ProteInOn: A Web Tool for Protein Semantic Similarity

Daniel Faria, Catia Pesquita, Francisco M. Couto and André O. Falcão

FACULDADE DE CIÊNCIAS UNIVERSIDADE DE LISBOA

bio XLDB Research Group

http://xldb.di.fc.ul.pt/biotools/proteinon/

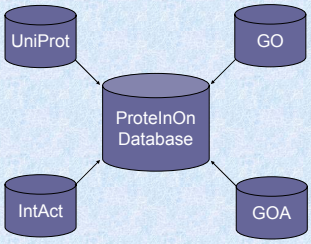
Motivation

The Gene Ontology (GO) provides a structure for comparing genes/proteins on the functional level.
Several measures have been used for this type of comparison (semantic similarity).
The tools available for the community are few and limited in application.

Abstract

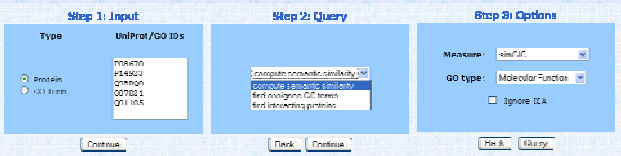
We have developed ProteInOn, an integrated web tool for computing GO based protein semantic similarity.
It implements eight distinct similarity measures, none of which were previously available online, including the novel simGIC measure developed in the context of this tool.
In addition to computing protein and GO term semantic similarity, ProteInOn combines protein interaction and annotation data, allowing the user to find proteins that interact with, or GO terms represented in a set of input proteins. The results of these queries can then be used as input for semantic similarity calculations (or other queries) providing a structure to answer more complex questions.

Database



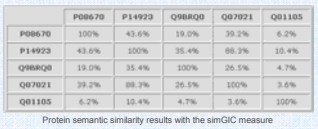
Interface

Simple and flexible 3-step query selection menu:



- 2-10 input entries
- proteins or GO terms
- 3 queries for proteins
- 2 queries for GO terms
- several options for each query

Fast and easy to read results:



	P08670	P14923	Q9BRQ0	Q07021	Q01105
P08670	100%	43.6%	19.0%	39.2%	6.2%
P14923	43.6%	100%	35.4%	88.3%	10.4%
Q9BRQ0	19.0%	35.4%	100%	26.5%	4.7%
Q07021	39.2%	88.3%	26.5%	100%	3.6%
Q01105	6.2%	10.4%	4.7%	3.6%	100%

Protein semantic similarity results with the simGIC measure

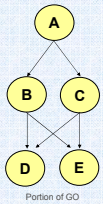
- semantic similarity results in all *vs.* all matrix
- color-coded results for easy interpretation
- term results ranked by representativity score
- results selectable for new queries
- protein and GO term ids link to source DBs

"Find assigned GO terms" results

Semantic Similarity

ProteInOn implements eight semantic similarity measures: three term similarity measures (Resnik's, Lin's and Jiang & Conrath's) with two distinct approaches (MICA and GraSM) plus two graph similarity measures (*simUI* and *simGIC*).
The three term similarity measures are information content (*IC*) based and rely on the notion of lowest common ancestor. As they are measures for single terms, applying them to proteins requires combining the similarities between the proteins' terms, which in ProteInOn is done with a best-match average.
By contrast, the graph similarity measures can be applied directly to both terms and proteins. They consider similarity between two terms (or term sets) as the ratio between the intersection and the union of the graphs they define, differing only in that *simUI* is edge based and *simGIC* is *IC* based.
All measures were evaluated by comparing protein semantic similarity with sequence similarity, and were found to correlate equally well. They differ only in resolution, which is the ordering criterion in ProteInOn's options selection menu.

GO term similarity:



Portion of GO

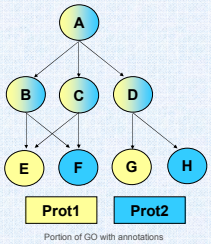
$$Resnik_{MICA}(D,E) = MAX(IC(B), IC(C))$$

$$Resnik_{GraSM}(D,E) = AVG(IC(B), IC(C))$$

$$Lin(D,E) = \frac{2 \times Resnik(D,E)}{IC(D) + IC(E)}$$

$$JiangConrath(D,E) = 1 + Resnik(D,E) - \frac{IC(D) + IC(E)}{2}$$

Protein similarity:



Portion of GO with annotations

$$simUI(Prot1, Prot2) = \frac{COUNT_{T \in Prot1 \cap Prot2}(T)}{COUNT_{T \in Prot1 \cup Prot2}(T)} = \frac{4}{8}$$

$$simGIC(Prot1, Prot2) = \frac{SUM_{T \in Prot1 \cap Prot2}(IC(T))}{SUM_{T \in Prot1 \cup Prot2}(IC(T))}$$

$$Resnik(Prot1, Prot2) = AVG(Resnik(E,F), Resnik(G,H))$$

Applications

Genomics/Proteomics:

- Find out which *biological process* terms are better represented and more meaningful in a set of upregulated genes/proteins.
- Measure the average *biological process* similarity of a set of co-expressed genes.

Comparative Genomics:

- Measure the *molecular function* similarity between sets of homologous genes from different species.

Interactomics:

- Measure the *biologic process* similarity between a protein and others it interacts with.
- Measure the *molecular function* similarity between sets of proteins that share interactors.