0007186	0.2452866	0.18637737	0.1526847	0.33604865	0.38350699	0.28268505
GO:0002695	0.3751807	0.33666581	0.1338785	0.06022107	0.06733108	0.05186616
GO:0010579	0.1612992	0.25275048	0.2139245	0.21985244	0.23921956	0.19568509
GO:0014068	0.3914530	0.29804305	0.2503953	0.26391601	0.29232594	0.22984118
GO:0030518	0.2111452	0.16311437	0.1346268	0.28867021	0.32300623	0.24839124
GO:0030819	0.1502851	0.30781242	0.2581913	0.05746362	0.06390262	0.04980768
GO:0032962	0.1238316	0.25810450	0.2182640	0.04724700	0.05151490	0.04194583
GO:0043401	0.1816741	0.14239968	0.1183181	0.48522580	0.72478273	0.88052109
GO:0045742	0.3770573	0.28809266	0.2424293	0.25410019	0.28033111	0.22236050
GO:0045745	0.3680040	0.28179904	0.2373774	0.24793151	0.27284186	0.21762227
GO:0050728	1.0000000	0.32353808	0.1289204	0.20315185	0.22596869	0.17603662

GO:0051281	0.3235381	1.00000000	0.2364896	0.05184028	0.05702387	0.04552712
GO:0070474	0.1289204	0.23648960	1.0000000	0.00000000	0.00000000	0.00000000
GO:0071356	0.2031519	0.05184028	0.0000000	1.00000000	0.60516659	0.47000721
GO:0071375	0.2259687	0.05702387	0.0000000	0.60516659	1.00000000	0.69984532
GO:0071392	0.1760366	0.04552712	0.0000000	0.47000721	0.69984532	1.00000000
GO:0090004	0.1344452	0.53976174	0.2345299	0.05134081	0.05642010	0.04514144
GO:0008284	0.1820470	0.36526526	0.3035415	0.06978875	0.07951998	0.05881015
GO:0030335	0.1676317	0.51848390	0.2832949	0.06418704	0.07232767	0.05478137
GO:0006954	0.8258406	0.00000000	0.0000000	0.23904322	0.27127403	0.20236550
GO:0007049	0.0000000	0.06752665	0.0000000	0.07891447	0.09158813	0.06515992
GO:0045087	0.6405987	0.00000000	0.0000000	0.25635723	0.29379169	0.21463757

	GO:0090004	GO:0008284	GO:0030335	GO:0006954	GO:0007049	GO:0045087
GO:0001934	0.31837899	0.52148479	0.47047325	0.0000000	0.10125241	0.0000000
GO:0001956	0.48644738	0.31932412	0.45733181	0.0000000	0.05821424	0.0000000
GO:0007204	0.13128821	0.18238716	0.16663498	0.0000000	0.08641867	0.0000000
GO:0008285	0.17795176	0.83460599	0.23058080	0.0000000	0.09733977	0.0000000
GO:0045909	0.24925026	0.32866354	0.30505729	0.0000000	0.00000000	0.0000000
GO:0010628	0.33163309	0.48876477	0.43832321	0.0000000	0.00000000	0.0000000
GO:0010629	0.16240362	0.23738239	0.21344797	0.0000000	0.00000000	0.0000000
GO:0019228	0.12477909	0.17006297	0.15628727	0.0000000	0.07980700	0.0000000
GO:0030263	0.26105619	0.05452169	0.05104167	0.0000000	0.05993654	0.0000000
GO:0030264	1.02058130	0.05309282	0.04978728	0.0000000	0.05821424	0.0000000
GO:0032024	0.57617755	0.39831119	0.56180407	0.0000000	0.07438889	0.0000000
GO:0043065	0.31770691	0.51989403	0.46917809	0.0000000	0.10089191	0.0000000
GO:0043280	0.16055023	0.22053153	0.20218546	0.0000000	0.08247807	0.0000000
GO:0043410	0.28957626	0.45589577	0.41642345	0.2589841	0.08668825	0.2794308
GO:0045599	0.14691652	0.19559881	0.18102954	0.0000000	0.07204021	0.0000000
GO:0045944	0.31490302	0.51328965	0.46379271	0.0000000	0.09939915	0.0000000
GO:0050769	0.27999240	0.43518626	0.39907660	0.0000000	0.08221389	0.0000000
GO:0051053	0.15462663	0.20950699	0.19288020	0.0000000	0.07782324	0.0000000
GO:0051055	0.13036730	0.17464963	0.16133926	0.0000000	0.00000000	0.0000000
GO:0051480	0.13216236	0.18407858	0.16804573	0.0000000	0.08733608	0.0000000
GO:0070374	0.27410197	0.42271783	0.38856648	0.2406889	0.07954792	0.2582508
GO:0071157	0.13719582	0.17873833	0.16649391	0.0000000	0.53371824	0.0000000
GO:0071333	0.11827606	0.15820761	0.14621792	0.2249962	0.07356535	0.2402701
GO:0090200	0.58609898	0.37918272	0.35147299	0.2165543	0.07039971	0.2306676
GO:2000353	0.22952691	0.33430145	0.31257520	0.0000000	0.06122166	0.0000000
GO:2001238	0.24758423	0.36890733	0.34262700	0.2108366	0.06827613	0.2241915
GO:0007186	0.18425690	0.26787217	0.24127903	0.2996003	0.10321131	0.3273061
GO:0002695	0.16055023	0.22053153	0.20218546	0.0000000	0.08247807	0.5397949
GO:0010579	0.22145124	0.31932412	0.29944313	0.1831309	0.05821424	0.1931233
GO:0014068	0.26076939	0.39520019	0.36519261	0.2254509	0.07373689	0.2407887

```
GO:0030518 0.16148789 0.22230455 0.20367476  0.2501880 0.08323263  0.2692184
GO:0030819 0.26923567 0.41256254 0.37996912  0.0000000 0.07739180  0.0000000
GO:0032962 0.22610477 0.32791800 0.30698758  0.0000000 0.05993654  0.0000000
GO:0043401 0.14115851 0.18552347 0.17236599  0.2098513 0.06791182  0.2230777
GO:0045742 0.25214097 0.37789345 0.35036498  0.2158373 0.07013252  0.2298543
GO:0045745 0.24668075 0.36713802 0.34110028  0.2098513 0.06791182  0.2230777
GO:0050728 0.13444522 0.18204697 0.16763172  0.8258406 0.00000000  0.6405987
GO:0051281 0.53976174 0.36526526 0.51848390  0.0000000 0.06752665  0.0000000
GO:0070474 0.23452986 0.30354148 0.28329493  0.0000000 0.00000000  0.0000000
GO:0071356 0.05134081 0.06978875 0.06418704  0.2390432 0.07891447  0.2563572
GO:0071375 0.05642010 0.07951998 0.07232767  0.2712740 0.09158813  0.2937917
GO:0071392 0.04514144 0.05881015 0.05478137  0.2023655 0.06515992  0.2146376
GO:0090004 1.00000000 0.31892193 0.51304937  0.0000000 0.06668164  0.0000000
GO:0008284 0.31892193 1.00000000 0.47152076  0.0000000 0.10154441  0.0000000
GO:0030335 0.51304937 0.47152076 1.00000000  0.0000000 0.09010291  0.0000000
GO:0006954 0.00000000 0.00000000 0.00000000  1.0000000 0.00000000  0.7875390
GO:0007049 0.06668164 0.10154441 0.09010291  0.0000000 1.00000000  0.0000000
GO:0045087 0.00000000 0.00000000 0.00000000  0.7875390 0.00000000  1.0000000
optimal assignment:
          GO:0001934 GO:0001956 GO:0007204 GO:0008285 GO:0045909 GO:0010628
```

	GO:0001934	GO:0001956	GO:0007204	GO:0008285	GO:0045909	GO:0010628
GO:0001934	1	0	0	0	0	0
GO:0001956	0	1	0	0	0	0
GO:0007204	0	0	1	0	0	0
GO:0008285	0	0	0	1	0	0
GO:0045909	0	0	0	0	1	0
GO:0010628	0	0	0	0	0	1
GO:0010629	0	0	0	0	0	0
GO:0019228	0	0	0	0	0	0
GO:0030263	0	0	0	0	0	0
GO:0030264	0	0	0	0	0	0
GO:0032024	0	0	0	0	0	0
GO:0043065	0	0	0	0	0	0
GO:0043280	0	0	0	0	0	0
GO:0043410	0	0	0	0	0	0
GO:0045599	0	0	0	0	0	0
GO:0045944	0	0	0	0	0	0
GO:0050769	0	0	0	0	0	0
GO:0051053	0	0	0	0	0	0
GO:0051055	0	0	0	0	0	0
GO:0051480	0	0	0	0	0	0
GO:0070374	0	0	0	0	0	0
GO:0071157	0	0	0	0	0	0

	GO:0010629	GO:0019228	GO:0030263	GO:0030264	GO:0032024	GO:0043065
GO:0071333	0	0	0	0	0	0
GO:0090200	0	0	0	0	0	0
GO:2000353	0	0	0	0	0	0
GO:2001238	0	0	0	0	0	0
GO:0007186	0	0	0	0	0	0
GO:0002695	0	0	0	0	0	0
GO:0010579	0	0	0	0	0	0
GO:0014068	0	0	0	0	0	0
GO:0030518	0	0	0	0	0	0
GO:0030819	0	0	0	0	0	0
GO:0032962	0	0	0	0	0	0
GO:0043401	0	0	0	0	0	0
GO:0045742	0	0	0	0	0	0
GO:0045745	0	0	0	0	0	0
GO:0050728	0	0	0	0	0	0
GO:0051281	0	0	0	0	0	0
GO:0070474	0	0	0	0	0	0
GO:0071356	0	0	0	0	0	0
GO:0071375	0	0	0	0	0	0
GO:0071392	0	0	0	0	0	0
GO:0090004	0	0	0	0	0	0
GO:0008284	0	0	0	0	0	0
GO:0030335	0	0	0	0	0	0
GO:0006954	0	0	0	0	0	0
GO:0007049	0	0	0	0	0	0
GO:0045087	0	0	0	0	0	0

	GO:0010629	GO:0019228	GO:0030263	GO:0030264	GO:0032024	GO:0043065
GO:0001934	0	0	0	0	0	0
GO:0001956	0	0	0	0	0	0
GO:0007204	0	0	0	0	0	0
GO:0008285	0	0	0	0	0	0
GO:0045909	0	0	0	0	0	0
GO:0010628	0	0	0	0	0	0
GO:0010629	1	0	0	0	0	0
GO:0019228	0	1	0	0	0	0
GO:0030263	0	0	1	0	0	0
GO:0030264	0	0	0	0	0	0
GO:0032024	0	0	0	0	1	0
GO:0043065	0	0	0	0	0	1
GO:0043280	0	0	0	0	0	0
GO:0043410	0	0	0	0	0	0
GO:0045599	0	0	0	0	0	0

GO:0045944	0	0	0	0	0	0
GO:0050769	0	0	0	0	0	0
GO:0051053	0	0	0	0	0	0
GO:0051055	0	0	0	0	0	0
GO:0051480	0	0	0	0	0	0
GO:0070374	0	0	0	0	0	0
GO:0071157	0	0	0	0	0	0
GO:0071333	0	0	0	0	0	0
GO:0090200	0	0	0	0	0	0
GO:2000353	0	0	0	0	0	0
GO:2001238	0	0	0	0	0	0
GO:0007186	0	0	0	0	0	0
GO:0002695	0	0	0	0	0	0
GO:0010579	0	0	0	0	0	0
GO:0014068	0	0	0	0	0	0
GO:0030518	0	0	0	0	0	0
GO:0030819	0	0	0	0	0	0
GO:0032962	0	0	0	0	0	0
GO:0043401	0	0	0	0	0	0
GO:0045742	0	0	0	0	0	0
GO:0045745	0	0	0	0	0	0
GO:0050728	0	0	0	0	0	0
GO:0051281	0	0	0	0	0	0
GO:0070474	0	0	0	0	0	0
GO:0071356	0	0	0	0	0	0
GO:0071375	0	0	0	0	0	0
GO:0071392	0	0	0	0	0	0
GO:0090004	0	0	0	1	0	0
GO:0008284	0	0	0	0	0	0
GO:0030335	0	0	0	0	0	0
GO:0006954	0	0	0	0	0	0
GO:0007049	0	0	0	0	0	0
GO:0045087	0	0	0	0	0	0

	GO:0043280	GO:0043410	GO:0045599	GO:0045944	GO:0050769	GO:0051053
GO:0001934	0	0	0	0	0	0
GO:0001956	0	0	0	0	0	0
GO:0007204	0	0	0	0	0	0
GO:0008285	0	0	0	0	0	0
GO:0045909	0	0	0	0	0	0
GO:0010628	0	0	0	0	0	0
GO:0010629	0	0	0	0	0	0
GO:0019228	0	0	0	0	0	0

GO:0030263	0	0	0	0	0	0
GO:0030264	0	0	0	0	0	0
GO:0032024	0	0	0	0	0	0
GO:0043065	0	0	0	0	0	0
GO:0043280	1	0	0	0	0	0
GO:0043410	0	1	0	0	0	0
GO:0045599	0	0	1	0	0	0
GO:0045944	0	0	0	0	0	0
GO:0050769	0	0	0	0	1	0
GO:0051053	0	0	0	0	0	1
GO:0051055	0	0	0	0	0	0
GO:0051480	0	0	0	0	0	0
GO:0070374	0	0	0	0	0	0
GO:0071157	0	0	0	0	0	0
GO:0071333	0	0	0	0	0	0
GO:0090200	0	0	0	0	0	0
GO:2000353	0	0	0	0	0	0
GO:2001238	0	0	0	0	0	0
GO:0007186	0	0	0	0	0	0
GO:0002695	0	0	0	0	0	0
GO:0010579	0	0	0	0	0	0
GO:0014068	0	0	0	0	0	0
GO:0030518	0	0	0	0	0	0
GO:0030819	0	0	0	1	0	0
GO:0032962	0	0	0	0	0	0
GO:0043401	0	0	0	0	0	0
GO:0045742	0	0	0	0	0	0
GO:0045745	0	0	0	0	0	0
GO:0050728	0	0	0	0	0	0
GO:0051281	0	0	0	0	0	0
GO:0070474	0	0	0	0	0	0
GO:0071356	0	0	0	0	0	0
GO:0071375	0	0	0	0	0	0
GO:0071392	0	0	0	0	0	0
GO:0090004	0	0	0	0	0	0
GO:0008284	0	0	0	0	0	0
GO:0030335	0	0	0	0	0	0
GO:0006954	0	0	0	0	0	0
GO:0007049	0	0	0	0	0	0
GO:0045087	0	0	0	0	0	0

	GO:0051055	GO:0051480	GO:0070374	GO:0071157	GO:0071333	GO:0090200
GO:0001934	0	0	0	0	0	0

GO:0001956	0	0	0	0	0	0
GO:0007204	0	0	0	0	0	0
GO:0008285	0	0	0	0	0	0
GO:0045909	0	0	0	0	0	0
GO:0010628	0	0	0	0	0	0
GO:0010629	0	0	0	0	0	0
GO:0019228	0	0	0	0	0	0
GO:0030263	0	0	0	0	0	0
GO:0030264	0	0	0	0	0	0
GO:0032024	0	0	0	0	0	0
GO:0043065	0	0	0	0	0	0
GO:0043280	0	0	0	0	0	0
GO:0043410	0	0	0	0	0	0
GO:0045599	0	0	0	0	0	0
GO:0045944	0	0	0	0	0	0
GO:0050769	0	0	0	0	0	0
GO:0051053	0	0	0	0	0	0
GO:0051055	1	0	0	0	0	0
GO:0051480	0	1	0	0	0	0
GO:0070374	0	0	1	0	0	0
GO:0071157	0	0	0	1	0	0
GO:0071333	0	0	0	0	1	0
GO:0090200	0	0	0	0	0	1
GO:2000353	0	0	0	0	0	0
GO:2001238	0	0	0	0	0	0
GO:0007186	0	0	0	0	0	0
GO:0002695	0	0	0	0	0	0
GO:0010579	0	0	0	0	0	0
GO:0014068	0	0	0	0	0	0
GO:0030518	0	0	0	0	0	0
GO:0030819	0	0	0	0	0	0
GO:0032962	0	0	0	0	0	0
GO:0043401	0	0	0	0	0	0
GO:0045742	0	0	0	0	0	0
GO:0045745	0	0	0	0	0	0
GO:0050728	0	0	0	0	0	0
GO:0051281	0	0	0	0	0	0
GO:0070474	0	0	0	0	0	0
GO:0071356	0	0	0	0	0	0
GO:0071375	0	0	0	0	0	0
GO:0071392	0	0	0	0	0	0
GO:0090004	0	0	0	0	0	0

GO:0008284	0	0	0	0	0	0
GO:0030335	0	0	0	0	0	0
GO:0006954	0	0	0	0	0	0
GO:0007049	0	0	0	0	0	0
GO:0045087	0	0	0	0	0	0

	GO:2000353	GO:2001238	GO:0007186	GO:0002695	GO:0010579	GO:0014068
GO:0001934	0	0	0	0	0	0
GO:0001956	0	0	0	0	0	0
GO:0007204	0	0	0	0	0	0
GO:0008285	0	0	0	0	0	0
GO:0045909	0	0	0	0	0	0
GO:0010628	0	0	0	0	0	0
GO:0010629	0	0	0	0	0	0
GO:0019228	0	0	0	0	0	0
GO:0030263	0	0	0	0	0	0
GO:0030264	0	0	0	0	0	0
GO:0032024	0	0	0	0	0	0
GO:0043065	0	0	0	0	0	0
GO:0043280	0	0	0	0	0	0
GO:0043410	0	0	0	0	0	0
GO:0045599	0	0	0	0	0	0
GO:0045944	0	0	0	0	0	0
GO:0050769	0	0	0	0	0	0
GO:0051053	0	0	0	0	0	0
GO:0051055	0	0	0	0	0	0
GO:0051480	0	0	0	0	0	0
GO:0070374	0	0	0	0	0	0
GO:0071157	0	0	0	0	0	0
GO:0071333	0	0	0	0	0	0
GO:0090200	0	0	0	0	0	0
GO:2000353	1	0	0	0	0	0
GO:2001238	0	1	0	0	0	0
GO:0007186	0	0	1	0	0	0
GO:0002695	0	0	0	1	0	0
GO:0010579	0	0	0	0	1	0
GO:0014068	0	0	0	0	0	1
GO:0030518	0	0	0	0	0	0
GO:0030819	0	0	0	0	0	0
GO:0032962	0	0	0	0	0	0
GO:0043401	0	0	0	0	0	0
GO:0045742	0	0	0	0	0	0
GO:0045745	0	0	0	0	0	0

GO:0050728	0	0	0	0	0	0
GO:0051281	0	0	0	0	0	0
GO:0070474	0	0	0	0	0	0
GO:0071356	0	0	0	0	0	0
GO:0071375	0	0	0	0	0	0
GO:0071392	0	0	0	0	0	0
GO:0090004	0	0	0	0	0	0
GO:0008284	0	0	0	0	0	0
GO:0030335	0	0	0	0	0	0
GO:0006954	0	0	0	0	0	0
GO:0007049	0	0	0	0	0	0
GO:0045087	0	0	0	0	0	0

	GO:0030518	GO:0030819	GO:0032962	GO:0043401	GO:0045742	GO:0045745
GO:0001934	0	0	0	0	0	0
GO:0001956	0	0	0	0	0	0
GO:0007204	0	0	0	0	0	0
GO:0008285	0	0	0	0	0	0
GO:0045909	0	0	0	0	0	0
GO:0010628	0	0	0	0	0	0
GO:0010629	0	0	0	0	0	0
GO:0019228	0	0	0	0	0	0
GO:0030263	0	0	0	0	0	0
GO:0030264	0	0	0	0	0	0
GO:0032024	0	0	0	0	0	0
GO:0043065	0	0	0	0	0	0
GO:0043280	0	0	0	0	0	0
GO:0043410	0	0	0	0	0	0
GO:0045599	0	0	0	0	0	0
GO:0045944	0	1	0	0	0	0
GO:0050769	0	0	0	0	0	0
GO:0051053	0	0	0	0	0	0
GO:0051055	0	0	0	0	0	0
GO:0051480	0	0	0	0	0	0
GO:0070374	0	0	0	0	0	0
GO:0071157	0	0	0	0	0	0
GO:0071333	0	0	0	0	0	0
GO:0090200	0	0	0	0	0	0
GO:2000353	0	0	0	0	0	0
GO:2001238	0	0	0	0	0	0
GO:0007186	0	0	0	0	0	0
GO:0002695	0	0	0	0	0	0
GO:0010579	0	0	0	0	0	0

GO:0014068	0	0	0	0	0	0
GO:0030518	1	0	0	0	0	0
GO:0030819	0	0	0	0	0	0
GO:0032962	0	0	1	0	0	0
GO:0043401	0	0	0	1	0	0
GO:0045742	0	0	0	0	1	0
GO:0045745	0	0	0	0	0	1
GO:0050728	0	0	0	0	0	0
GO:0051281	0	0	0	0	0	0
GO:0070474	0	0	0	0	0	0
GO:0071356	0	0	0	0	0	0
GO:0071375	0	0	0	0	0	0
GO:0071392	0	0	0	0	0	0
GO:0090004	0	0	0	0	0	0
GO:0008284	0	0	0	0	0	0
GO:0030335	0	0	0	0	0	0
GO:0006954	0	0	0	0	0	0
GO:0007049	0	0	0	0	0	0
GO:0045087	0	0	0	0	0	0

	GO:0050728	GO:0051281	GO:0070474	GO:0071356	GO:0071375	GO:0071392
GO:0001934	0	0	0	0	0	0
GO:0001956	0	0	0	0	0	0
GO:0007204	0	0	0	0	0	0
GO:0008285	0	0	0	0	0	0
GO:0045909	0	0	0	0	0	0
GO:0010628	0	0	0	0	0	0
GO:0010629	0	0	0	0	0	0
GO:0019228	0	0	0	0	0	0
GO:0030263	0	0	0	0	0	0
GO:0030264	0	0	0	0	0	0
GO:0032024	0	0	0	0	0	0
GO:0043065	0	0	0	0	0	0
GO:0043280	0	0	0	0	0	0
GO:0043410	0	0	0	0	0	0
GO:0045599	0	0	0	0	0	0
GO:0045944	0	0	0	0	0	0
GO:0050769	0	0	0	0	0	0
GO:0051053	0	0	0	0	0	0
GO:0051055	0	0	0	0	0	0
GO:0051480	0	0	0	0	0	0
GO:0070374	0	0	0	0	0	0
GO:0071157	0	0	0	0	0	0

GO:0071333	0	0	0	0	0	0
GO:0090200	0	0	0	0	0	0
GO:2000353	0	0	0	0	0	0
GO:2001238	0	0	0	0	0	0
GO:0007186	0	0	0	0	0	0
GO:0002695	0	0	0	0	0	0
GO:0010579	0	0	0	0	0	0
GO:0014068	0	0	0	0	0	0
GO:0030518	0	0	0	0	0	0
GO:0030819	0	0	0	0	0	0
GO:0032962	0	0	0	0	0	0
GO:0043401	0	0	0	0	0	0
GO:0045742	0	0	0	0	0	0
GO:0045745	0	0	0	0	0	0
GO:0050728	1	0	0	0	0	0
GO:0051281	0	1	0	0	0	0
GO:0070474	0	0	1	0	0	0
GO:0071356	0	0	0	1	0	0
GO:0071375	0	0	0	0	1	0
GO:0071392	0	0	0	0	0	1
GO:0090004	0	0	0	0	0	0
GO:0008284	0	0	0	0	0	0
GO:0030335	0	0	0	0	0	0
GO:0006954	0	0	0	0	0	0
GO:0007049	0	0	0	0	0	0
GO:0045087	0	0	0	0	0	0

	GO:0090004	GO:0008284	GO:0030335	GO:0006954	GO:0007049	GO:0045087
GO:0001934	0	0	0	0	0	0
GO:0001956	0	0	0	0	0	0
GO:0007204	0	0	0	0	0	0
GO:0008285	0	0	0	0	0	0
GO:0045909	0	0	0	0	0	0
GO:0010628	0	0	0	0	0	0
GO:0010629	0	0	0	0	0	0
GO:0019228	0	0	0	0	0	0
GO:0030263	0	0	0	0	0	0
GO:0030264	1	0	0	0	0	0
GO:0032024	0	0	0	0	0	0
GO:0043065	0	0	0	0	0	0
GO:0043280	0	0	0	0	0	0
GO:0043410	0	0	0	0	0	0
GO:0045599	0	0	0	0	0	0

GO:0045944	0	0	0	0	0	0
GO:0050769	0	0	0	0	0	0
GO:0051053	0	0	0	0	0	0
GO:0051055	0	0	0	0	0	0
GO:0051480	0	0	0	0	0	0
GO:0070374	0	0	0	0	0	0
GO:0071157	0	0	0	0	0	0
GO:0071333	0	0	0	0	0	0
GO:0090200	0	0	0	0	0	0
GO:2000353	0	0	0	0	0	0
GO:2001238	0	0	0	0	0	0
GO:0007186	0	0	0	0	0	0
GO:0002695	0	0	0	0	0	0
GO:0010579	0	0	0	0	0	0
GO:0014068	0	0	0	0	0	0
GO:0030518	0	0	0	0	0	0
GO:0030819	0	0	0	0	0	0
GO:0032962	0	0	0	0	0	0
GO:0043401	0	0	0	0	0	0
GO:0045742	0	0	0	0	0	0
GO:0045745	0	0	0	0	0	0
GO:0050728	0	0	0	0	0	0
GO:0051281	0	0	0	0	0	0
GO:0070474	0	0	0	0	0	0
GO:0071356	0	0	0	0	0	0
GO:0071375	0	0	0	0	0	0
GO:0071392	0	0	0	0	0	0
GO:0090004	0	0	0	0	0	0
GO:0008284	0	1	0	0	0	0
GO:0030335	0	0	1	0	0	0
GO:0006954	0	0	0	1	0	0
GO:0007049	0	0	0	0	1	0
GO:0045087	0	0	0	0	0	1

```
=====================
```

term similarity matrix:

	GO:0001934	GO:0001956	GO:0007204	GO:0008285	GO:0045909	GO:0010628
GO:0010629	0.88341800	0.14323644	0.18738474	0.54501949	0.1674750	0.9394387
GO:0046885	0.37227565	0.31645835	0.41734827	0.18660546	0.3577173	0.3615608
GO:0006874	0.18956951	0.36642792	0.96327998	0.18383542	0.4229081	0.2000490
GO:0006979	0.00000000	0.00000000	0.00000000	0.00000000	0.0000000	0.0000000
GO:0007566	0.00000000	0.00000000	0.00000000	0.00000000	0.1968291	0.0000000
GO:0030968	0.22401252	0.24108839	0.15808124	0.21764415	0.1455048	0.2052091

```
GO:0033280 0.00000000 0.00000000 0.00000000 0.00000000 0.0000000 0.0000000
GO:0040015 0.15268665 0.10744042 0.12676207 0.35578731 0.3546344 0.1587928
GO:0043434 0.00000000 0.00000000 0.00000000 0.00000000 0.0000000 0.0000000
GO:0046697 0.00000000 0.00000000 0.00000000 0.00000000 0.1879061 0.0000000
GO:0071456 0.06712798 0.04504801 0.06026934 0.06538553 0.0000000 0.0000000
GO:2001256 0.14034178 0.38899661 0.11735835 0.13744912 0.1126994 0.1454839
           GO:0010629 GO:0019228 GO:0030263 GO:0030264 GO:0032024 GO:0043065
GO:0010629  1.0000000 0.17439994 0.54907611 0.00000000 0.17951462 0.23603440
GO:0046885  0.3549046 0.39577287 0.13940443 0.04311900 0.64144684 0.19084364
GO:0006874  0.1954228 0.47714979 0.05118915 0.04992759 0.45042420 0.18904533
GO:0006979  0.0000000 0.00000000 0.00000000 0.00000000 0.00000000 0.00000000
GO:0007566  0.0000000 0.21844329 0.00000000 0.00000000 0.00000000 0.00000000
GO:0030968  0.2007658 0.31016500 0.04907904 0.04791817 0.29364399 0.22343135
GO:0033280  0.0000000 0.00000000 0.00000000 0.00000000 0.00000000 0.00000000
GO:0040015  0.3721151 0.19629550 0.00000000 0.00000000 0.12663682 0.15237651
GO:0043434  0.0000000 0.00000000 0.00000000 0.00000000 0.00000000 0.00000000
GO:0046697  0.0000000 0.20750745 0.00000000 0.00000000 0.00000000 0.00000000
GO:0071456  0.0000000 0.05697733 0.04607250 0.04504801 0.05416098 0.06696934
GO:2001256  0.1432364 0.11212971 0.00000000 0.00000000 0.45377292 0.14007972
           GO:0043280 GO:0043410 GO:0045599 GO:0045944 GO:0050769 GO:0051053
GO:0010629 0.73552249  0.4286789 0.41552981 0.86910408 0.19656919 0.69783664
GO:0046885 0.30345710  0.3370771 0.15276537 0.43221174 0.16720175 0.31359590
GO:0006874 0.16111130  0.1677056 0.14419635 0.18686592 0.16069324 0.15366975
GO:0006979 0.00000000  0.2424541 0.00000000 0.00000000 0.00000000 0.00000000
GO:0007566 0.00000000  0.0000000 0.23259552 0.00000000 0.28241049 0.00000000
GO:0030968 0.19216964  0.3558245 0.17295825 0.22101285 0.19169741 0.18374426
GO:0033280 0.00000000  0.2052803 0.00000000 0.00000000 0.00000000 0.00000000
GO:0040015 0.13516123  0.1393507 0.29564479 0.15108208 0.39691205 0.31065885
GO:0043434 0.00000000  0.2543398 0.00000000 0.00000000 0.00000000 0.00000000
GO:0046697 0.00000000  0.0000000 0.22172749 0.00000000 0.29190372 0.00000000
GO:0071456 0.05832589  0.2876131 0.05290517 0.06630835 0.05819365 0.05595895
GO:2001256 0.12539701  0.1289950 0.11576418 0.13898504 0.12516602 0.12123256
           GO:0051055 GO:0051480 GO:0070374 GO:0071157 GO:0071333 GO:0090200
GO:0010629  0.6671415 0.18917058  0.3966884 0.37895249  0.1619543  0.1706975
GO:0046885  0.3532486 0.42025312  0.3182968 0.14228290  0.3743134  0.1503213
GO:0006874  0.1475498 0.97146738  0.1564457 0.13258230  0.7034463  0.1414616
GO:0006979  0.0000000 0.00000000  0.2263471 0.00000000  0.2124147  0.2048747
GO:0007566  0.0000000 0.00000000  0.0000000 0.00000000  0.0000000  0.0000000
GO:0030968  0.1539868 0.15935032  0.3331681 0.15964221  0.5391736  0.3027555
GO:0033280  0.0000000 0.00000000  0.1936150 0.00000000  0.4084756  0.1776853
GO:0040015  0.3010081 0.12757680  0.1321480 0.27664626  0.1145900  0.1221846
GO:0043434  0.0000000 0.00000000  0.2366725 0.00000000  0.4934850  0.2132975
```

GO:0046697	0.0000000	0.00000000	0.0000000	0.00000000	0.0000000	0.0000000
GO:0071456	0.0000000	0.06071413	0.2706841	0.04909791	0.4573328	0.2476841
GO:2001256	0.1177218	0.11805636	0.1227992	0.10879127	0.1068504	0.1141495

	GO:2000353	GO:2001238	GO:0007186	GO:0002695	GO:0010579	GO:0014068
GO:0010629	0.1500891	0.1659695	0.2408168	0.46988842	0.5344116	0.1780793
GO:0046885	0.1359974	0.1471068	0.1935507	0.16756089	0.2995666	0.1552580
GO:0006874	0.1257599	0.1378898	0.1924032	0.16111130	0.1204615	0.1470025
GO:0006979	0.0000000	0.1997499	0.2776981	0.00000000	0.1747083	0.2128199
GO:0007566	0.0000000	0.0000000	0.0000000	0.00000000	0.0000000	0.0000000
GO:0030968	0.1517719	0.2954612	0.4049366	0.19216964	0.2596200	0.3140368
GO:0033280	0.0000000	0.1738176	0.2299946	0.00000000	0.1545423	0.1836310
GO:0040015	0.1112504	0.1197429	0.1543554	0.32216121	0.1074404	0.1259208
GO:0043434	0.0000000	0.2077483	0.2934024	0.00000000	0.1807964	0.2219232
GO:0046697	0.0000000	0.0000000	0.0000000	0.00000000	0.0000000	0.0000000
GO:0071456	0.0468281	0.2421200	0.3237220	0.05832589	0.2145087	0.2562529
GO:2001256	0.1045497	0.1120156	0.1417504	0.12539701	0.1011779	0.1174040

	GO:0030518	GO:0030819	GO:0032962	GO:0043401	GO:0045742	GO:0045745
GO:0010629	0.1987664	0.69432266	0.5490761	0.1651560	0.1701040	0.1651560
GO:0046885	0.1685825	0.36691042	0.3060813	0.1465495	0.1499200	0.1465495
GO:0006874	0.1623026	0.15297184	0.1235053	0.1372734	0.1410142	0.1372734
GO:0006979	0.2347282	0.00000000	0.0000000	0.1988652	0.2042329	0.1988652
GO:0007566	0.0000000	0.00000000	0.0000000	0.0000000	0.0000000	0.0000000
GO:0030968	0.3449739	0.18295194	0.1491631	0.5060426	0.3018427	0.2942007
GO:0033280	0.1997148	0.00000000	0.0000000	0.8463625	0.1772024	0.1731474
GO:0040015	0.1359240	0.12987743	0.1096368	0.1193189	0.1218802	0.1193189
GO:0043434	0.2458512	0.00000000	0.0000000	0.6434940	0.2126020	0.2067916
GO:0046697	0.0000000	0.00000000	0.0000000	0.0000000	0.0000000	0.0000000
GO:0071456	0.2795270	0.05573554	0.0460725	0.4311230	0.2469888	0.2411566
GO:2001256	0.1260533	0.12083618	0.1031233	0.1116445	0.1138838	0.1116445

	GO:0050728	GO:0051281	GO:0070474	GO:0071356	GO:0071375	GO:0071392
GO:0010629	0.4447040	0.39160266	0.1544103	0.00000000	0.00000000	0.00000000
GO:0046885	0.1400797	0.35246126	0.1211354	0.05351699	0.05905924	0.04681524
GO:0006874	0.1533251	0.78669393	0.1290810	0.06442044	0.07262417	0.05495129
GO:0006979	0.4135955	0.00000000	0.0000000	0.22489114	0.25319268	0.19213013
GO:0007566	0.0000000	0.00000000	0.1844556	0.00000000	0.00000000	0.00000000
GO:0030968	0.3967368	0.16428383	0.1355411	0.56953487	0.63789352	0.48951240
GO:0033280	0.5165396	0.00000000	0.0000000	0.42901743	0.47442112	0.82129547
GO:0040015	0.3101200	0.28332785	0.3342800	0.00000000	0.00000000	0.00000000
GO:0043434	0.2317917	0.00000000	0.0000000	0.52378374	0.97040777	0.62086240
GO:0046697	0.0000000	0.00000000	0.1765969	0.00000000	0.00000000	0.00000000
GO:0071456	0.3672759	0.05042972	0.0000000	0.48115018	0.53408293	0.41795952
GO:2001256	0.1210370	0.63522824	0.1066283	0.00000000	0.00000000	0.00000000

```
            GO:0090004 GO:0008284 GO:0030335 GO:0006954 GO:0007049 GO:0045087
GO:0010629 0.16240362  0.2373824 0.21344797  0.0000000 0.00000000  0.0000000
GO:0046885 0.14465464  0.1916099 0.17760756  0.0000000 0.07039971  0.0000000
GO:0006874 0.13518396  0.1899935 0.17296137  0.0000000 0.09056352  0.0000000
GO:0006979 0.00000000  0.0000000 0.00000000  0.4947236 0.00000000  0.5348280
GO:0007566 0.00000000  0.0000000 0.00000000  0.0000000 0.00000000  0.0000000
GO:0030968 0.16263407  0.2244824 0.20550140  0.4707938 0.08416176  0.5069705
GO:0033280 0.00000000  0.0000000 0.00000000  0.2214949 0.00000000  0.2362815
GO:0040015 0.11787561  0.1529372 0.14263294  0.0000000 0.00000000  0.0000000
GO:0043434 0.00000000  0.0000000 0.00000000  0.2797096 0.00000000  0.3037114
GO:0046697 0.00000000  0.0000000 0.00000000  0.0000000 0.00000000  0.0000000
GO:0071456 0.04995693  0.0672562 0.06203847  0.4298750 0.07569159  0.4598363
GO:2001256 0.38299885  0.1405534 0.45733181  0.0000000 0.00000000  0.0000000
optimal assignment:
            GO:0010629 GO:0046885 GO:0006874 GO:0006979 GO:0007566 GO:0030968
GO:0001934       0          0          0          0          0          0
GO:0001956       0          0          0          0          0          0
GO:0007204       0          0          0          0          0          0
GO:0008285       0          0          0          0          0          0
GO:0045909       0          0          0          0          0          0
GO:0010628       0          0          0          0          0          0
GO:0010629       0          0          0          0          0          0
GO:0019228       0          0          0          1          0          0
GO:0030263       0          0          0          0          0          0
GO:0030264       0          0          0          0          0          0
GO:0032024       0          0          0          0          0          0
GO:0043065       0          0          0          0          0          0
GO:0043280       0          0          0          0          0          0
GO:0043410       0          0          0          0          0          0
GO:0045599       0          0          0          0          0          0
GO:0045944       0          0          0          0          0          0
GO:0050769       0          0          0          0          0          0
GO:0051053       0          0          0          0          0          0
GO:0051055       0          0          0          0          0          0
GO:0051480       0          0          0          0          0          0
GO:0070374       0          0          0          0          0          0
GO:0071157       0          0          0          0          0          0
GO:0071333       0          0          0          0          0          0
GO:0090200       0          0          0          0          0          0
GO:2000353       0          0          0          0          0          0
GO:2001238       0          1          0          0          0          0
GO:0007186       0          0          0          0          0          0
```

32

GO:0002695	0	0	0	0	0	0
GO:0010579	0	0	0	0	0	0
GO:0014068	0	0	0	0	0	0
GO:0030518	0	0	0	0	0	0
GO:0030819	0	0	0	0	0	0
GO:0032962	0	0	0	0	0	0
GO:0043401	0	0	0	0	0	0
GO:0045742	0	0	0	0	1	0
GO:0045745	0	0	0	0	0	0
GO:0050728	0	0	0	0	0	0
GO:0051281	0	0	0	0	0	0
GO:0070474	0	0	0	0	0	0
GO:0071356	0	0	0	0	0	0
GO:0071375	0	0	0	0	0	0
GO:0071392	0	0	0	0	0	0
GO:0090004	0	0	0	0	0	0
GO:0008284	0	0	0	0	0	0
GO:0030335	0	0	0	0	0	0
GO:0006954	1	0	0	0	0	0
GO:0007049	0	0	0	0	0	1
GO:0045087	0	0	1	0	0	0

	GO:0033280	GO:0040015	GO:0043434	GO:0046697	GO:0071456	GO:2001256
GO:0001934	1	0	0	0	0	0
GO:0001956	0	0	0	0	1	0
GO:0007204	0	0	0	0	0	0
GO:0008285	0	0	0	0	0	0
GO:0045909	0	0	0	0	0	0
GO:0010628	0	0	0	0	0	0
GO:0010629	0	0	0	0	0	0
GO:0019228	0	0	0	0	0	0
GO:0030263	0	0	0	0	0	0
GO:0030264	0	0	0	0	0	0
GO:0032024	0	0	0	0	0	0
GO:0043065	0	0	0	0	0	0
GO:0043280	0	0	0	0	0	0
GO:0043410	0	0	0	0	0	0
GO:0045599	0	0	0	1	0	0
GO:0045944	0	0	0	0	0	1
GO:0050769	0	0	0	0	0	0
GO:0051053	0	0	0	0	0	0
GO:0051055	0	0	0	0	0	0
GO:0051480	0	0	0	0	0	0

```
GO:0070374            0         0         0         0         0         0
GO:0071157            0         0         0         0         0         0
GO:0071333            0         0         0         0         0         0
GO:0090200            0         0         0         0         0         0
GO:2000353            0         0         0         0         0         0
GO:2001238            0         0         0         0         0         0
GO:0007186            0         0         0         0         0         0
GO:0002695            0         0         0         0         0         0
GO:0010579            0         0         0         0         0         0
GO:0014068            0         0         0         0         0         0
GO:0030518            0         0         0         0         0         0
GO:0030819            0         1         0         0         0         0
GO:0032962            0         0         0         0         0         0
GO:0043401            0         0         0         0         0         0
GO:0045742            0         0         0         0         0         0
GO:0045745            0         0         1         0         0         0
GO:0050728            0         0         0         0         0         0
GO:0051281            0         0         0         0         0         0
GO:0070474            0         0         0         0         0         0
GO:0071356            0         0         0         0         0         0
GO:0071375            0         0         0         0         0         0
GO:0071392            0         0         0         0         0         0
GO:0090004            0         0         0         0         0         0
GO:0008284            0         0         0         0         0         0
GO:0030335            0         0         0         0         0         0
GO:0006954            0         0         0         0         0         0
GO:0007049            0         0         0         0         0         0
GO:0045087            0         0         0         0         0         0
=====================
         8614      2852
8614 1.0000000 0.3111701
2852 0.3111701 1.0000000
```

Note the difference to a gene similarity that is just based on the maximum GO term
similarity and to a gene similarity that is based on the average of best matching GO
terms:

```
> getGeneSim(c("8614","2852"),similarity="max",similarityTerm="Lin",verbose=FALSE)

filtering out genes not mapping to the currently set GO category ... ===> list of  2
         8614      2852
8614 1.0000000 0.9018423
2852 0.9018423 1.0000000
```

```
> getGeneSim(c("8614","2852"),similarity="funSimMax",similarityTerm="Lin",verbose=
```

```
filtering out genes not mapping to the currently set GO category ... ===> list of  2
          8614      2852
8614 1.0000000 0.6419092
2852 0.6419092 1.0000000
```

2.2.5   Gene Similarities In the Spirit of Hausdorff Metrics

Hausdorff metrics are a general concept for measuring distances between compact subsets of a metric space. Let X and Y be the two sets of GO terms associated to genes g and g', and let $d(t, t')$ denote the distanc between GO terms t and t'. Then the Hausdorff distance X and Y is defined as

$$d_{Hausdorff}(X, Y) = \max\{\sup_{t \in X} \inf_{t' \in Y} d(t, t'), \sup_{t' \in Y} \inf_{t \in X} d(t, t')\} \tag{11}$$

Using Hausdorff metrics for measuring gene functional distances was proposed in del Pozo et al. (2008). We translate the idea to define a similarity measure between g and g' (see the difference to previous GOSim versions):

$$sim_{gene}(g, g') = \exp(-d_{Hausdorff}(g, g')) \tag{12}$$

```
> getGeneSim(c("8614","2852"),similarity="hausdorff",similarityTerm="Lin",verbose=
```

```
filtering out genes not mapping to the currently set GO category ... ===> list of  2
          8614      2852
8614 1.0000000 0.9873622
2852 0.9873622 1.0000000
```

2.2.6   Feature Space Embedding of Gene Products

The Simple Approach   Mistry and Pavlidis (2008) proposed to represent each gene by a feature vector describing the presence/absence of all GO terms. The absence of each GO term is additionally weighted by its information content. In the feature space similarities arise as dot products. Hence, the similarity between two GO terms t and t' is implicitly defined as the product of their information content values, hence igoring the exact DAG structure of the Gene Ontology as employed by the GO term similarity measures explained in the beginning of this document.

```
> getGeneSim(c("8614","2852"),similarity="dot",method="Tanimoto", verbose=FALSE)
```

```
filtering out genes not mapping to the currently set GO category ... ===> list of  2
     8614 2852
8614    1  NaN
2852  NaN    1
```

This will calculate the Tanimoto coefficient between feature vectors as a similarity measure. It is possible to retrieve the feature vectors via:

```
> features = getGeneFeatures(c("8614","2852"))
```

```
filtering out genes not mapping to the currently set GO category ... ===> list of  2
```

Embeddings via GO Term Similarities to Prototype Genes This approach is due to Speer et al. (2005); Fröhlich et al. (2006). The idea is to define a feature vector for each gene by its pairwise GO term similarity to certain prototype genes, i.e. the prototype genes form a (nonorthogonal) basis, and each gene is defined relative to this basis. The prototype genes can eithed be defined a priori or one can use one of the heuristics implemented in the function `selectPrototypes`. The default behavior is to select the 250 best annotated genes, i.e. which have been annotated with GO terms most often, but here we just use 5 for computational reasons:

```
> proto = selectPrototypes(n=5,verbose=FALSE)
```

We now calculate for each gene g feature vectors $\phi(g)$ by using their similarity to all prototypes $p_1, ..., p_n$:

$$\phi(g) = (sim'(g, p_1), ..., sim'(g, p_n))^T \qquad (13)$$

Here sim' by default is the maximum pairwise GO term similarity. Alternatively, one can use other similarity measures for sim' as well. These similarity measures can by itself again be combined with arbitrary GO term similarity concepts. The default is the Jiang-Conrath term similarity.

Because the feature vectors are very high-dimensional we usually perform a principal component analysis (PCA) to project the data into a lower dimensional subspace:

```
> PHI = getGeneFeaturesPrototypes(genes,prototypes=proto,verbose=FALSE)
```

```
filtering out genes not mapping to the currently set GO category ... ===> list of  1
filtering out genes not mapping to the currently set GO category ... ===> list of  5
```

This uses the above define prototypes to calculate feature vectors and performs a PCA afterwards. The number of principal components is chosen such that at least 95% of the total variance in feature space can be explained (this is a relatively conservatve criterion).

We can now plot our genes in the space spanned by the first 2 principal components to get an impression of the relative "position" of the genes to each other in the feature space (see Fig. **??**). The feature vectors are normalized to Euclidian norm 1 by default:

```
> x=seq(min(PHI$features[,1]),max(PHI$features[,1]),length.out=100)
> y=seq(min(PHI$features[,2]),max(PHI$features[,2]),length.out=100)
> plot(x,y,xlab="principal component 1",ylab="principal component 2",type="n")
> text(PHI$features[,1],PHI$features[,2],labels=genes)
```
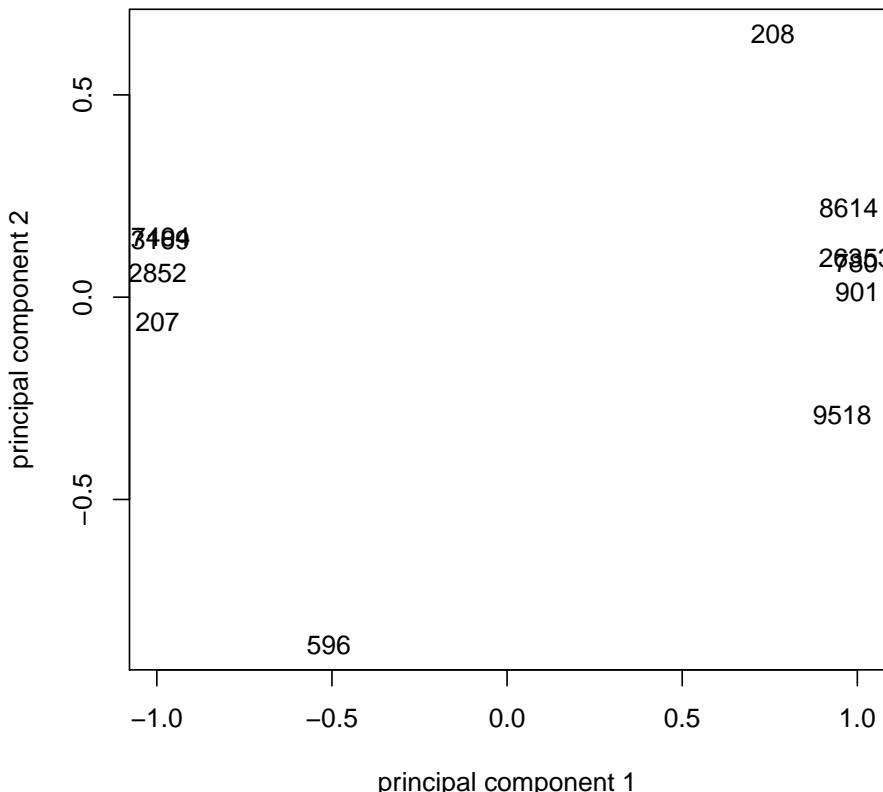
Finally, we can directly calculate the similarities of the genes to each other, this time using the Resnik's GO term similarity concept. These similarities may then be used to cluster genes with respect to their function:

```
> sim = getGeneSimPrototypes(genes,prototypes=proto,similarityTerm="Resnik",verbose
> h=hclust(as.dist(1-sim$similarity),"ward")
> plot(h,xlab="")
```

This produces a hierarchical clustering of all genes using Ward's method (see Fig. 1).

2.2.7 Combination of Similarities from Different Ontologies

It should be mentioned that up to now all similarity computations were performed within the ontology "biological process". One could imagine to combine functional similarities between gene products with regard to different taxonomies. An obvious way for doing so would be to consider the sum of the respective similarities:

$$sim_{total}(g, g') = sim_{Ontology1}(g, g') + sim_{Ontology2}(g, g') \tag{14}$$

37
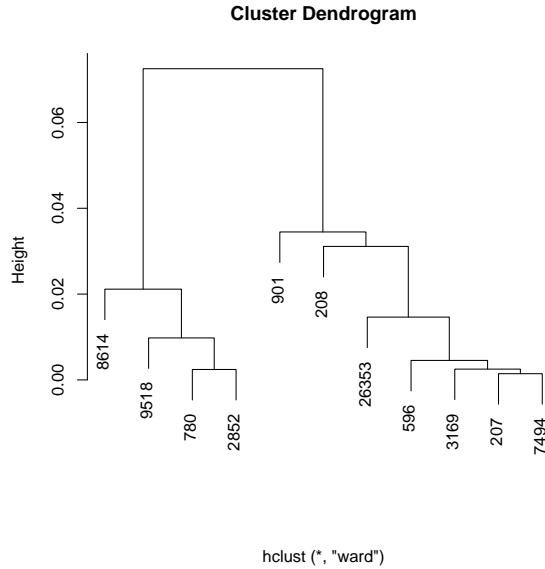
Figure 1: Possible functional clustering of the genes using Ward's method.

Of course, one could also use a weighted averaging scheme here, if desired.

2.3 Cluster Evaluations

GOSim has the possibility to evaluate a given clustering of genes or terms by means of their GO similarities. Supposed, based on other experiments (e.g. microarry), we have decided to put genes "8614", "9518", "780", "2852" in one group, genes "3169", "207", "7494", "596" in a second and the rest in a third group. Then we can ask ourselves, how similar these groups are with respect to their GO annotations:

```
> ev = evaluateClustering(c(2,3,2,3,1,2,1,1,3,1,2), sim$similarity)
> plot(ev$clustersil,main="")
```

A good indiciation of the clustering qualitiy can be obtained by looking at the cluster silhouettes (Rousseeuw, 1987) (see Fig. 2). This shows that clusters 1 and 2 are relatively homogenous with respect to the functional similarity of the genes contained in it, while the genes in cluster 3 are more dissimilar.

2.4 GO Enrichment Analysis

Since version 1.1 *GOSim* also offers the possibility of a GO enrichment analysis. Suppose, we may now want to get a clearer picture of the genes involved in cluster 1. For this purpose we use the topGO tool (Alexa et al., 2006).
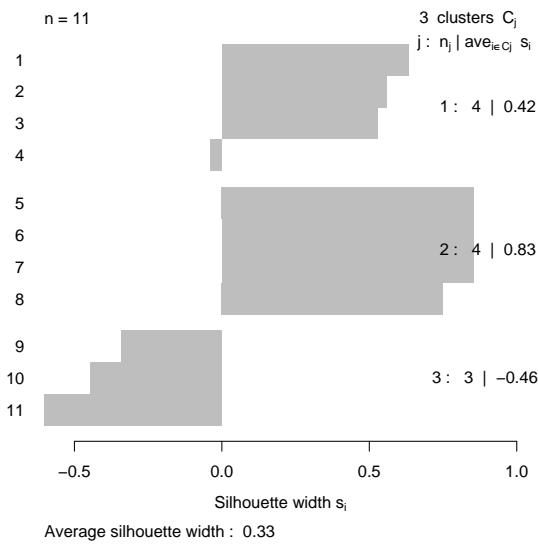
Figure 2: Silhouette plot of a possible given grouping of genes.

```
> library(org.Hs.eg.db)
> library(topGO)

groupGOTerms:        GOBPTerm, GOMFTerm, GOCCTerm environments built.

> allgenes = union(c("8614", "9518", "780", "2852"), sample(keys(org.Hs.egGO), 100
> GOenrichment(c("8614", "9518", "780", "2852"), allgenes) # print out what cluste

Building most specific GOs .....        ( 1404 GO terms found. )

Build GO DAG topology ..........        ( 3769 GO terms and 8407 relations. )

Annotating nodes ...............        ( 328 genes annotated to the GO terms. )

                    -- Elim Algorithm --

          the algorithm is scoring 683 nontrivial nodes
          parameters:
                test statistic:  fisher
                cutOff:  0.01

     Level 16:        2 nodes to be scored        (0 eliminated genes)
```

```
       Level 15:        4 nodes to be scored        (0 eliminated genes)

       Level 14:        4 nodes to be scored        (0 eliminated genes)

       Level 13:        5 nodes to be scored        (0 eliminated genes)

       Level 12:       13 nodes to be scored        (0 eliminated genes)

       Level 11:       29 nodes to be scored        (0 eliminated genes)

       Level 10:       42 nodes to be scored        (6 eliminated genes)

       Level 9:        56 nodes to be scored       (11 eliminated genes)

       Level 8:        73 nodes to be scored       (11 eliminated genes)

       Level 7:       102 nodes to be scored       (11 eliminated genes)

       Level 6:       113 nodes to be scored       (34 eliminated genes)

       Level 5:       115 nodes to be scored       (44 eliminated genes)

       Level 4:        72 nodes to be scored       (64 eliminated genes)

       Level 3:        35 nodes to be scored       (82 eliminated genes)

       Level 2:        17 nodes to be scored       (82 eliminated genes)

       Level 1:         1 nodes to be scored       (82 eliminated genes)
$GOTerms
             go_id                                             Term
16520 GO:0006874                      cellular calcium ion homeostasis
16999 GO:0007167 enzyme linked receptor protein signaling pathway
17677 GO:0007566                                    embryo implantation
18479 GO:0008285          negative regulation of cell proliferation
24496 GO:0010817                         regulation of hormone levels
33256 GO:0022411                     cellular component disassembly
42622 GO:0033993                                     response to lipid
47876 GO:0040008                                regulation of growth
51441 GO:0043434                         response to peptide hormone
65340 GO:0048609     multicellular organismal reproductive process
71984 GO:0051924                    regulation of calcium ion transport
```

40

```
79394 GO:0071310              cellular response to organic substance
83873 GO:0097305                            response to alcohol


16520
16999          Any series of molecular signals initiated by the binding of an extra
17677
18479
24496          Any process that modulates the levels of hormone within an organism
33256
42622
47876
51441 Any process that results in a change in state or activity of a cell or an orga
65340
71984
79394
83873


$p.values
  GO:0097305    GO:0071310    GO:0007566    GO:0033993    GO:0051924    GO:0007167
0.0011051224 0.0045276194 0.0003342728 0.0083386986 0.0016508672 0.0013219313
  GO:0022411    GO:0048609    GO:0043434    GO:0040008    GO:0010817    GO:0008285
0.0048712799 0.0083386986 0.0048712799 0.0083386986 0.0039132312 0.0096878977
  GO:0006874
0.0048712799


$genes
$genes$`GO:0097305`
[1] "2852" "2903" "5723" "6347" "8614"


$genes$`GO:0071310`
 [1] "10555"  "11213"  "128506" "148022" "1796"   "1977"   "2253"   "2308"
 [9] "2633"   "2651"   "2658"   "27230"  "2852"   "2908"   "30849"  "3133"
[17] "3456"   "4054"   "4504"   "4792"   "4851"   "5245"   "5293"   "5582"
[25] "56034"  "5788"   "6347"   "6566"   "7297"   "7473"   "7709"   "81285"
[33] "8614"   "8808"   "9114"   "9518"


$genes$`GO:0007566`
[1] "708"  "780"  "8614"


$genes$`GO:0033993`
 [1] "11213"  "128506" "148022" "2643"   "2852"   "2908"   "4792"   "5069"
 [9] "5723"   "6347"   "7473"   "81285"  "8614"
```

```
$genes$`GO:0051924`
[1] "23566" "2852"  "6347"  "774"   "7779"  "8614"


$genes$`GO:0007167`
 [1] "1796"  "1977"  "2048"  "2253"  "2308"  "2651"  "2658"  "2852"  "30849"
[10] "4054"  "4504"  "4792"  "4851"  "4878"  "5293"  "5582"  "56034" "6347"
[19] "63893" "780"   "79849" "8038"  "9114"  "9518"


$genes$`GO:0022411`
 [1] "11213" "2107"  "2852"  "317"   "51765" "6133"  "6604"  "7443"  "780"
[10] "832"


$genes$`GO:0048609`
 [1] "10876"  "11113"  "1447"   "147912" "1525"   "2302"   "29118"  "378807"
 [9] "57820"  "6347"   "7473"   "780"    "8614"


$genes$`GO:0043434`
 [1] "1407"  "1796"  "1977"  "2253"  "2308"  "2852"  "30849" "4878"  "8614"
[10] "9114"


$genes$`GO:0040008`
 [1] "2253"  "23566" "2658"  "27230" "3304"  "4504"  "4851"  "4878"  "5245"
[10] "7473"  "780"   "8614"  "8838"


$genes$`GO:0010817`
[1] "1407"  "2266"  "27230" "27284" "2852"  "2908"  "6566"  "8447"  "8614"


$genes$`GO:0008285`
 [1] "147912" "2302"   "23641"  "2658"   "2852"   "3304"   "3398"   "4851"
 [9] "5245"   "5784"   "5828"   "65268"  "780"    "8558"


$genes$`GO:0006874`
 [1] "23566" "2852"  "3827"  "488"   "55584" "5788"  "6347"  "64072" "7779"
[10] "8614"
```

References

Alexa, A., Rahnenführer, J., and Lengauer, T. (2006). Improved scoring of functional groups from gene expression data by decorrelating GO graph structure. *Bioinformatics*, 22(13):1600 − 1607.

Cortes, C. and Vapnik, V. (1995). Support vector networks. *Machine Learning*, 20:273 – 297.

Couto, F., Silva, M., and Coutinho, P. (2003). Implementation of a Functional Semantic Similarity Measure between Gene-Products. Technical Report DI/FCUL TR 03–29, Department of Informatics, University of Lisbon.

Couto, F., Silva, M., and Coutinho, P. (2005). Semantic Similarity over the Gene Ontology: Family Correlation and Selecting Disjunctive Ancestors. In *Conference in Information and Knowledge Management*.

del Pozo, A., Pazos, F., and Valencia, A. (2008). Defining functional distances over gene ontology. *BMC Bioinformatics*, 9:50.

Fröhlich, H., Speer, N., Poustka, A., and Beissbarth, T. (2007). GOSim - An R-Package for Computation of Information Theoretic GO Similarities Between Terms and Gene Products. *BMC Bioinformatics*, 8:166.

Fröhlich, H., Speer, N., and Zell, A. (2006). Kernel based functional gene grouping. In *Proc. Int. Joint Conf. Neural Networks*, pages 6886 – 6891.

Jiang, J. and Conrath, D. (1998). Semantic similarity based on corpus statistics and lexical taxonomy. In *Proceedings of the International Conference on Research in Computational Linguistics*, Taiwan.

Lerman, G. and Shakhnovich, B. E. (2007). Defining functional distance using manifold embeddings of gene ontology annotations. *Proc Natl Acad Sci U S A*, 104(27):11334–11339.

Lin, D. (1998). An information-theoretic definition of similarity. In Kaufmann, M., editor, *Proceedings of the 15th International Conference on Machine Learning*, volume 1, pages 296–304, San Francisco, CA.

Lord, P., Stevens, R., Brass, A., and Goble, C. (2003). Semantic similarity measures as tools for exploring the gene ontology. In *Proceedings of the Pacific Symposium on Biocomputing*, pages 601–612.

Mehlhorn, K. and Näher, S. (1999). *The LEDA Platform of Combinatorial and Geometric Computing*. Cambridge University Press.

Mistry, M. and Pavlidis, P. (2008). Gene ontology term overlap as a measure of gene functional similarity. *BMC Bioinformatics*, 9:327.

Pesquita, C., Faria, D., Bastos, H., Falcao, A., and Couto, F. (2007). Evaluating go-based semantic similarity measures. In *Proc. 10th Annual Bio-Ontologies Meeting 2007*, volume 2007, pages 37 – 40.

Resnik, P. (1995). Using information content to evaluate semantic similarity in a taxonomy. In *Proceedings of the 14th International Joint Conference on Artificial Intelligence*, volume 1, pages 448–453, Montreal.

Resnik, P. (1999). Semantic similarity in a taxonomy: An information-based measure and its application to problems of ambigiguity in natural language. *Journal of Artificial Intelligence Research*, 11:95–130.

Rousseeuw, P. (1987). Silhouettes: a graphical aid to the interpretation and validation of cluster analysis. *J. Comp. and Applied Mathematics*, 20:53–65.

Schlicker, A., Domingues, F. S., Rahnenführer, J., and Lengauer, T. (2006). A new measure for functional similarity of gene products based on Gene Ontology. *BMC Bioinformatics*, 7:302.

Schölkopf, B. and Smola, A. J. (2002). *Learning with Kernels*. MIT Press, Cambridge, MA.

Speer, N., Fröhlich, H., Spieth, C., and Zell, A. (2005). Functional grouping of genes using spectral clustering and gene ontology. In *Proc. Int. Joint Conf. Neural Networks*, pages 298 – 303.

The Gene Ontology Consortium (2004). The gene ontology (GO) database and informatics resource. *Nucleic Acids Research*, 32:D258–D261.