TEXT MINING

Bioinformatics and Computational Biology

Summer School – University Complutense of Madrid

LECTURE OVERVIEW

- The Biomedical literature
- Introduction to Natural Language Processing
- Information Retrieval in Biology
- Functional annotations: Gene Ontology
- Information Extraction in Biology
- Evaluation of Text mining tools
- Conclusions and outlook
- Useful links, reviews and articles

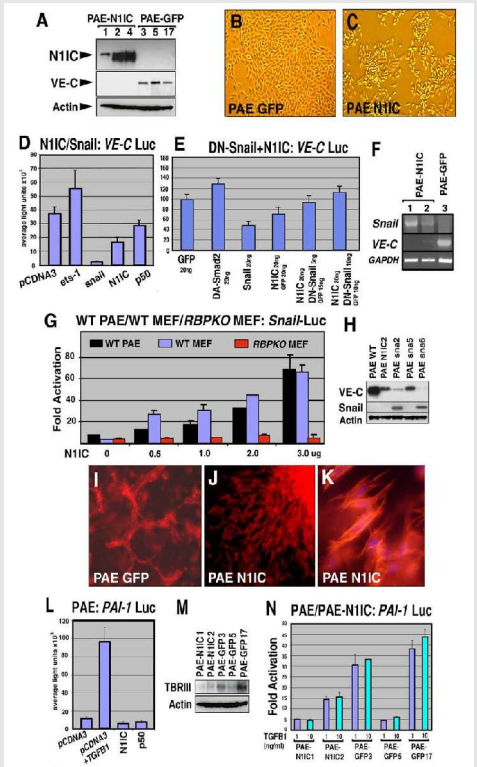
FROM EXPERIMENTS TO ARTICLES

1- Experiments

Planning and carrying out experiments (lab work)

2- Results

Processing and interpretation of obtained results



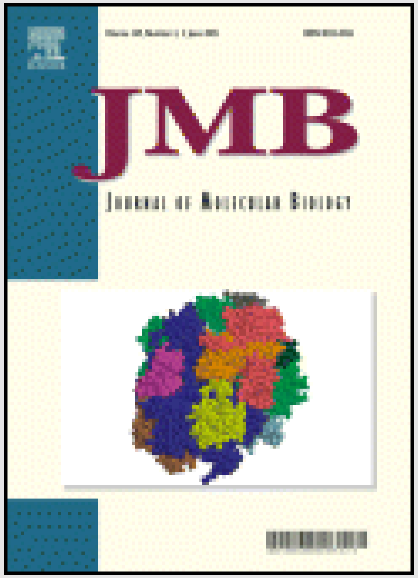
3- Scientific articles

'Relevant' results are published in scientific journals

TEXT MINING (2005)

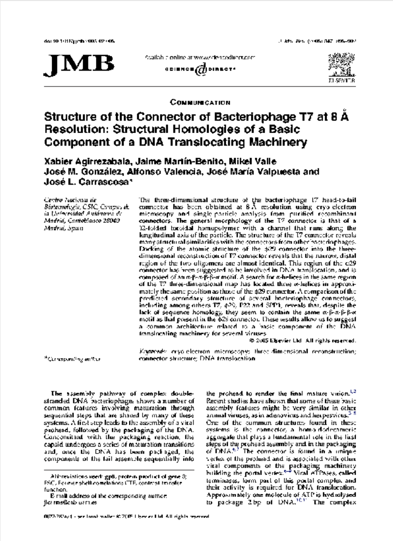
DATA IN SCIENTIFIC ARTICLES

Scientific Journals



- Format
- Paper structure
- Article type

FREE TEXT


JMB

Available online at www.sciencedirect.com

Communication

Structure of the Connector of Bacteriophage T7 at 8 Å Resolution: Structural Homologies of a Basic Component of a DNA Translocating Machinery

Xabier Agirrezabala, Jaime Martín-Benito, Mikel Valle, José M. González, Alfonso Valencia, José María Valpuesta and José L. Carrascosa*

Centro Nacional de Biotecnología, CSIC, Campus de la Universidad Autónoma de Madrid, Cantoblanco 28049 Madrid, Spain

Title

Abstracts

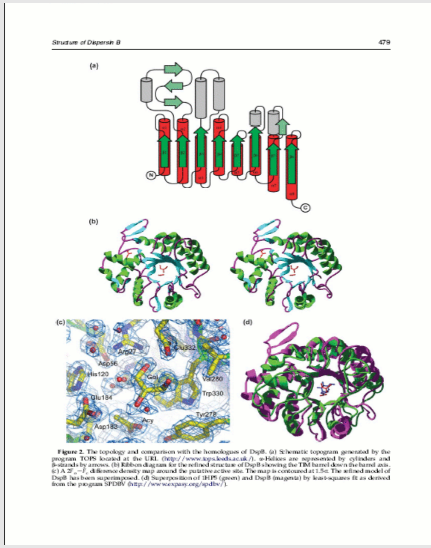
Keywords

Text body

References

TABLES

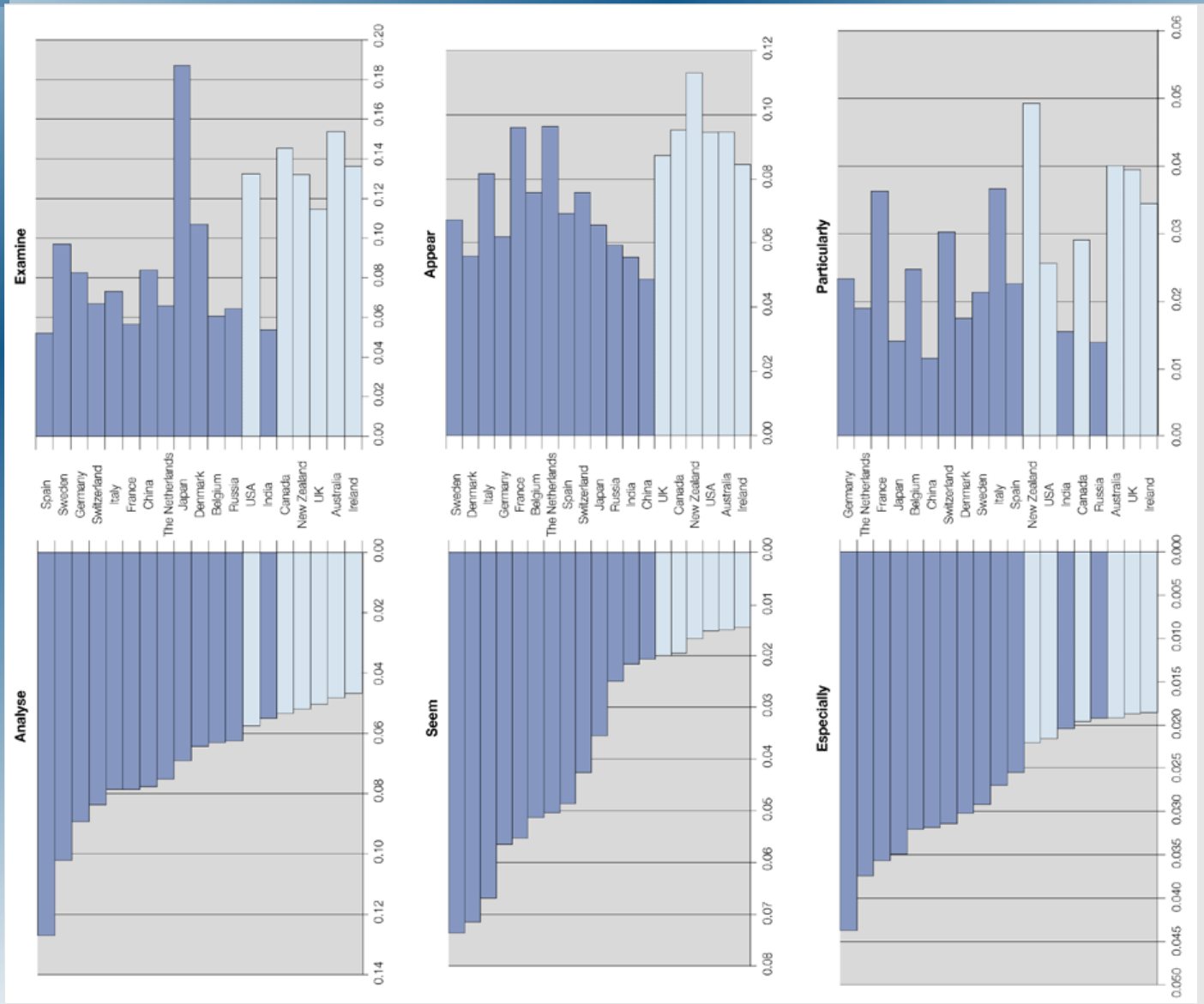
FIGURES



BIOMEDICAL LITERATURE CHARACTERISTICS

- Heavy use of domain specific terminology (12% biochemistry related technical terms).
- Polysemic words (word sense disambiguation), e.g. Drosophila genes like 'archipelago', 'capicua' or 'ebony'.
- Most words with low frequency (data sparseness).
- New names and terms created.
- Typographical variants
- Different writing styles (native languages)

SCIENTIFIC ENGLISH ?



- Most in English.
- Different native languages.
- Different word usage (preferences)

Netzel R, Perez-Iratxeta C, Bork P, Andrade MA
The way we write. EMBO Rep. 2003 May;4(5):446-51

DIFFERENT COUNTRIES – DIFFERENT WORD USAGE

Table 2 | Most frequently used words in various countries

Country	Adjectives	Nouns	Verbs	Adverbs	Example sentence	PMID ref
Spain	Infrequent, bibliographic	Repercussion, evolution, existence, **sunflower**, **olive**, **wine**	–	Basically	Prevalence of CYP2D6 gene duplication and its **repercussion** on the oxidative phenotype in a white population.	7697944
Japan	Useful	**Bullfrog**, **shadow** (in radiography)	Clarify	Faintly, next, suddenly, scarcely	MDR-1 protein was **faintly** expressed in one of four chemoresistant patients, but Bcl-2 were [**sic**] clearly detected in four patients.	12538495
UK	Unsuitable, unlinked, unfamiliar	Marmoset, **consultant**, **questionnaire**	Lie, mirror, arise, tackle	Wholly, principally, particularly	The morphology of these projection neurons was revealed in great detail and confirmed that the projection **arises wholly** from pyramidal cells.	11602231
Russia	**Gravitational**	(Space) **mission**, **quantum**, **hibernate**, peculiarity, regularity, realization	–	**Thermo-dynamically**	The article is devoted to the question of **peculiarity** of bronchopulmonary system's pathology in the workers of the animal fodder production [**sic**].	10341521
India	**Malarial**, -wise (as in stepwise), ascorbic	Malaria, buffalo, peanut, garlic, catfish,	Impart (convey)	Appreciable	Hydroxypropylmethylcellulose (HPMC) was used to **impart** strength and sphericity to the agglomerates.	12476867
France	Exceptional, digestive	Trouble	Envisage (imagine)	Successively (sequentially), essentially, sometimes	These 2 cells [**sic**] lines being able to clone, it is hard to **envisage** clonogenic assays.	3051563
China	**Medicinal**, **radiant** (heat), **noxious** (heat)	**Acupuncture**, **coal**, **tea**	**Burn**, replenish, alleviate	Obviously, meanwhile	Because only a catalytic amount of ERK2/pTpY is required, this method **alleviates** the need for large quantities of phospho-ERK2.	12056917
Germany	Satisfying practicable, unremarkable	Hint, precondition multitude	–	Additionally, exactly,	In clinically presumed spontaneous spinal cord infarction and **unremarkable** signaling of the spinal cord during sequential MRI investigations vertebral body infarction may serve as the only confirmatory sign of spinal cord ischemic stroke.	11987007
US	**Federal**, investigational, supplemental	Residency, **cocaine**, **payment**, **veteran**, **reimbursement**, physician, care, plan, **noncompliance**, effort, **profit**	Sponsor, mandate	–	Loss of revenue, mainly from **noncompliance** with charge capture resulted in the hospital billing only US$386,794.32 with a total **reimbursement** of US$165,779.86.	12488156

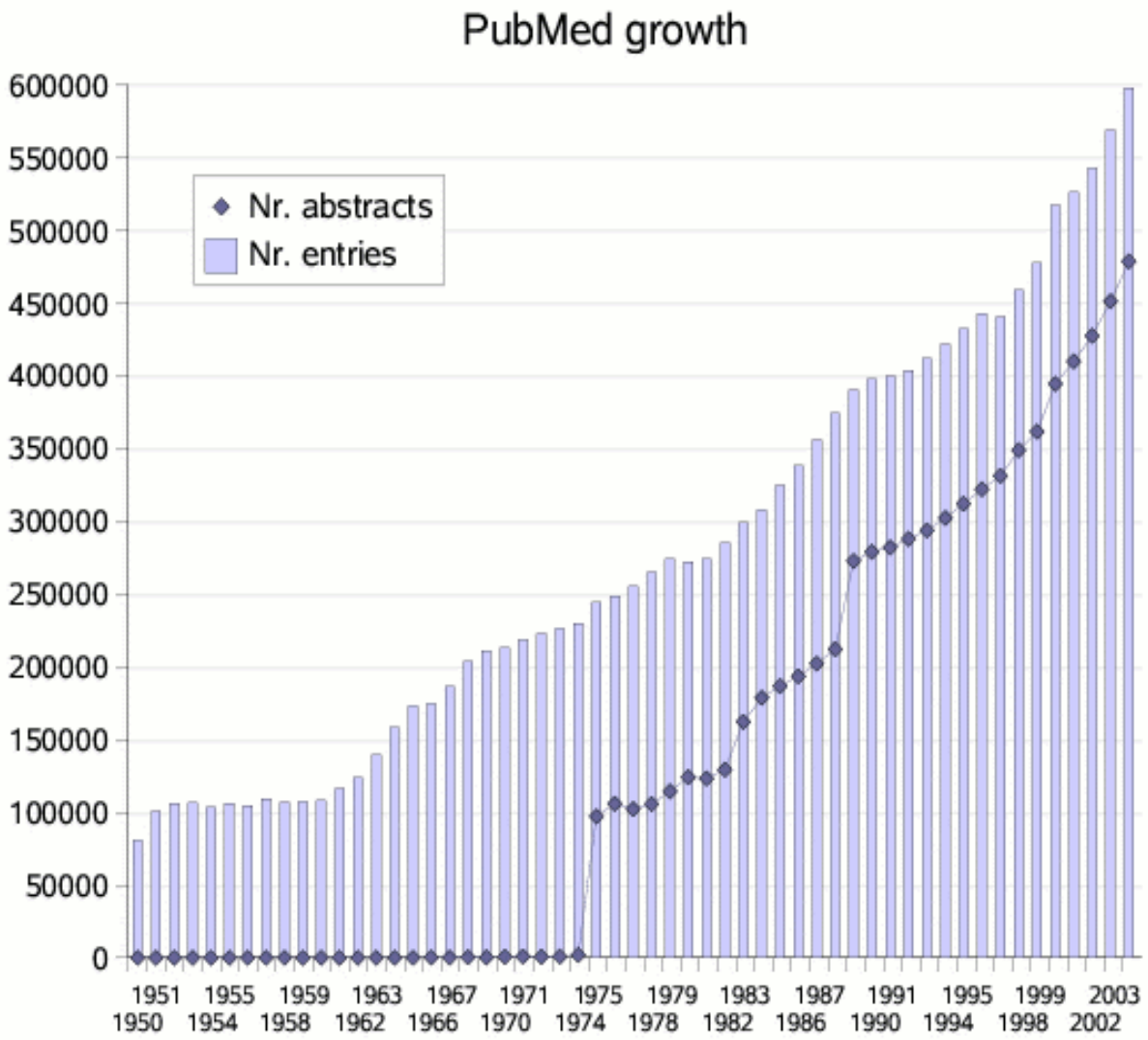
Words in bold typeface have specific meanings and are probably related to local research rather than to local language usage. The bold and underlined words in the example sentences indicate the most abundant country-specific terms. The words shown were found to be more common in the abstracts of the corresponding country than in the abstracts of any other of the 19 representative countries (as in Fig. 2). Note that most of the sentences are grammatically correct, but the usage of the marked (bold and underlined) words is unusual. PMID ref, PubMed reference number.

Netzel R, Perez-Iratxeta C, Bork P, Andrade MA. The way we write. EMBO Rep. 2003 May;4(5):446-51

PubMed DATABASE

- Developed by the National Center for Biotechnology Information (NCBI) at the National Library of Medicine NLM.
- Devoted mainly life science literature.
- Access through NCBI Entrez retrieval system: http://www.ncbi.nlm.nih.gov/entrez/
- Entrez: text-based search and retrieval system.
- Publishers submit their citations electronically to PubMed.
- Over 14 million citations from the 50th until today.
- More than 48,000 journals
- Some articles are indexed with MeSH terms publication types and GenBank Accession nr.

PubMed GROWTH

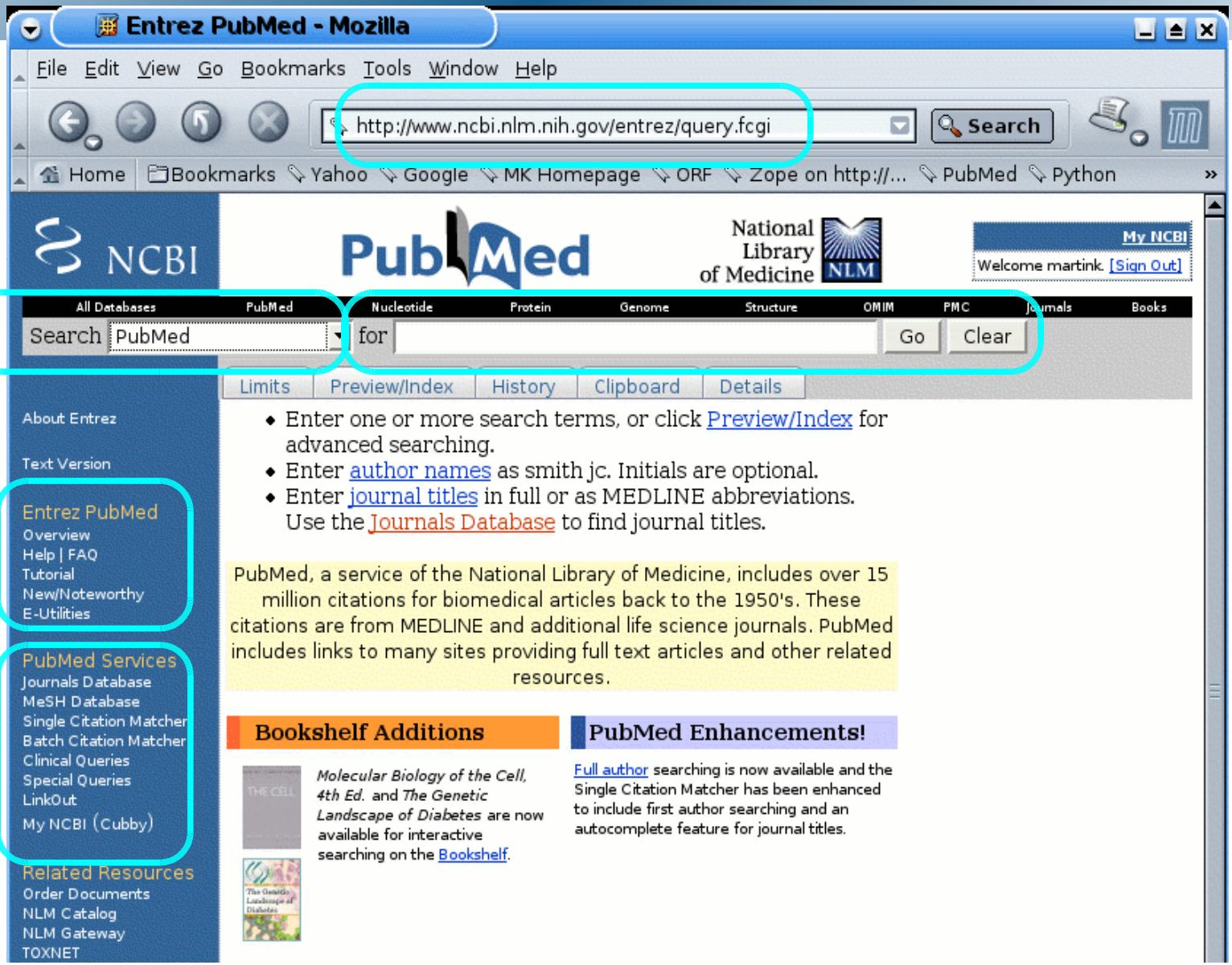


PubMed

~ 450,000 new abstracts/a

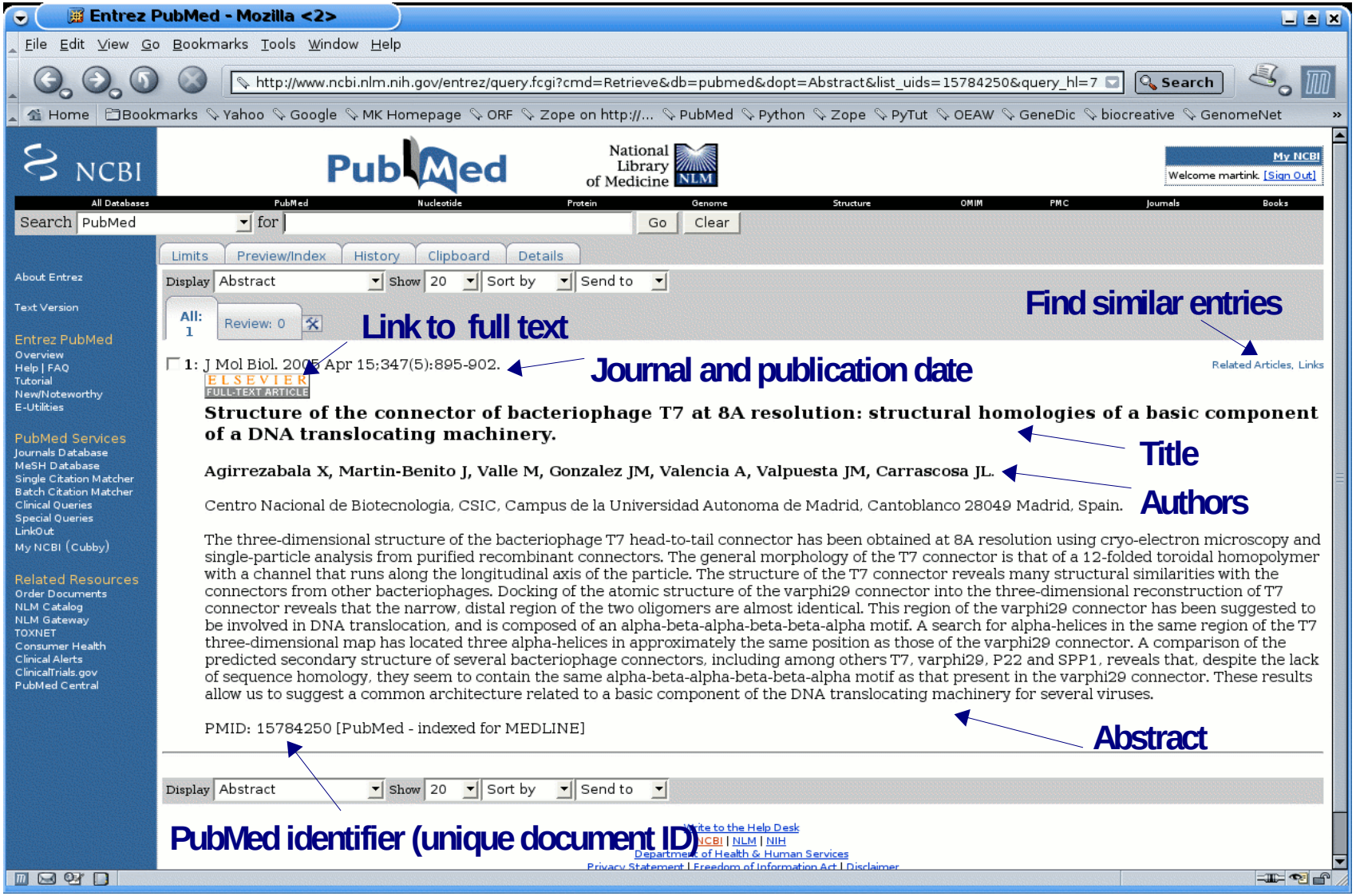
> 4,800 biomedical journals

PubMed web-interface



PubMed retrieval

PubMed retrieval



Exercise 1.1 : PubMed

1.1. Carry out a PubMed search for 'HIV' using the 'Limits' option. How many articles did you retrieve? Now try to follow the research interest in HIV over time through the associated publications deposited in PubMed by constructing a 'Publication time period' vs 'number of retrieved publications' table. Start from 1980 and use time intervals of 5 years (e.g. 1980-1984, 1985-1990,...). Describe your results?

Comment: The aim of search exercise is to explore an easy way to monitor research interests related to a certain topic of research. For instance pharmaceutical companies are often interested in monitoring research interests of other companies to obtain competitive intelligence.

http://www.pdg.cnb.uam.es/martink/LINKS/tm_sc_ucm2005.htm

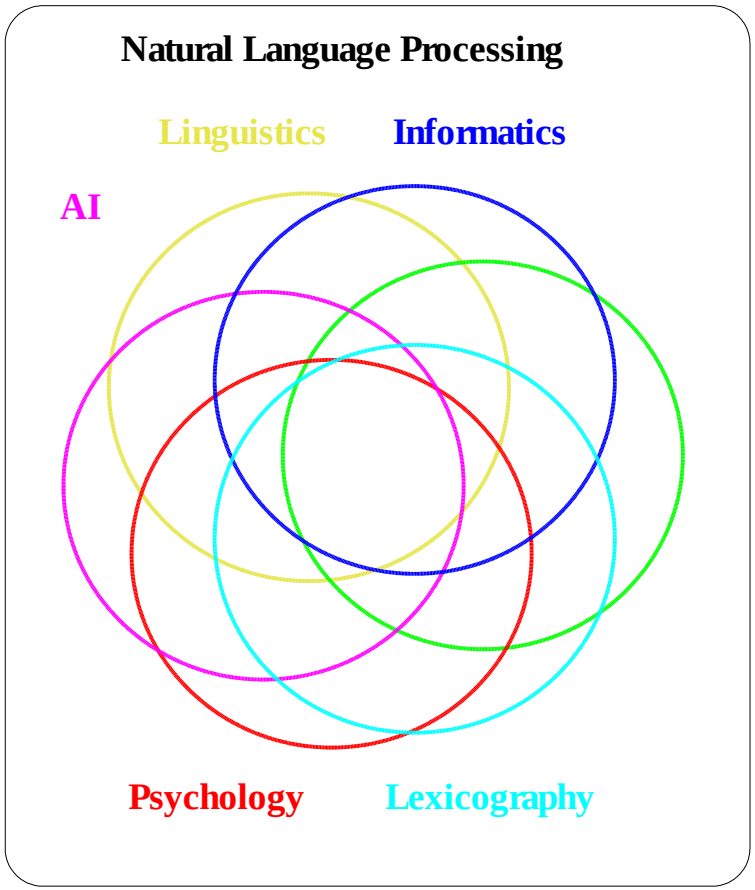
Exercises 1.2. - 1.3. : PubMed

1.2. Retrieve articles from PubMed for the Escherichia coli gene TRME_ECOLI. How many articles did your retrieve? Which problems did you encounter? Comment the obtained results. Notice that your worked with this gene before in the

1.3. Perform the same search for the Escherichia coli gene MRAZ_ECOLI Notice that you worked with that protein before, in the " Redes de Interaccion de Proteinas" session; and for the yeast gene RPE_YEAST (used in the Analisis de Secuencias session). What are the difficulties your encountered? How many documents did you retrieve?

http://www.pdg.cnb.uam.es/martink/LINKS/tm_sc_ucm2005.htm

Natural language processing (NLP)



- **Techniques that analyse, understand and generate language** (free text, speech).
- Linguistic tools, e.g. syntactic analyser and semantic classification.
- Multidisciplinary field.
- Strongly language dependent.
- Create computational models of language.
- Learn statistical properties of language.
- Methods: statistical analysis, machine learning, rule-based, pattern-matching, AI, etc...
- Domain dependent (biomedical) vs generic NLP.

MAIN NLP TOPICS

- Information Retrieval (IR).
- Information extraction/Text mining (IE).
- Question Answering (QA).
- Natural Language Generation (NLG).

- Automatic summarisation.
- Machine translation.
- Text proofing.
- Speech recognition.
- Optical character recognition (OCR).

INFORMATION RETRIEVAL (IR)

- IR: process of **recovery of those documents** from a collection of documents which satisfy a given information demand.
- Information demand often posed in form of a **search query**.
- Example: retrieval of web-pages using search engines, e.g. Google.
- First step: indexing document collection:
  - Tokenization
  - Case folding
  - Stemming
  - Stop word removal
- Efficient indexing to reduce vocabulary of terms and query formulations.
- Example: 'Glycogenin *AND* binding' and 'glycogenin *AND* bind'.
- Query types: Boolean query and Vector Space Model based query.

BOOLEAN QUERY

- Based on **combination of terms** using Boolean operators.
- Basic **Boolean operators**: AND, OR and NOT.
- Queries matched against the terms in the inverted index file.
- Entrez – Boolean search in PubMed.
- Fast, easy to implement.
- **Search engines**: often stop word removal and case folding.
- Stop word removal : space saving speed improvement.
- Return a **unranked list**.
- Return large list of documents, many not relevant.
- Terms have different information content ->
  better weighted query.

GOOGLE SCHOLAR

- Search engine for scholarly literature.
- URL: http://scholar.google.com/
- Include:
  - peer-reviewed papers
  - theses
  - books
  - preprints
  - abstracts
  - technical reports,...
- Return a ranked list according to relevance to user query.
- Ranking uses: full text, authors, publication type/journal, nr of citations in scholarly literature.

EXERCISE 2: GOOGLE SCHOLAR

Google developed Google Scholar, in order to provide a search engine specifically for academic and research users. Try out the search queries proposed in exercises 1.3 and 1.4. using the advanced Scholar Search. Compare the results with the results of PubMed. What are the advantages and disadvantages when using Google Scholar?

http://www.pdg.cnb.uam.es/martink/LINKS/tm_sc_ucm2005.htm

SELECTIVE DISSEMINATION OF INFORMATION SERVICES (SDI)

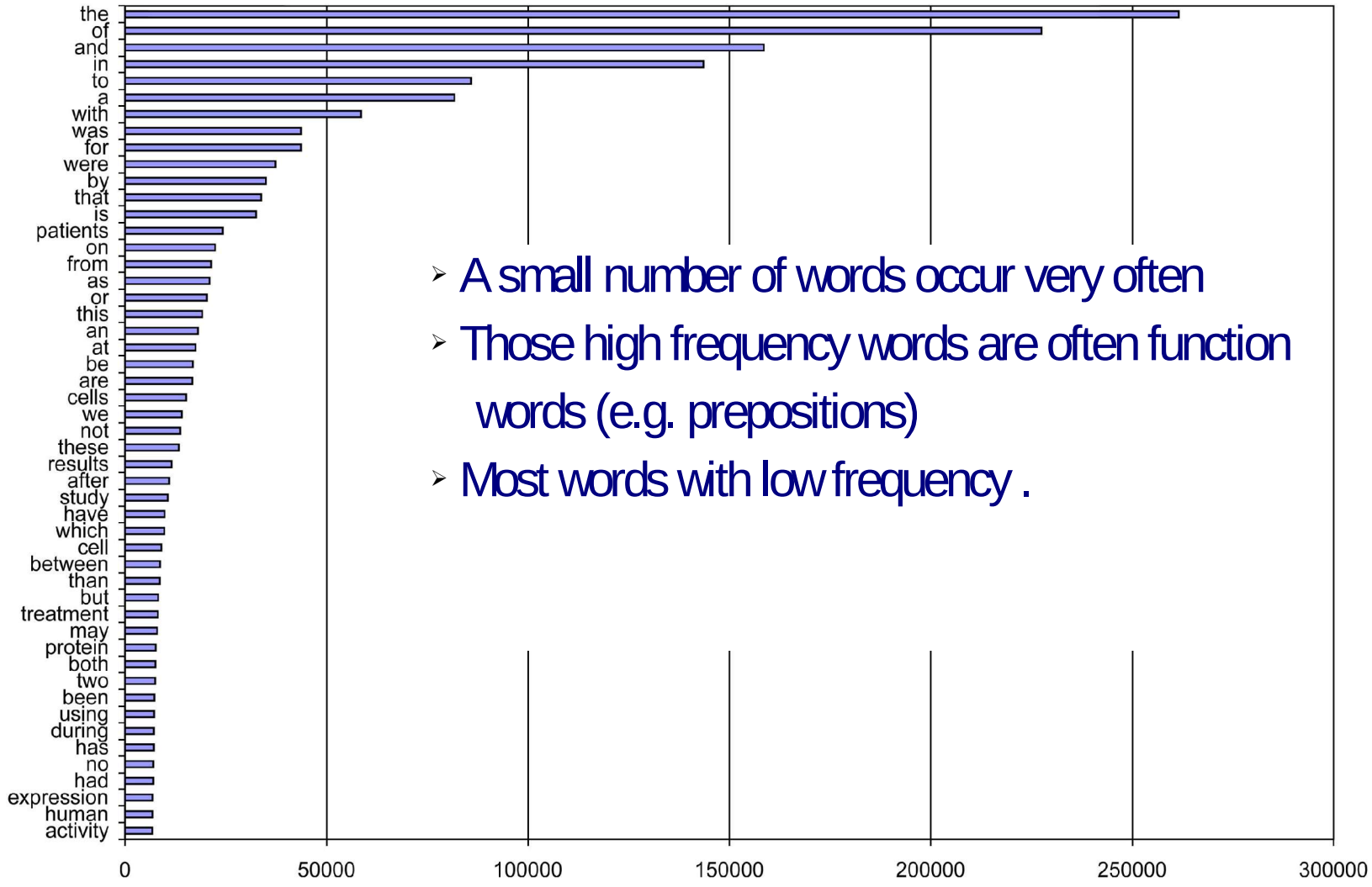
- Service provided by a library or data repository institution which periodically alerts users of new publications.
- New publications can be associated to certain subjects or information demands
- Often based on automated iterative/periodical IR queries.
- Advantages: new publications are automatically anounced (e.g. using e-mail alerts)
- Disadvantages: implicit to IR based on Boolean queries, often unrelevant articles.
- Free SDI services based on PubMed / Biomedical literature:
  - Cubby (NCBI)
  - PubCrawler
  - BioMail

EXERCISE 3: SDI

1.2. Set up your own selective dissemination of information service (SDI) query using the My NCBI Cubby service for a query topic of your own interest or of one of the genes discussed before.

http://www.pdg.cnb.uam.es/martink/LINKS/tm_sc_ucm2005.htm

ZIPF'S LAW



- A small number of words occur very often
- Those high frequency words are often function words (e.g. prepositions)
- Most words with low frequency .

From: Rebholz-Schuhmann D, Kirsch H, Couto F (2005) Facts from Text—Is Text Mining Ready to Deliver? PLoS Biol 3(2): e65

STOP WORD FILTERING

after	also	an	and
as	at	be	because
before	between	but	before
for	however	from	if
in	into	of	or
other	out	since	such
than	that	the	these
there	this	those	to
under	upon	when	where
whether	which	with	within
without	.	.	.

VECTOR SPACE MODEL (VSM)

- Measure **similarity** between query and documents.
- (1) Document indexing , (2) Term weighting,
  (3) similarity coefficient
- Query: a list of terms or even whole documents.
- Query as **vectors of terms**.
- **Term weighting** (w) according to their frequency:
  - within the document (i)
  - within the document collection (d)
- Widespread term weigthing: tf x idf.
- Calculate similarity between those vectors.
- Cosine similarity often used.
- Return a ranked list.
- Example: related article search in PubMed

$$w_{i,j} = tf_{i,j} \times idf_j$$

w: term weight
tf: term frequency

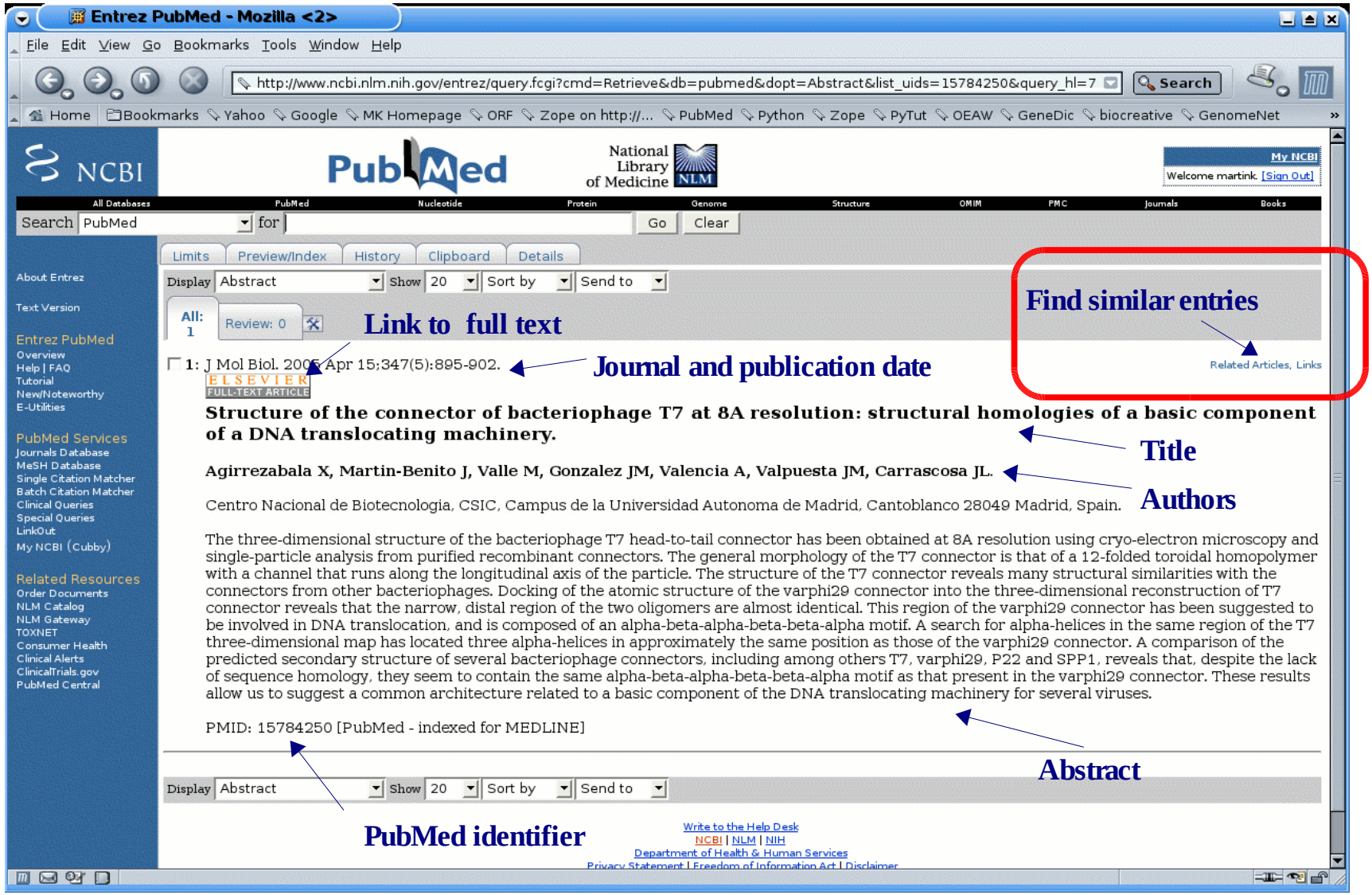
$$idf_j = \log\left(\frac{N}{df_j}\right)$$

idf: inverted document frequency

$$sim(Q,D) = \frac{\sum_{j=1}^{V} w_{Q,j} \times w_{i,j}}{\sqrt{\sum_{j=1}^{V} w_{Q,j} \times \sum_{j=1}^{V} w_{i,j}^2}}$$

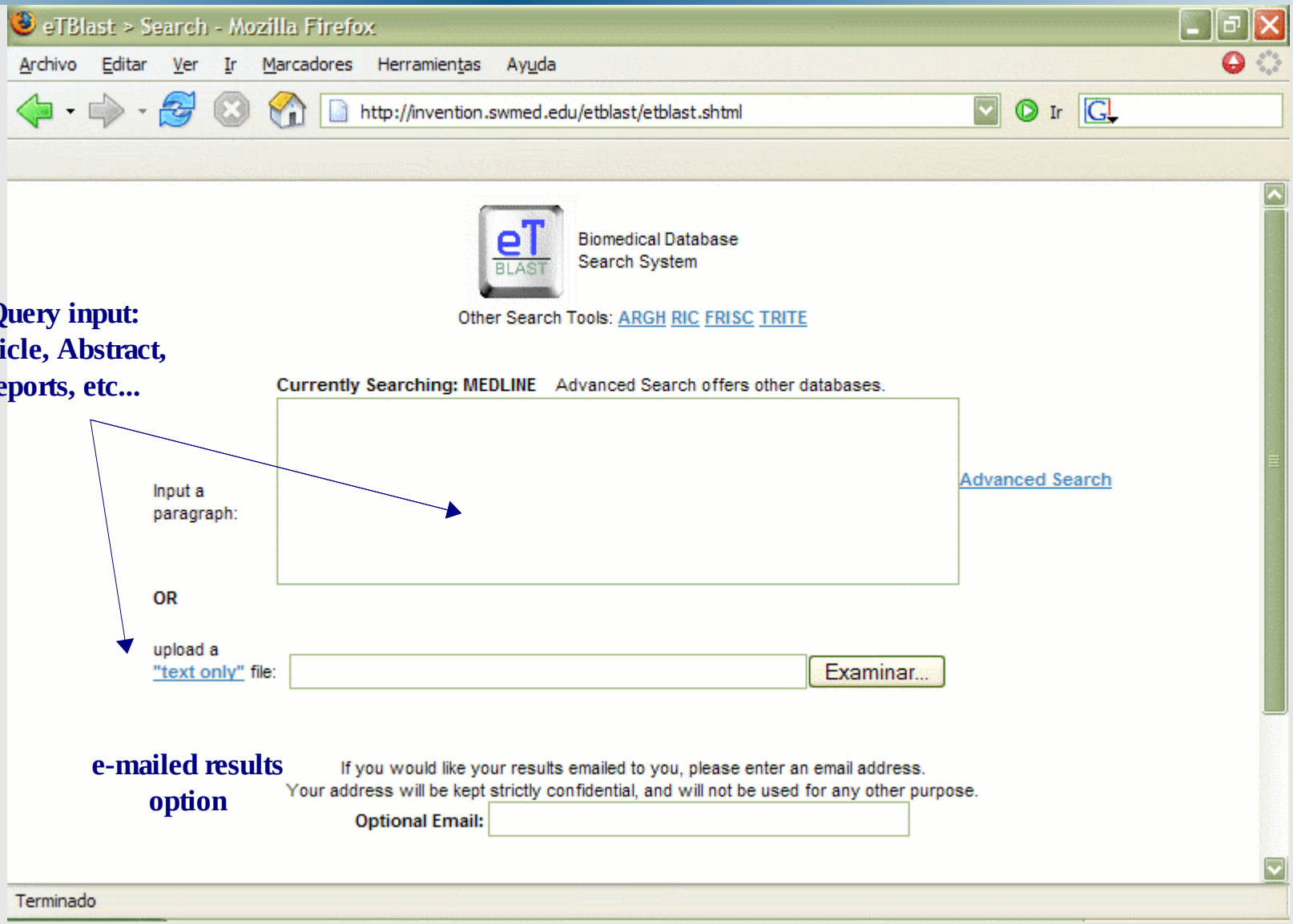
sim(Q,D): similarity between query and document

PubMed related article search



eTBlast system

http://invention.swmed.edu/etblast/index.shtml

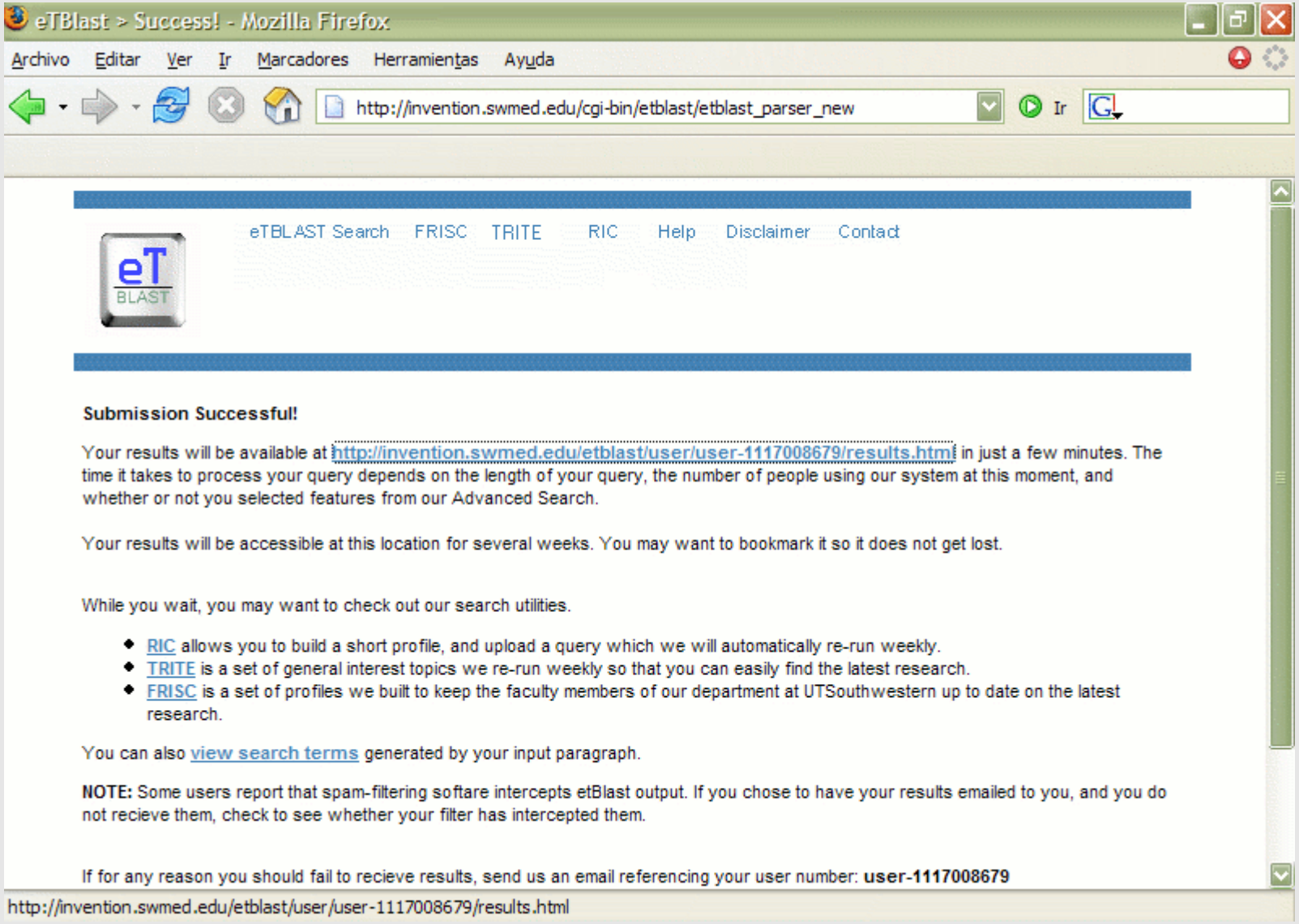


Query input: Article, Abstract, reports, etc...

e-mailed results option

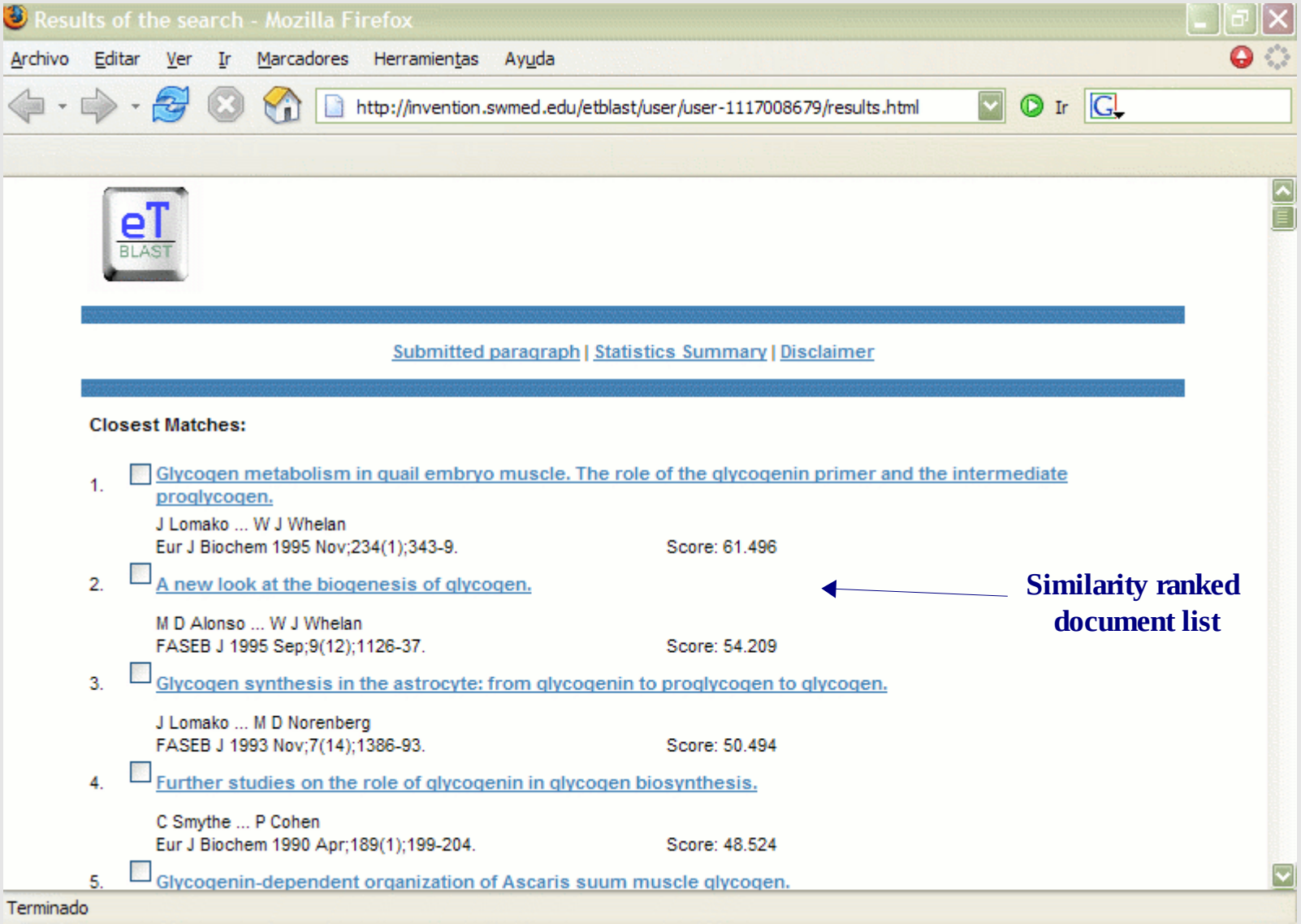
eTBlast submission

http://invention.swmed.edu/etblast/index.shtml



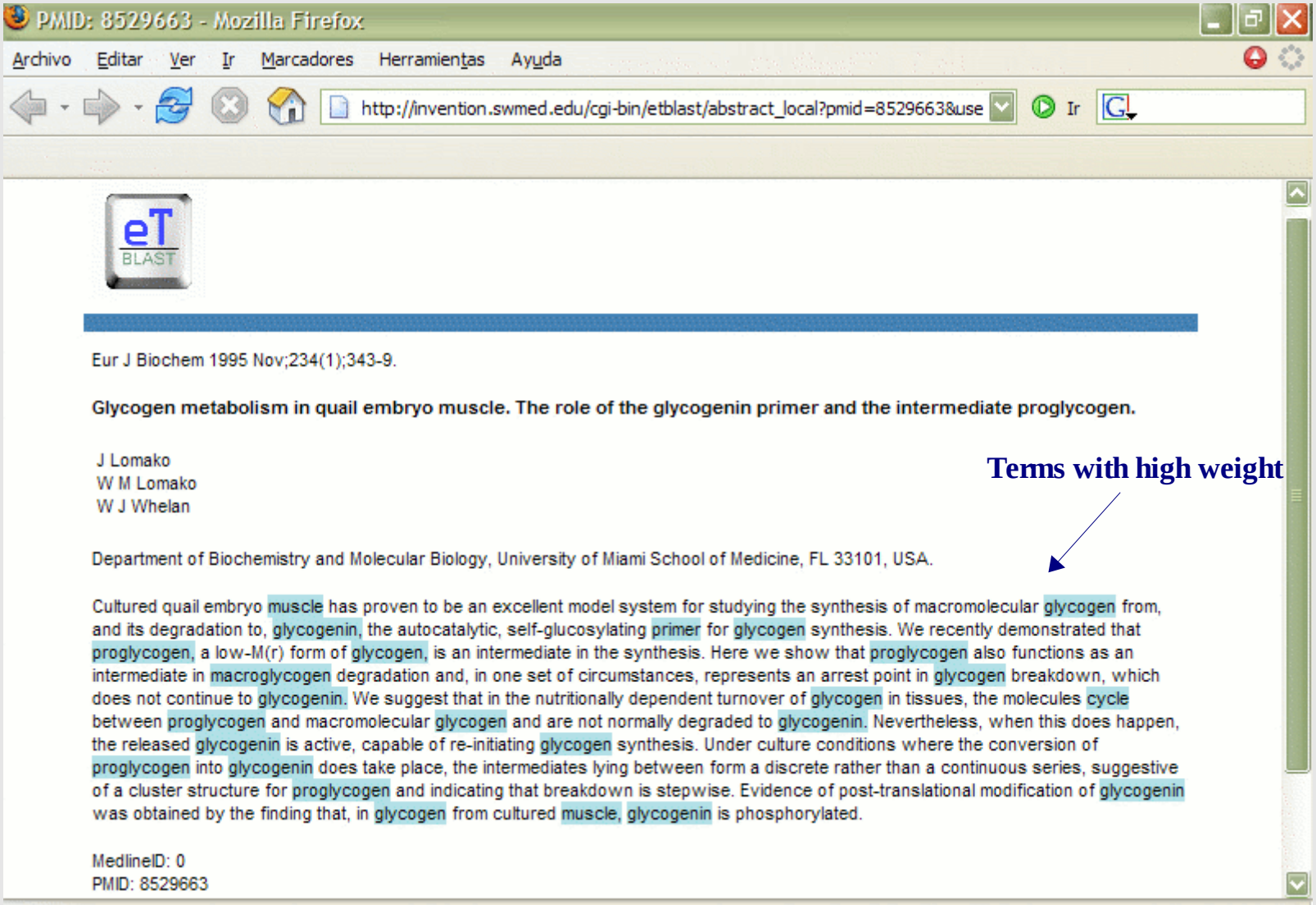
eTBlast results

http://invention.swmed.edu/etblast/index.shtml



eTBlast results

http://invention.swmed.edu/etblast/index.shtml



EXERCISE 4. eTBlast

http://invention.swmed.edu/etblast/index.shtml

While writing a scientific article, report or a grant application, people often want to retrieve a set of documents which are related/relevant to this given work. What could/should you do in such situations? A PubMed search using alternative Boolean queries? Typically people use Boolean queries against PubMed to obtain their set of references.

You can use eTBlast instead and upload or past your free text to obtain similar articles. You can even iterate the search by selecting a subset of relevant documents retrieved in the first eTBlast round.

In case you have your own input document or are interested in certain PubMed article you can use it as your query text (or else try some of the following files: etblast_sample1.txt, etblast_sample1_trmE.txt).

Notice that eTBlast is relatively slow. Use the advance search mode, you can try out different metrics for calculating the document similarity. You can try out uploading your own stop word file: stop_word_list.txt to filter those for when calculating the document similarity.

Explain the output (ranked list). Compare the list of similar documents for a given abstract in PubMed (related article search) with the results of eTBlast. What are the advantages of using eTBlast and what are the disadvantages. Are the highlighted word (with high weight) according to your opinion relevant and discriminative?

http://www.pdg.cnb.uam.es/martink/LINKS/tm_sc_ucm2005.htm

IR performance

- **Precision**: fraction of relevant documents retrieved divided by the total returned documents
- **Recall**: proportion of relevant documents returned divided by the total number of relevant documents
- **F-score**: the harmonic mean of precision and recall
- Precision-recall curves

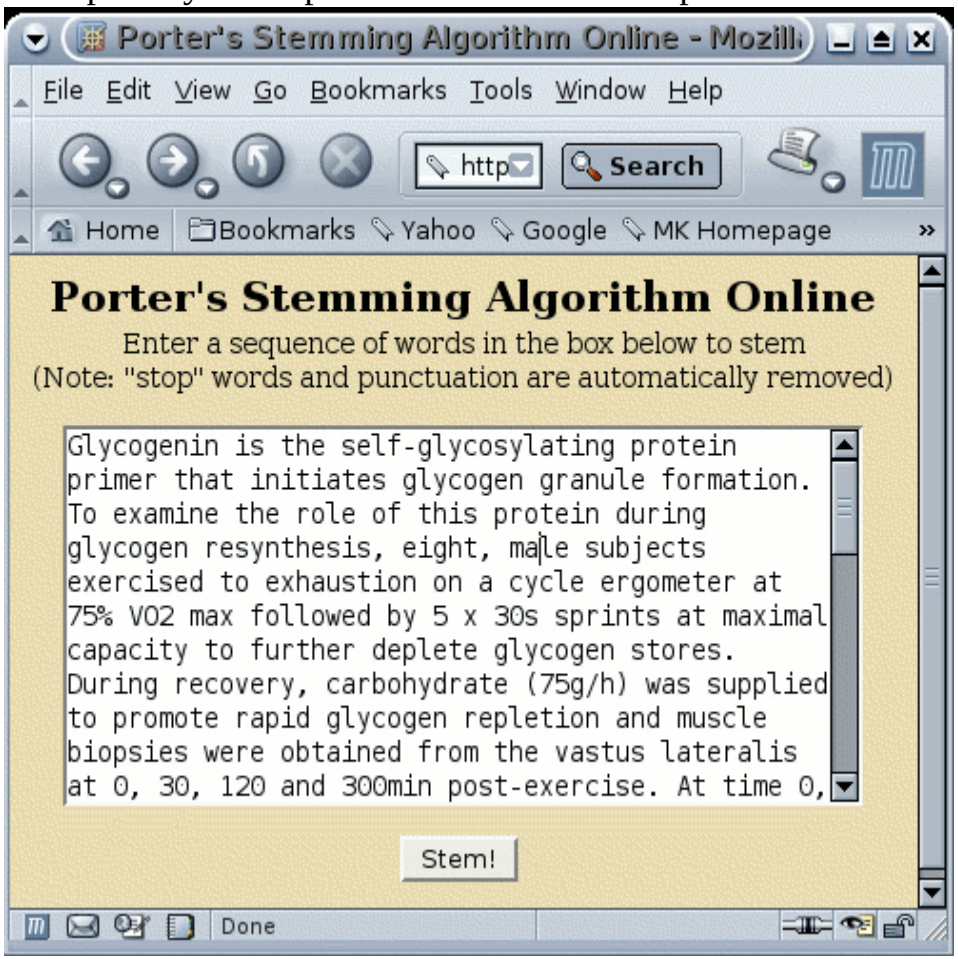
Information extraction and text mining

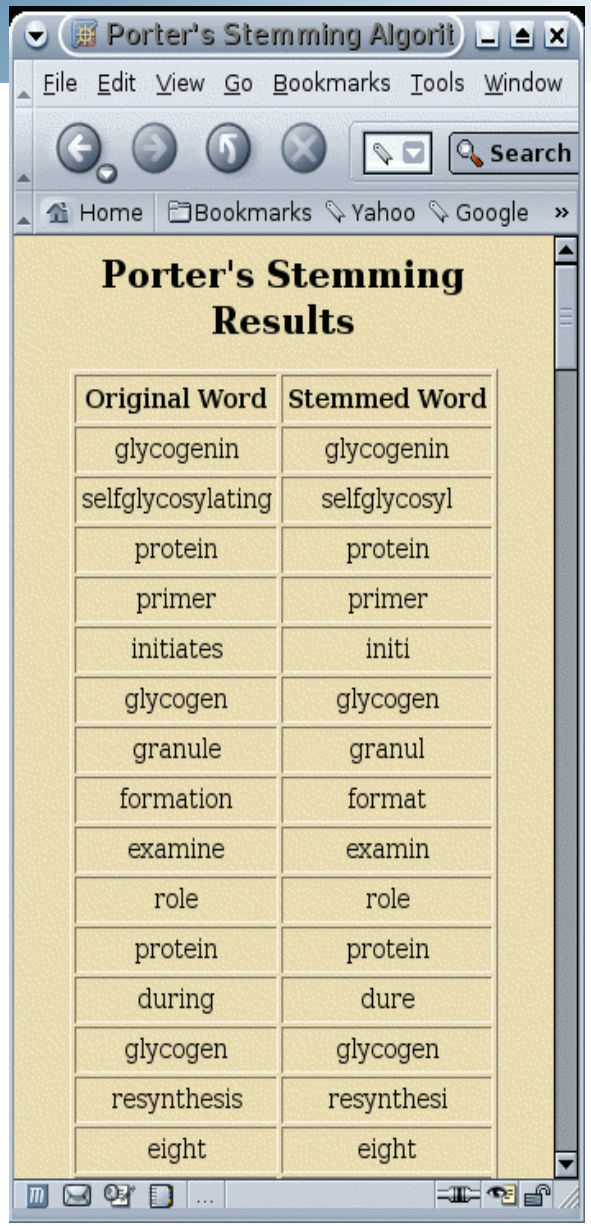
- Identification of **semantic structures** within free text.
- Use of syntactic and Part of Speech (POS) information.
- Integration of domain specific knowledge (e.g. ontologies).
- Identification of textual patterns.
- Extraction of predefined **entities** (NER), **relations**, **facts**.
- Entities like: companies, places or proteins, drugs.
- Relations like: protein interactions
- Methods: heuristics, rule-based systems, machine learning and statistical techniques, regular expressions,..

Stemming

- Process of removing affixes of words transforming them to their corresponding morphological base form or root.

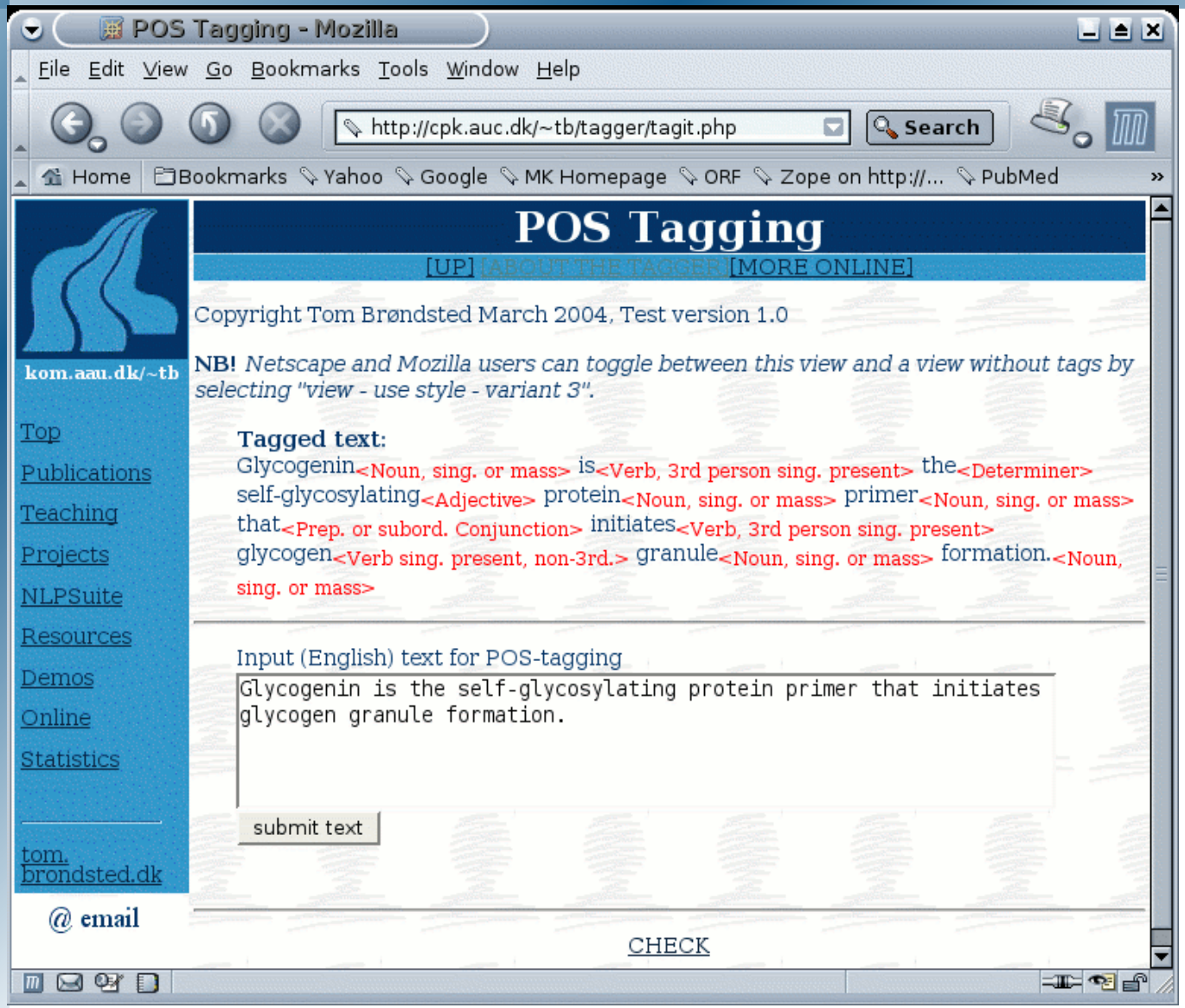
http://maya.cs.depaul.edu/~classes/ds575/porter.html





Original Word	Stemmed Word
glycogenin	glycogenin
selfglycosylating	selfglycosyl
protein	protein
primer	primer
initiates	initi
glycogen	glycogen
granule	granul
formation	format
examine	examin
role	role
protein	protein
during	dure
glycogen	glycogen
resynthesis	resynthesi
eight	eight

POS tagging



Providing each word given a sentence with its corresponding part of speech label , e.g. whether it is a noun, verb, preposition, article, etc.

Question Answering (QA)

- Humans formulate questions using natural language.
- Example: *What are the molecular functions of Glycogenin?*.
- QA: **automatic generation of answers** to queries in form NL expressions from document collections.
- Most systems limited to generic literature or newswire.
- QA difficult: heterogeneous, poorly formalised domain, new scientific terms
- Ad hoc retrieval task of the TREC Genomics Track 2005.
- Galitsky system (semantic skeletons (SSK), logical programming).

Natural Language Generation

- NLG: constructing automatically natural language texts.
- Display the content of databases: reports, error messages.
- Based on semantic input, providing computer-internal representation of the information.
- Different degrees of complexity.
- Biology: modelling the domain language difficult.
- Simpathica/XSSYS trace analysis tool.

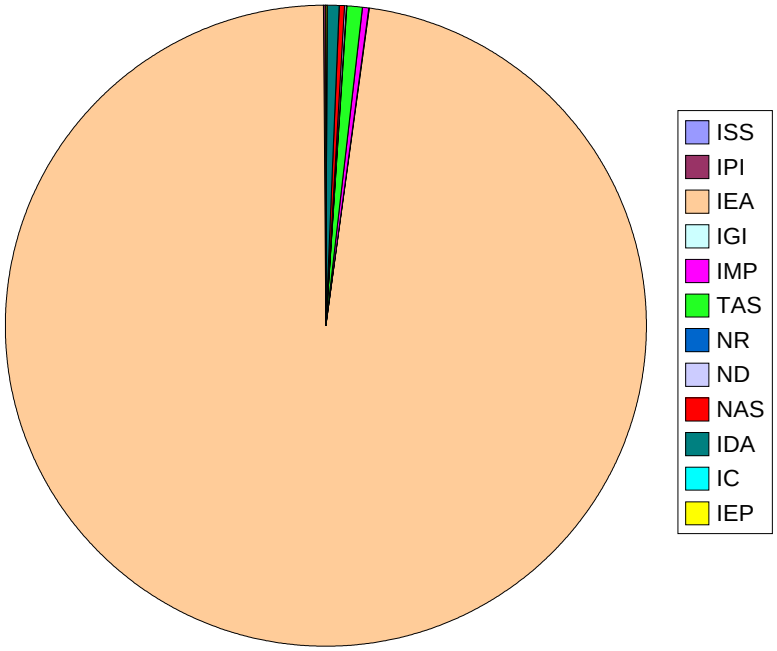
Annotation of gene products: Gene Ontology

http://www.geneontology.org/

- Ontology deacyclic graph structure.
- Controlled vocabulary of concepts.
- Three main categories:
  - Molecular Function
  - Cellular Component
  - Biological Process
- Describe relevant biological aspects of gene products
- Synonyms, links to external keywords.
- Currently most important source annotation terms.

Gene Ontology Annotation

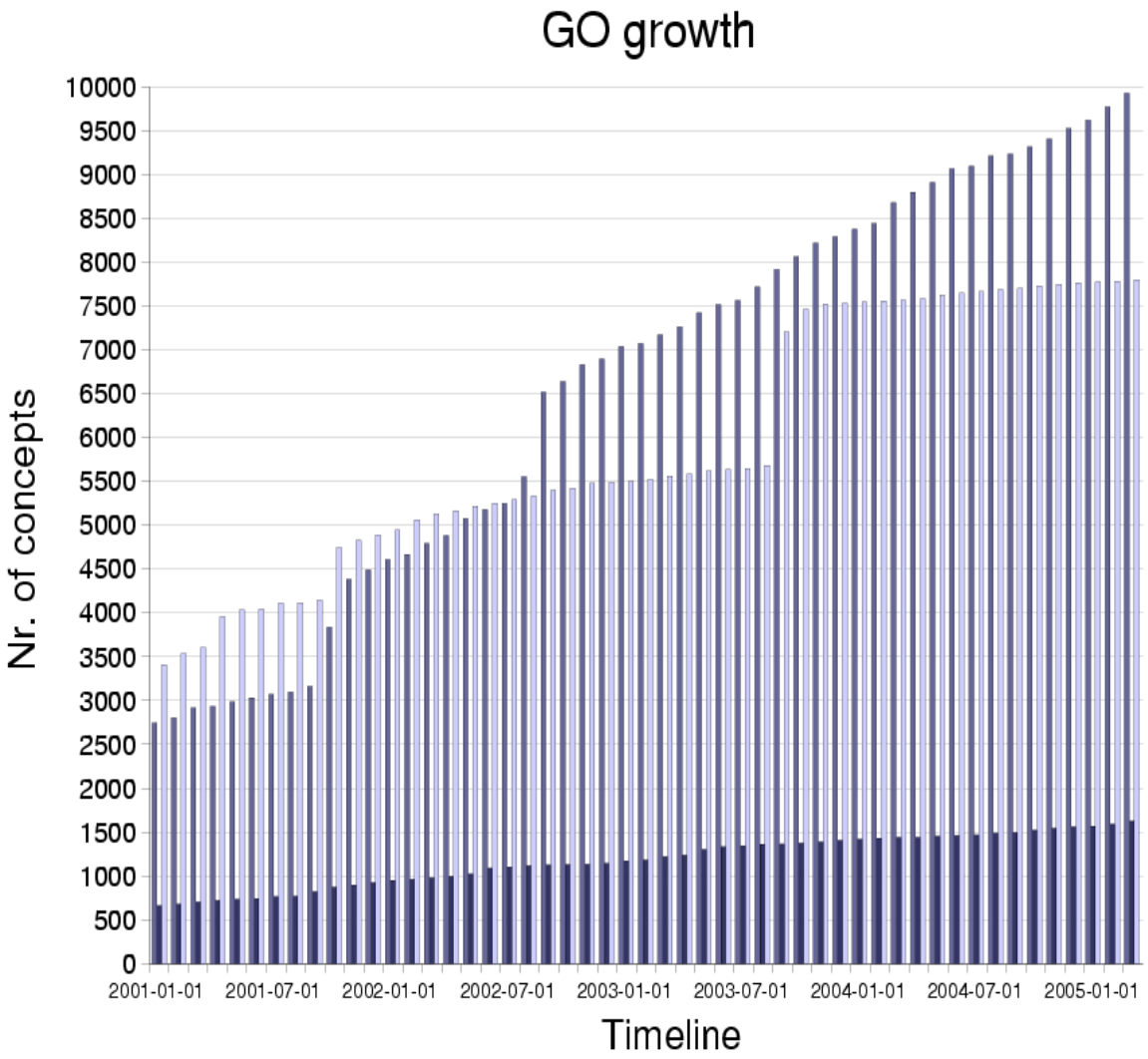
http://www.ebi.ac.uk/GOA/ 04/22/05



Ev.C.	Annot	Perc.	
IEA	**6421817**	**0.97529**	
ISS	19576	0.00297	**Electronic/ sequence-based annotation**
NR	2191	0.00033	
ND	4433	0.00067	
IPI	7130	0.00108	
IGI	3014	0.00046	
IMP	19072	0.00290	**Experimental evidence**
IDA	38862	0.00590	
IEP	1495	0.00023	
IC	831	0.00013	
TAS	49630	0.00754	**Curator knowledge**
NAS	16456	0.00250	

TAS: Traceable Author Statement; IDA: Inferred by direct assay; IC: Inferred by curator ; ND:No data; IMP:Inferred from mutant phenotype; IGI: Inferred from genetic interaction; 3.8) IPI :Inferred from physical interaction; ISS: Inferred from sequence similarity; IEP: Inferred from expression pattern; NAS: Non traceable author statement; IEA: Inferred by electronic annotation; NR: Not recorded;

Gene Ontology Growth



- MF:Molecular Function
- CC: Cellular Component
- BP: Biological Process

Exercise 5: Gene Ontology

Gene Ontology (GO) aims to provide standardized concepts or terms to describe relevant biological aspects. Try to use GO retrieve the ontology sub-structure for a set of terms: apoptosis, caspase, glycogenin, transcription factor (or in case you are interested in some particular function/process/compartment use your own query instead). What did you retrieve. Browse through the results and visualize the corresponding ontology graphs. What kind of relationships between terms did you find? What are the advantages of using such an ontology?

Try to explore annotation for a set of proteins, namely:

1) CASP9_HUMAN (P55211) (formerly known as ICE9_HUMAN),

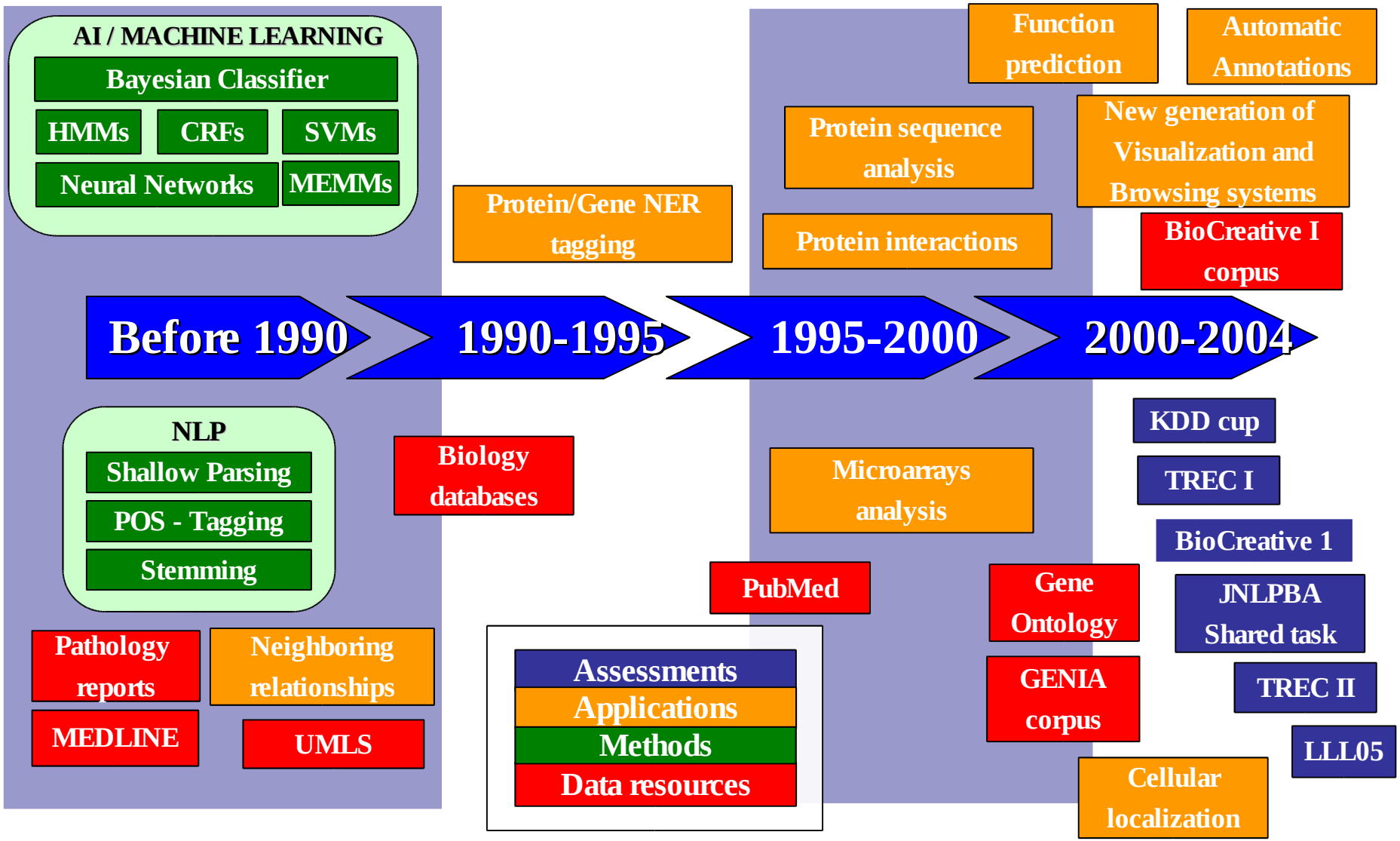
2) Y1333_MYCTU (P64811) formerly known as YD33_MYCTU

3) RPE_YEAST (P46969)

by Searching the Gene Ontology Annotation database GOA. Those proteins have been used in the practical part of the Patrones, perfiles y dominios session. What are one of the weak points when using GO annotations for bioinformatics annotations? (Hint: think about domains).

http://www.pdg.cnb.uam.es/martink/LINKS/tm_sc_ucm2005.htm

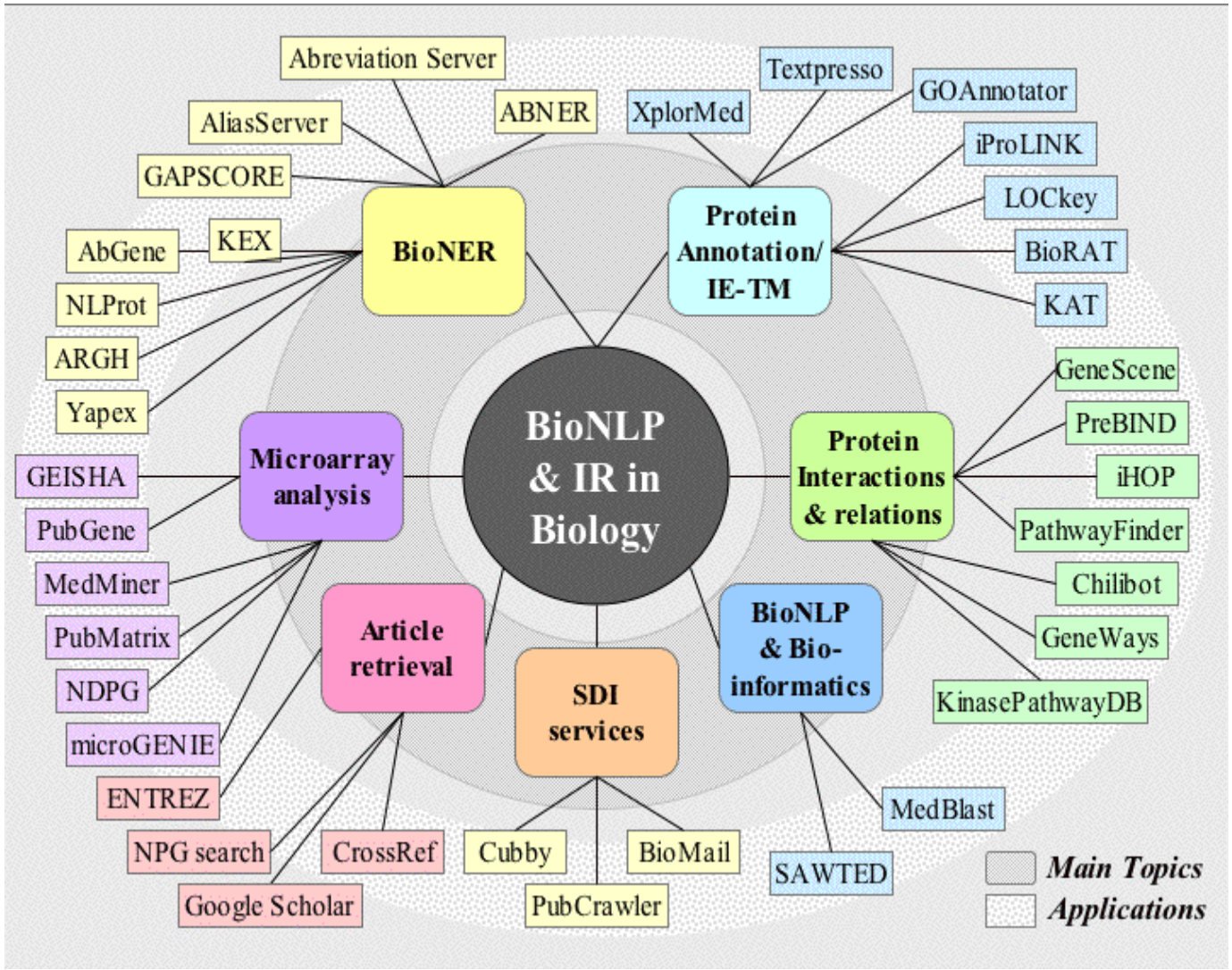
NLP in Molecular Biology - timeline



Text Mining applications in Biology

- NER: tagging biological entities.
- Automatic annotation: associating proteins to functional descriptions.
- Protein interactions: extracting interactions of proteins, genes and drugs.
- Microarray analysis: providing biological context through literature mining
- Protein localisation
- Improving sequence-based homology detection.

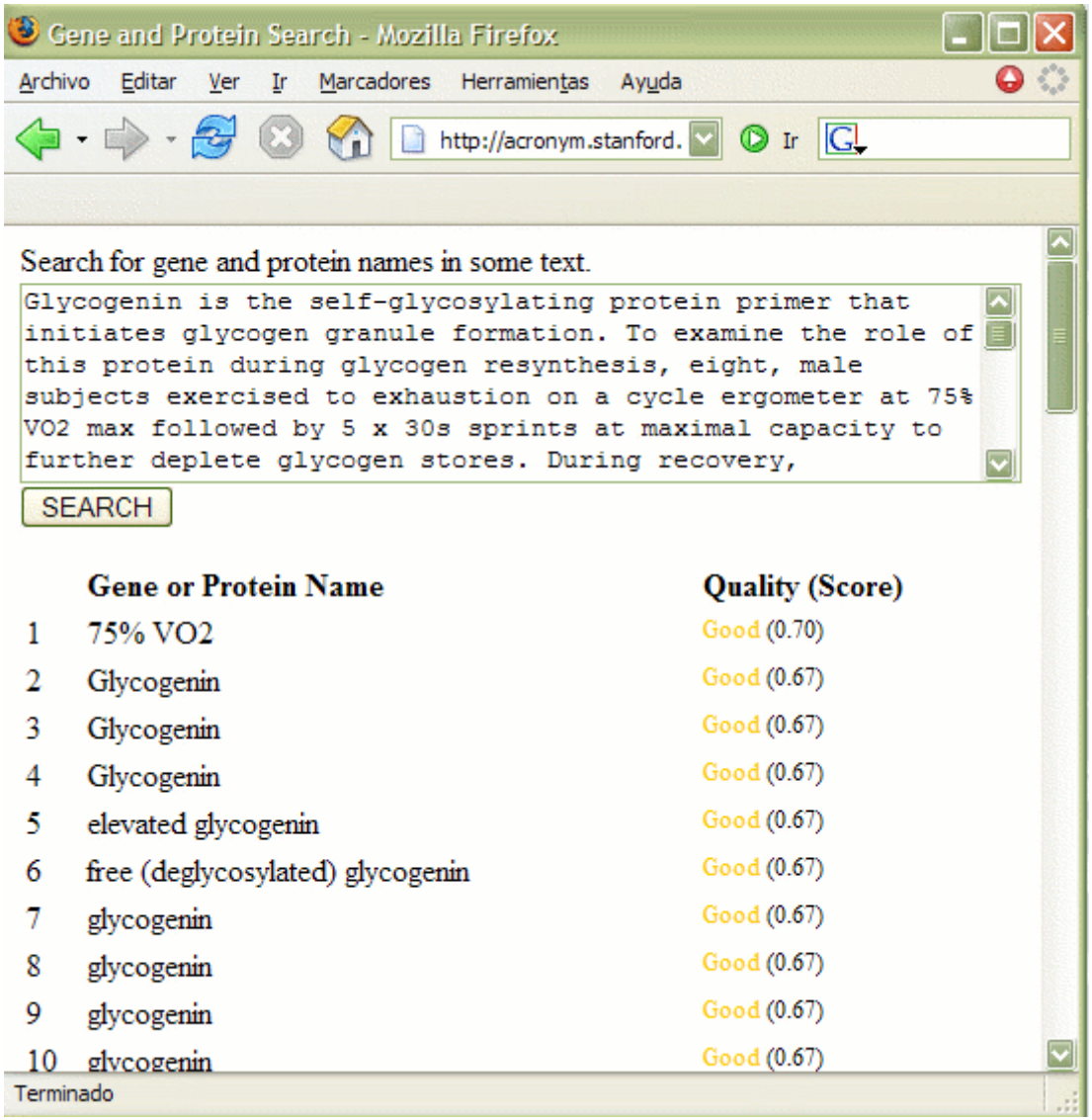
Text Mining applications in Biology



Tagging biological names

- Aim: **Identify** biological entities in articles and to **link** them to entries in biological databases.
- Generic NER: corporate names and places (0.9 f-score).
- Biology NER: more complex (synonyms, disambiguation, typographical variants, official symbols not used,..).
- Bioinformatics vs NLP approach.
- Performance organism dependent.
- Methods: POS tagging, rule-based, flexible matching, statistics, ML (naïve Bayes, ME, SVM, CRF, HMM).

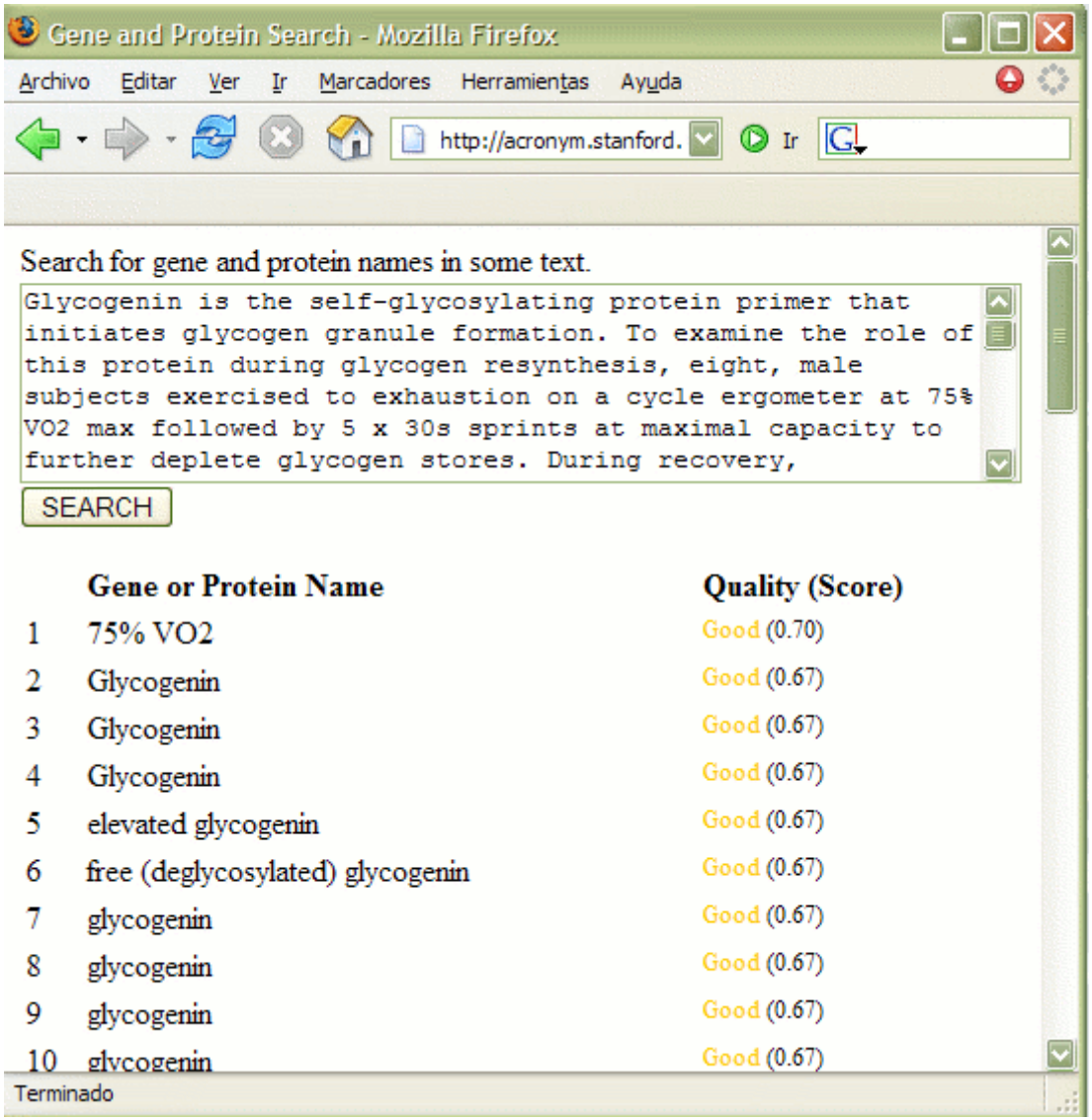
GAPSCORE



- Scores words based on a statistical model of gene names
- Quantifies:
  - Appearance
  - Morphology
    - Context.
- Online.

http://bionlp.stanford.edu/gapscore/

GAPSCORE



- Scores words based on a statistical model of gene names
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  - Appearance
  - Morphology
    - Context.
- Online.

http://bionlp.stanford.edu/gapscore/

Chang JT, Schütze H, and Altman RB. GAPSCORE: Finding Gene and Protein Names One Word at a Time. *Bioinformatics*. 2004 Jan 22;20(2):216-25.

NLProt

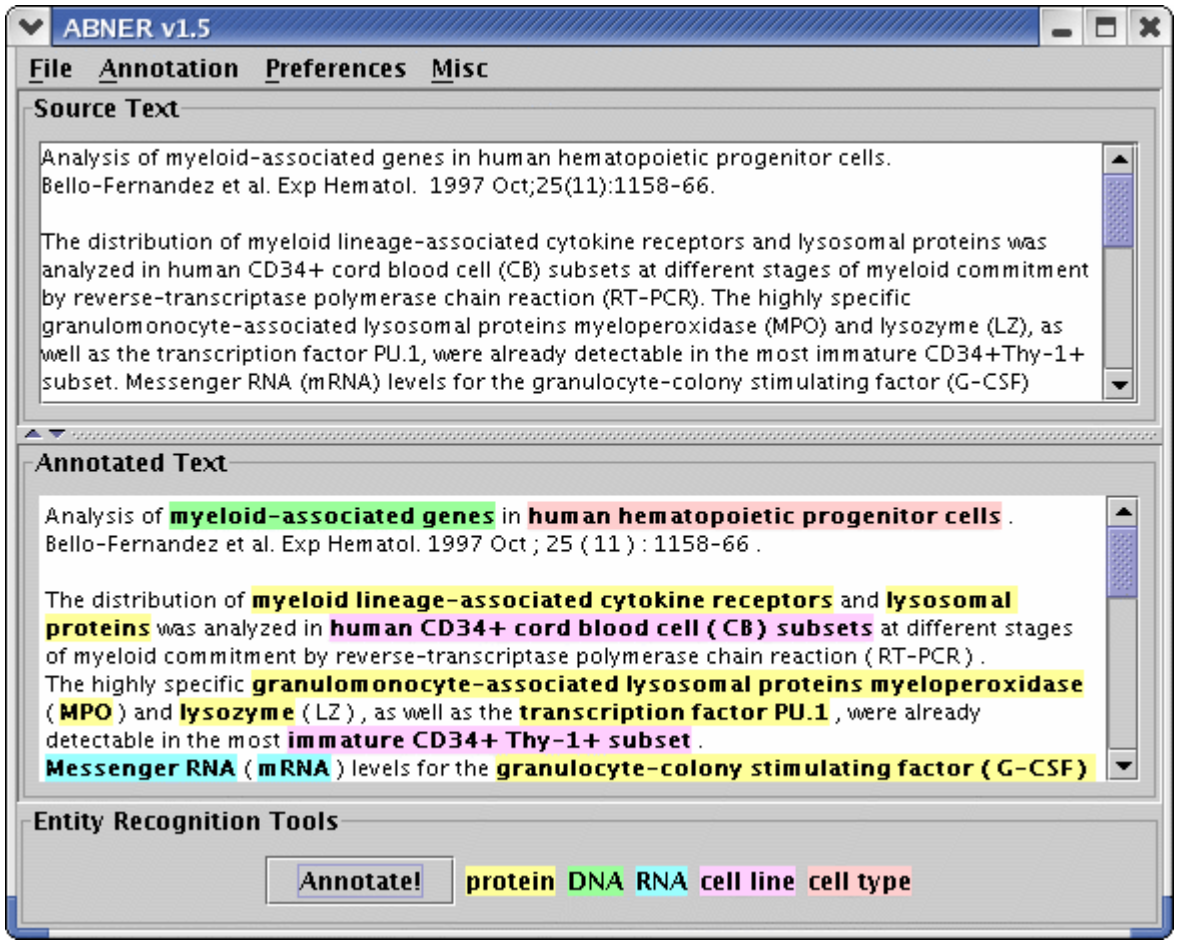
NAME	ORGANISM	TXT-POS	SCORE	METHOD	DB-ID(S)
Glycogenin	homo sapiens	1	1.040	SVM	GYG2_HUMAN (86%)
glycogenin	homo sapiens	96	0.856	SVM	GYG2_HUMAN (91%)
glycogenin	homo sapiens	103	1.040	SVM	GYG2_HUMAN (91%)
Glycogenin	homo sapiens	109	0.871	SVM	GYG2_HUMAN (86%)
glycogenin	homo sapiens	138	0.980	SVM	GYG2_HUMAN (91%)
Glycogenin	homo sapiens	157	0.971	SVM	GYG2_HUMAN (86%)
glycogenin	homo sapiens	161	0.311	SVM	GYG2_HUMAN (91%)
glycogenin	homo sapiens	214	0.819	SVM	GYG2_HUMAN (91%)
glycogenin	homo sapiens	234	0.747	SVM	GYG2_HUMAN (91%)

- Online (e-mail alert).
- Downloadable.
- SVM-based
- Pre-processing dictionary
- Rule-based filtering step
- PubMed words.
- Precision of 75%
- Recall of 76%

http://cubic.bioc.columbia.edu/services/nlprot/

Chang JT, Schutze H, Altman RB. GAPSCORE: finding gene and protein names one word at a time. *Bioinformatics*. 2004 Jan 22;20(2):216-25.

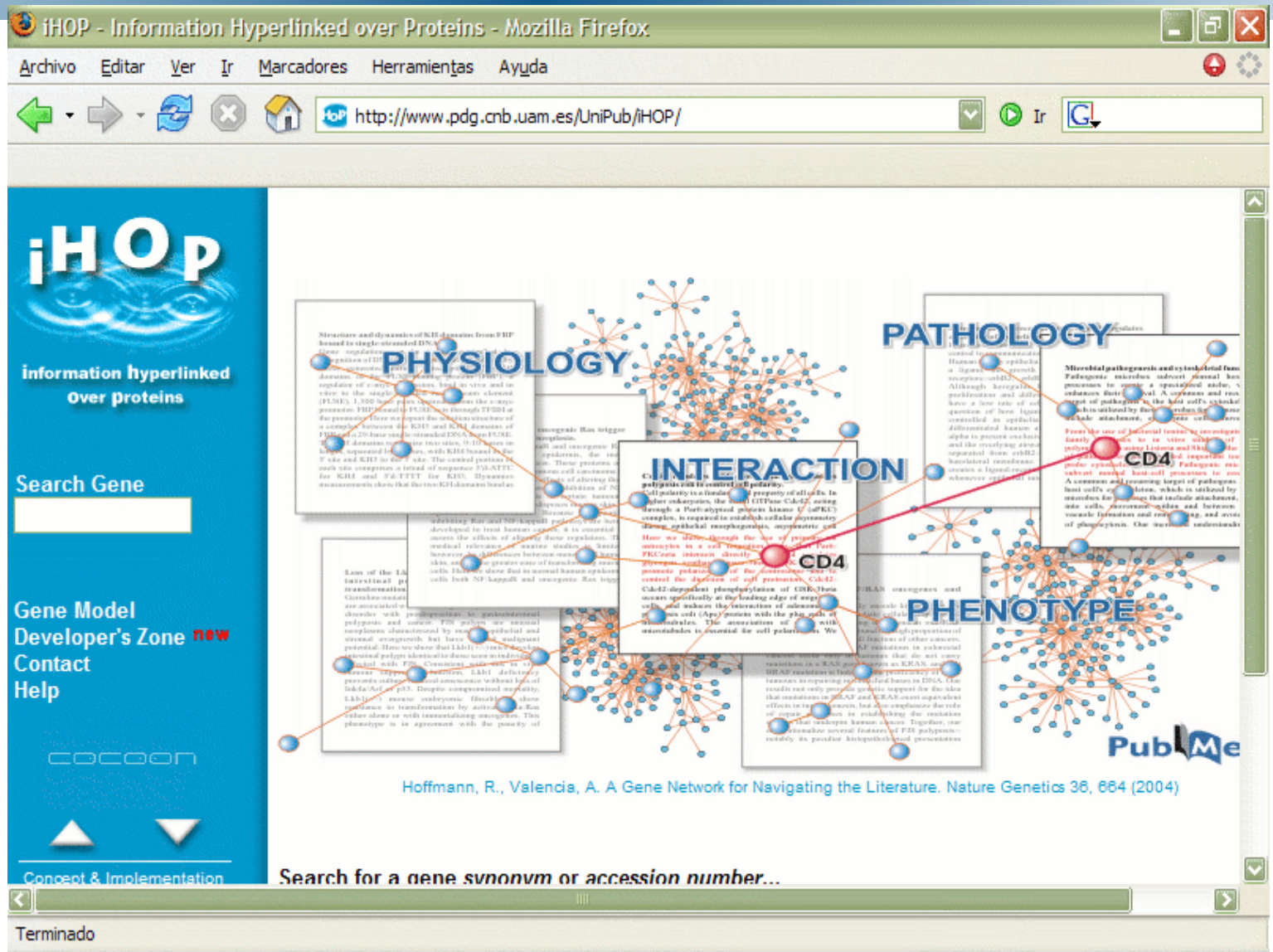
ABNER



Burr Settles. "ABNER: A Biomedical Named Entity Recognizer." http://www.cs.wisc.edu/~bsettles/abner/. 2004.

- A Biomedical Named Entity Recogniser
- Downloadable.
- CRF-based
- Trained on BioCreative and GENIA
- orthographic and contextual features
- Can be trained on new corpora

iHOP



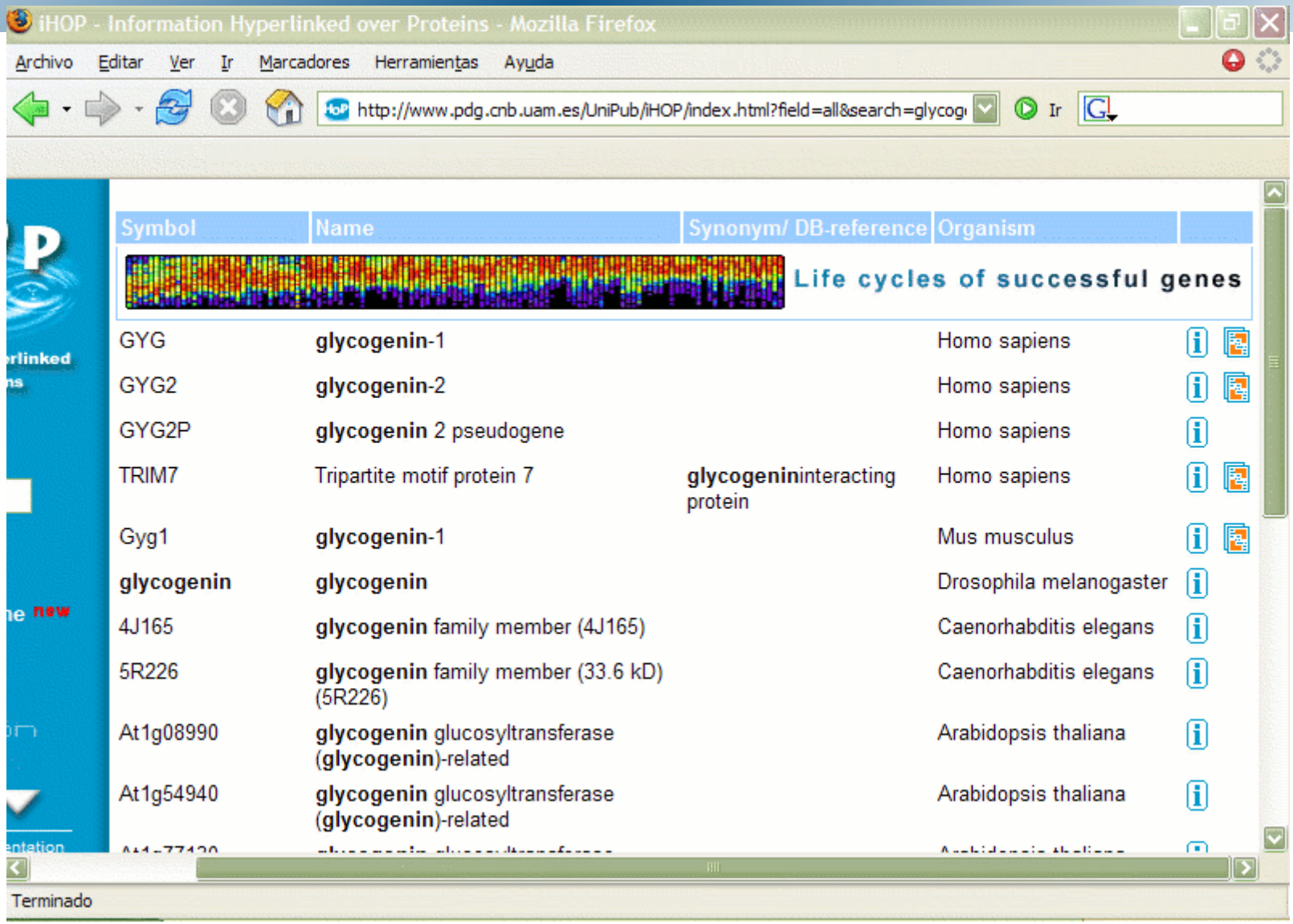
Hoffmann R, Valencia A. A gene network for navigating the literature *Nat Gene*t. 2004 Jul;36(7):664.

iHOP

- Protein centric: nucleates the literature around protein name.
- For a range of model organisms (e.g. Human, yeast,..)
- Hyperlinks proteins through co-occurrence
- Highlight direct associations between proteins and functional terms.
- Online, fast, easy to use.

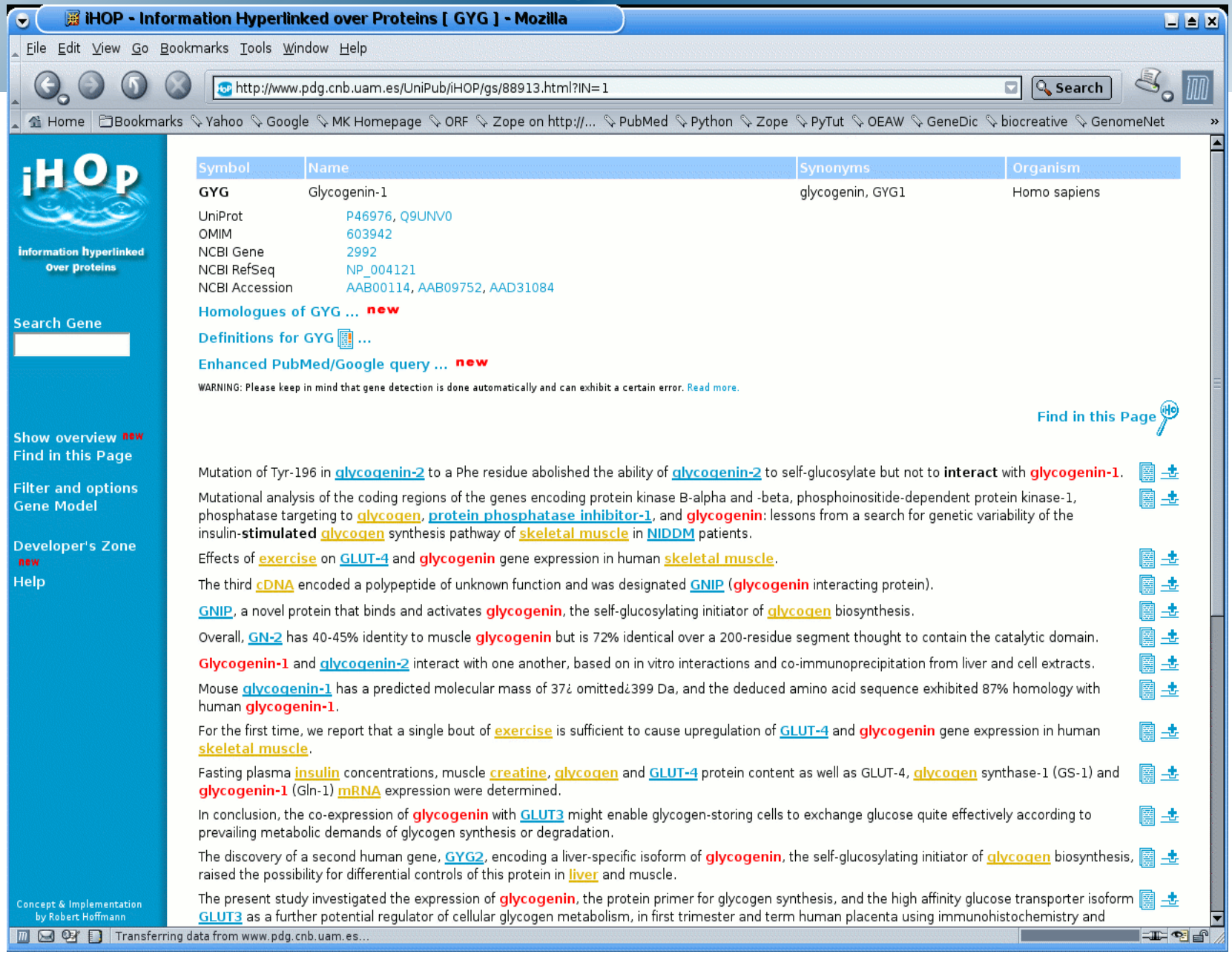
Hoffmann R, Valencia A. A gene network for navigating the literature *Nat Gene*t. 2004 Jul;36(7):664.

iHOP

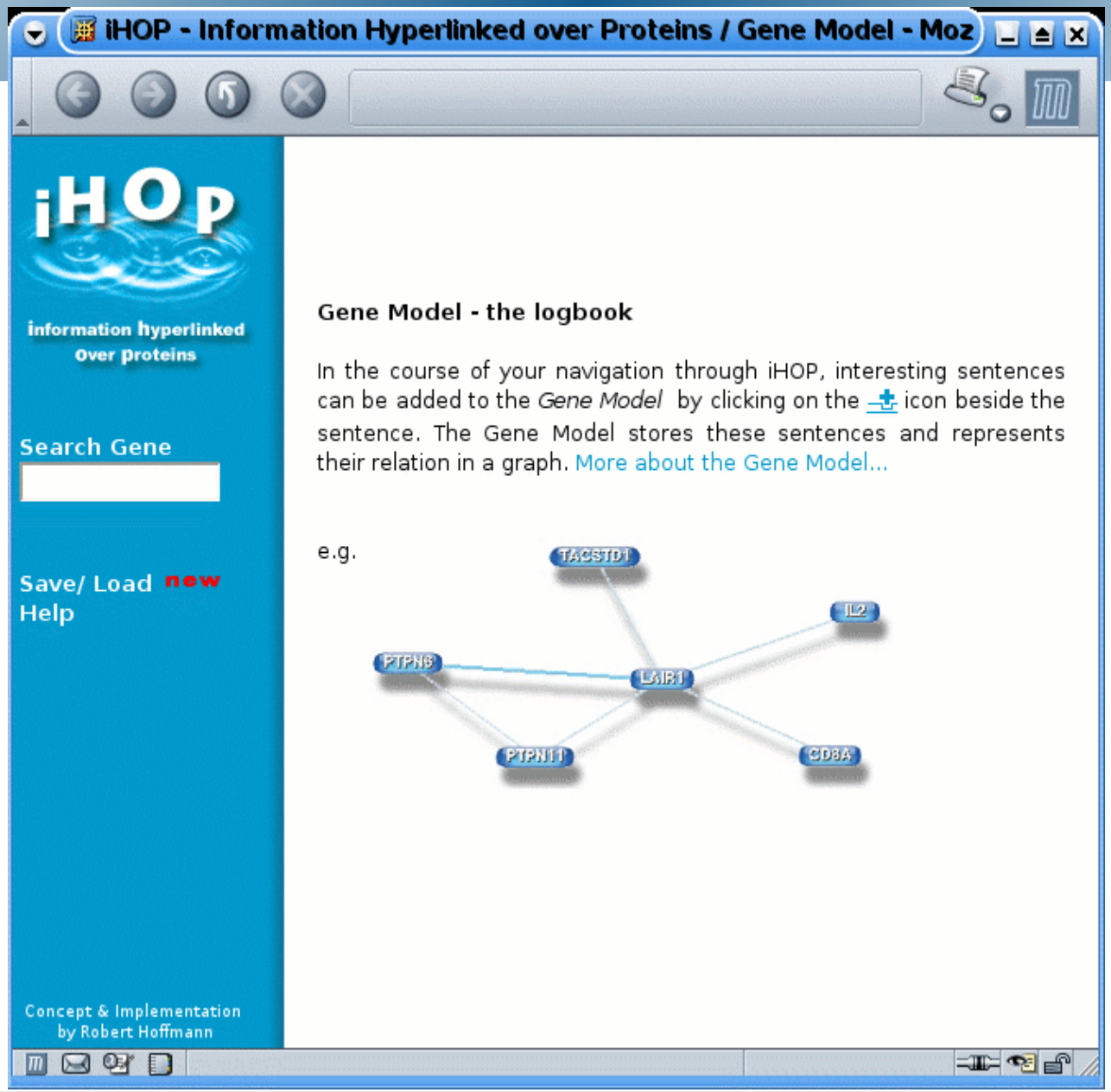


Hoffmann R, Valencia A. A gene network for navigating the literature *Nat Gene*t. 2004 Jul;36(7):664.

iHOP


iHOP - Information Hyperlinked over Proteins [GYG] - Mozilla
File Edit View Go Bookmarks Tools Window Help
http://www.pdg.cnb.uam.es/UniPub/iHOP/gs/88913.html?IN=1
Search
Home Bookmarks Yahoo Google MK Homepage ORF Zope on http://... PubMed Python Zope PyTut OEAW GeneDic biocreative GenomeNet
iHOP
information hyperlinked over proteins
Search Gene
Show overview new
Find in this Page
Filter and options
Gene Model
Developer's Zone new
Help
Concept & Implementation by Robert Hoffmann
Symbol Name Synonyms Organism
GYG Glycogenin-1 glycogenin, GYG1 Homo sapiens
UniProt P46976, Q9UNV0
OMIM 603942
NCBI Gene 2992
NCBI RefSeq NP_004121
NCBI Accession AAB00114, AAB09752, AAD31084
Homologues of GYG ... new
Definitions for GYG ...
Enhanced PubMed/Google query ... new
WARNING: Please keep in mind that gene detection is done automatically and can exhibit a certain error. Read more.
Find in this Page
Mutation of Tyr-196 in glycogenin-2 to a Phe residue abolished the ability of glycogenin-2 to self-glucosylate but not to interact with glycogenin-1.
Mutational analysis of the coding regions of the genes encoding protein kinase B-alpha and -beta, phosphoinositide-dependent protein kinase-1, phosphatase targeting to glycogen, protein phosphatase inhibitor-1, and glycogenin: lessons from a search for genetic variability of the insulin-stimulated glycogen synthesis pathway of skeletal muscle in NIDDM patients.
Effects of exercise on GLUT-4 and glycogenin gene expression in human skeletal muscle.
The third cDNA encoded a polypeptide of unknown function and was designated GNIP (glycogenin interacting protein).
GNIP, a novel protein that binds and activates glycogenin, the self-glucosylating initiator of glycogen biosynthesis.
Overall, GN-2 has 40-45% identity to muscle glycogenin but is 72% identical over a 200-residue segment thought to contain the catalytic domain.
Glycogenin-1 and glycogenin-2 interact with one another, based on in vitro interactions and co-immunoprecipitation from liver and cell extracts.
Mouse glycogenin-1 has a predicted molecular mass of 37¿ omitted¿399 Da, and the deduced amino acid sequence exhibited 87% homology with human glycogenin-1.
For the first time, we report that a single bout of exercise is sufficient to cause upregulation of GLUT-4 and glycogenin gene expression in human skeletal muscle.
Fasting plasma insulin concentrations, muscle creatine, glycogen and GLUT-4 protein content as well as GLUT-4, glycogen synthase-1 (GS-1) and glycogenin-1 (Gln-1) mRNA expression were determined.
In conclusion, the co-expression of glycogenin with GLUT3 might enable glycogen-storing cells to exchange glucose quite effectively according to prevailing metabolic demands of glycogen synthesis or degradation.
The discovery of a second human gene, GYG2, encoding a liver-specific isoform of glycogenin, the self-glucosylating initiator of glycogen biosynthesis, raised the possibility for differential controls of this protein in liver and muscle.
The present study investigated the expression of glycogenin, the protein primer for glycogen synthesis, and the high affinity glucose transporter isoform GLUT3 as a further potential regulator of cellular glycogen metabolism, in first trimester and term human placenta using immunohistochemistry and
Transferring data from www.pdg.cnb.uam.es...

iHOP



iHOP: Visualization of protein interactions using network graphs

EXERCISE 6: BIO-NER

Retrieve a given abstract from PubMed searching for genes of your own research interest or alternatively for some of the following genes gene names: Caspase-9 (CASP-9, APAF-3), RPE1 (EPI1, POS18), Orc-1, Bcl-2, glycogenin, p53. Then try to tag gene and protein names from some those abstracts using different gene/protein NER tools and compare the results. If your need GenBank ids (e.g. gi:20986531) or SwissProt accession numbers (Q07817 / BCLX_HUMAN) use: NCBI or UniProt Use some of the online applications NLProt, GAPSCORE, Yapex or BioNE recognizer (you can also download ABNER).

How do they perform? What are the common error? Which differences do you encounter? What are the main difficulties ? Which taggers do you think are useful in practice?

Explore for some of the gene symbols previously used (e.g. CASP-9, RPE1, Orc-1, glycogenin, p53) or for genes of your own research interest iHOP. This tool was developed at out group (PDG) at the CNB. Create a gene model for your query gene, check the results carefully, and surf through the virtual gene network of iHOP. What kind of results are obtained by iHOP? What are the advantages/disadvatages when using iHOP instead of other bio-NER tools or the PubMed retireval search?

http://www.pdg.cnb.uam.es/martink/LINKS/tm_sc_ucm2005.htm

EXERCISE 7: From sequence to abstracts

From sequence to abstracts

You have been using protein sequences for a range of analysis purposes in previous lectures of this course. Traditionally in case you want to obtain information related to a query sequence , after doing a sequence search (e.g. Blast against NCBI), retrieving the query genes, extracting their gene names or symbols and searching with those names PubMed you obtained the associated literature. This is a lot of work, with a lot of corresponding working steps. Those steps are integrated in the MedBlast tool.

Lets try to obtain the corresponding literature for some of the protein sequences used in other lectures (or your own query sequence of interest) for this exercise.:

Use MedBlast, a NLP based retrieval system to return relevant articles for your sequence. Notice that this system is low and sensitive to server overload! Describe the obtained results. What are the main difficulties when linking a query sequence to scientific articles?

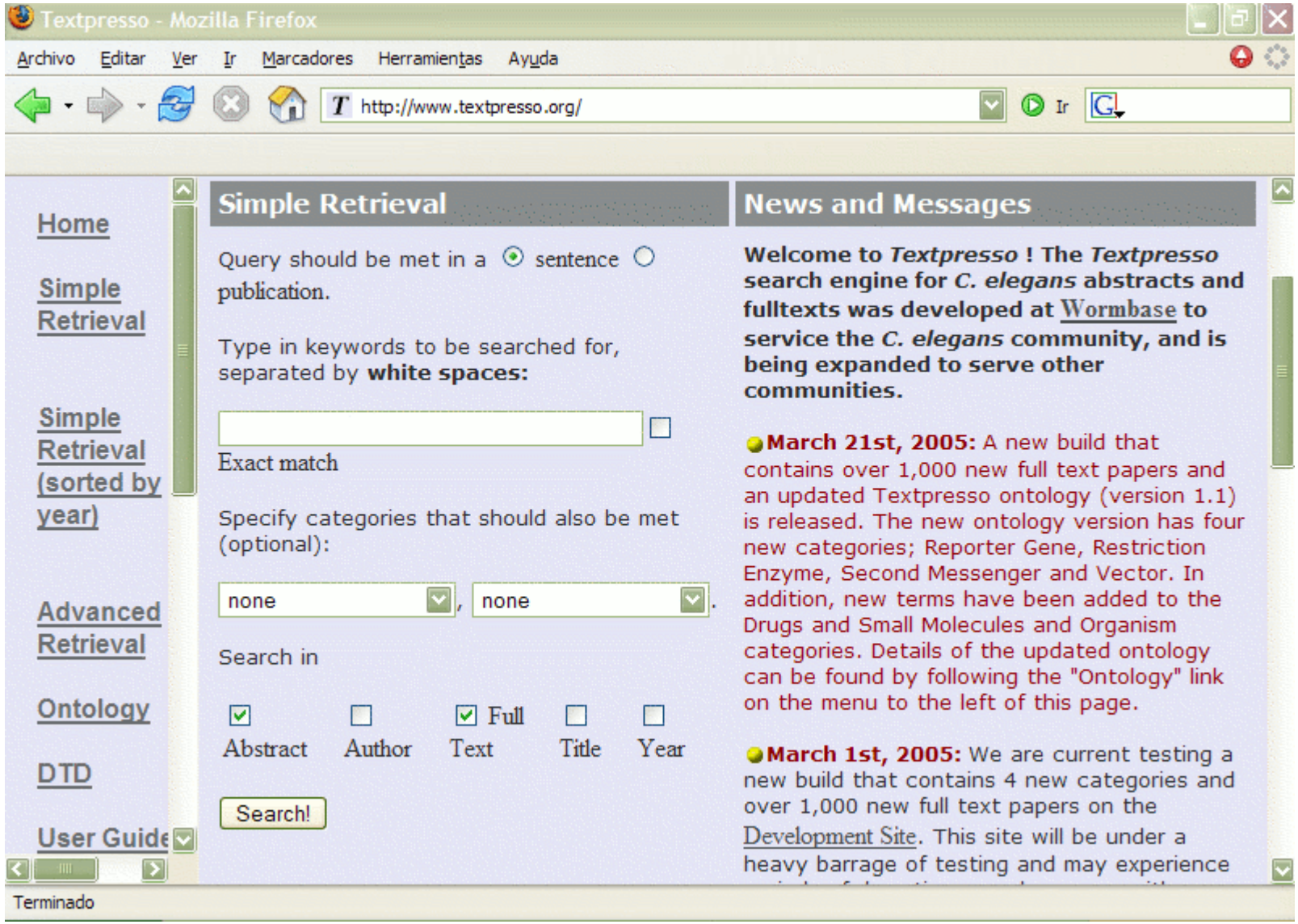
http://www.pdg.cnb.uam.es/martink/LINKS/tm_sc_ucm2005.htm

Extracting functional Annotations

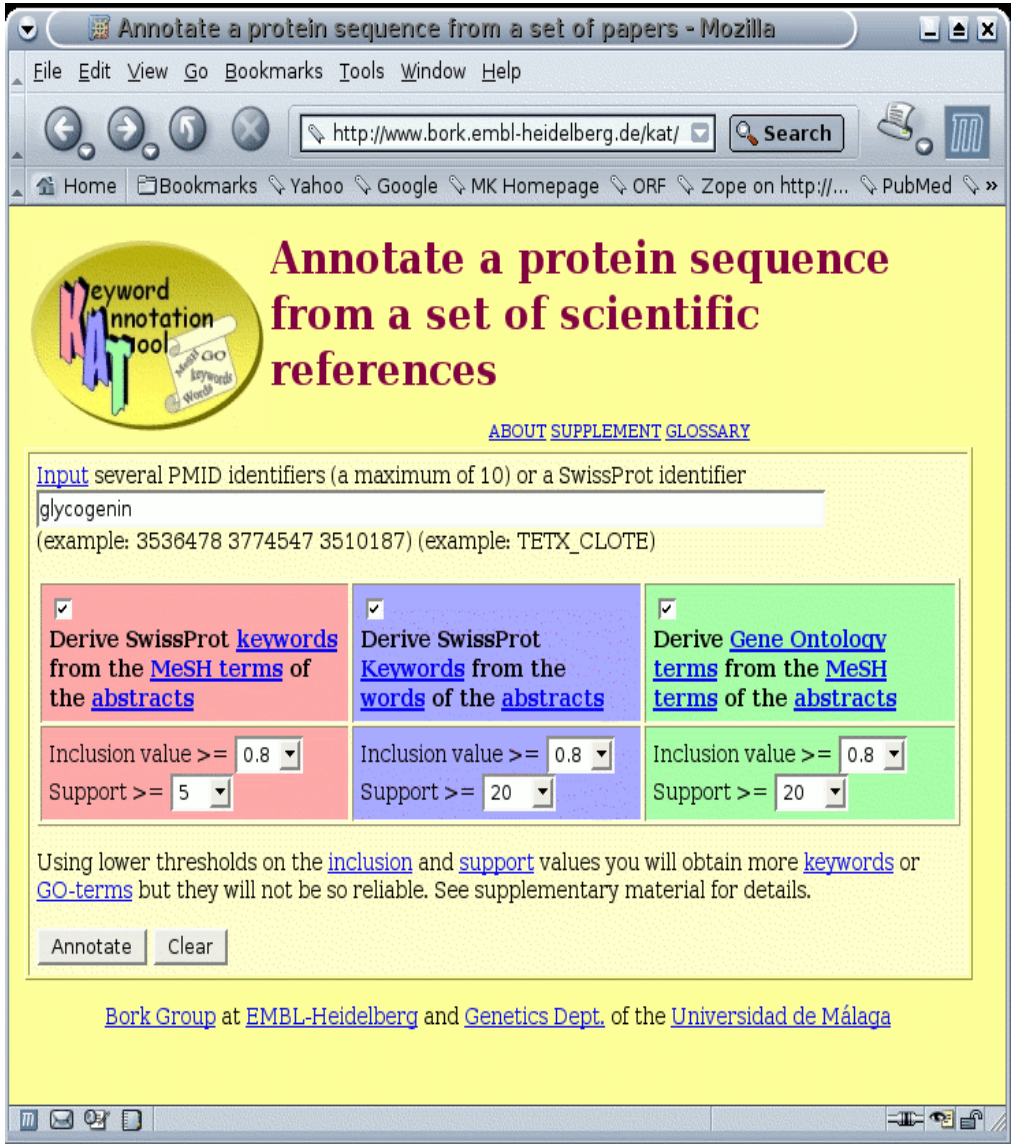
- **Manual annotation** extraction by database curators.
  - Scientific literature analysis.
  - Time-consuming & labour-intensive.
  - Example: Gene Ontology annotation (GOA).

- **Text mining** to assist annotation extraction:
  - Identification of annotation relevant sentences.
  - Identification of protein-term associations.

Textpresso


Textpresso - Mozilla Firefox
Archivo Editar Ver Ir Marcadores Herramientas Ayuda
http://www.textpresso.org/
Ir
Home
Simple Retrieval
Simple Retrieval (sorted by year)
Advanced Retrieval
Ontology
DTD
User Guide
Simple Retrieval
Query should be met in a sentence publication.
Type in keywords to be searched for, separated by white spaces:
Exact match
Specify categories that should also be met (optional):
none
none
Search in
Abstract
Author
Full Text
Title
Year
Search!
News and Messages
Welcome to Textpresso ! The Textpresso search engine for C. elegans abstracts and fulltexts was developed at Wormbase to service the C. elegans community, and is being expanded to serve other communities.
March 21st, 2005: A new build that contains over 1,000 new full text papers and an updated Textpresso ontology (version 1.1) is released. The new ontology version has four new categories; Reporter Gene, Restriction Enzyme, Second Messenger and Vector. In addition, new terms have been added to the Drugs and Small Molecules and Organism categories. Details of the updated ontology can be found by following the "Ontology" link on the menu to the left of this page.
March 1st, 2005: We are current testing a new build that contains 4 new categories and over 1,000 new full text papers on the Development Site. This site will be under a heavy barrage of testing and may experience
Terminado

KEYWORD ANNOTATION TOOL (KAT)



- Extraction of mappings between related terms using a model of fuzzy associations
- Mesh terms/SwissProt keywords/GO terms

Perez AJ, Perez-Iratxeta C, Bork P, Thode G, Andrade MA.Gene annotation from scientific literature using mappings between keyword systems. Bioinformatics. 2004 Sep 1;20(13): 2084-91. Epub 2004 Apr 1.

Suppl. EXERCISE 8: PROTEIN FUNCTION

- The functional annotations contained in databases such as Gene
- Ontology annotation (GOA) was directly or indirectly extracted from the literature.
- Several applications have been developed to associate proteins with functional terms.
- Try to use text mining applications and GOA annotations to find functional information for your query proteins:
  - GOAnnotator
  - iHOP
  - GOA

PROTEIN INTERACTIONS

- Advances in experimental large scale protein interaction analysis
- Exp. Methods for protein interaction characterization:
  - protein arrays
  - mRNA expression microarrays
  - Yeast two-hybrid
  - Affinity purification with MS
  - X-ray, NMRFRET, chemical cross-linking,..
- Bioinformatics methods for protein characterization:
  - Genome-based
  - Sequence-based

PROTEIN INTERACTION DATABASES

Database Name	Reference	URL
BIND	(Bader *et al*., 2003)	http://bind.ca
DIP	(Xenarios *et al*., 2002)	http://dip.doe-mbi.ucla.edu
GRID	(Breitkreutz *et al*. 2003)	http://biodata.mshri.on.ca/grid
HPID	(Han *et al*., 2004)	http://www.hpid.org
HPRD	(Peri *et al*., 2004)	http://www.hprd.org
IntAct	(Hermjakob *et al*., 2004)	http:/www.ebi.ac.uk/intact
MINT	(Zanzoni *et al*., 2002)	http://cbm.bio.uniroma2.it/mint
STRING	(vonMering et al., 2003)	http://string.embl.de
ECID	(Juan *et al*., 2004)	http://www.pdg.cnb.uam.es/ECID

TEXT MINING & PROTEIN INTERACTIONS

- Extract automatically those interactions from articles.
- NL used to characterise the nature of the interaction and its directionality.
- Literature-derived interaction networks:
  - power law distribution
  - scale free topology
- Visualised using network graphs.
- Methods range from: simple occurrence, expert derived word patterns (frames) to machine learning.

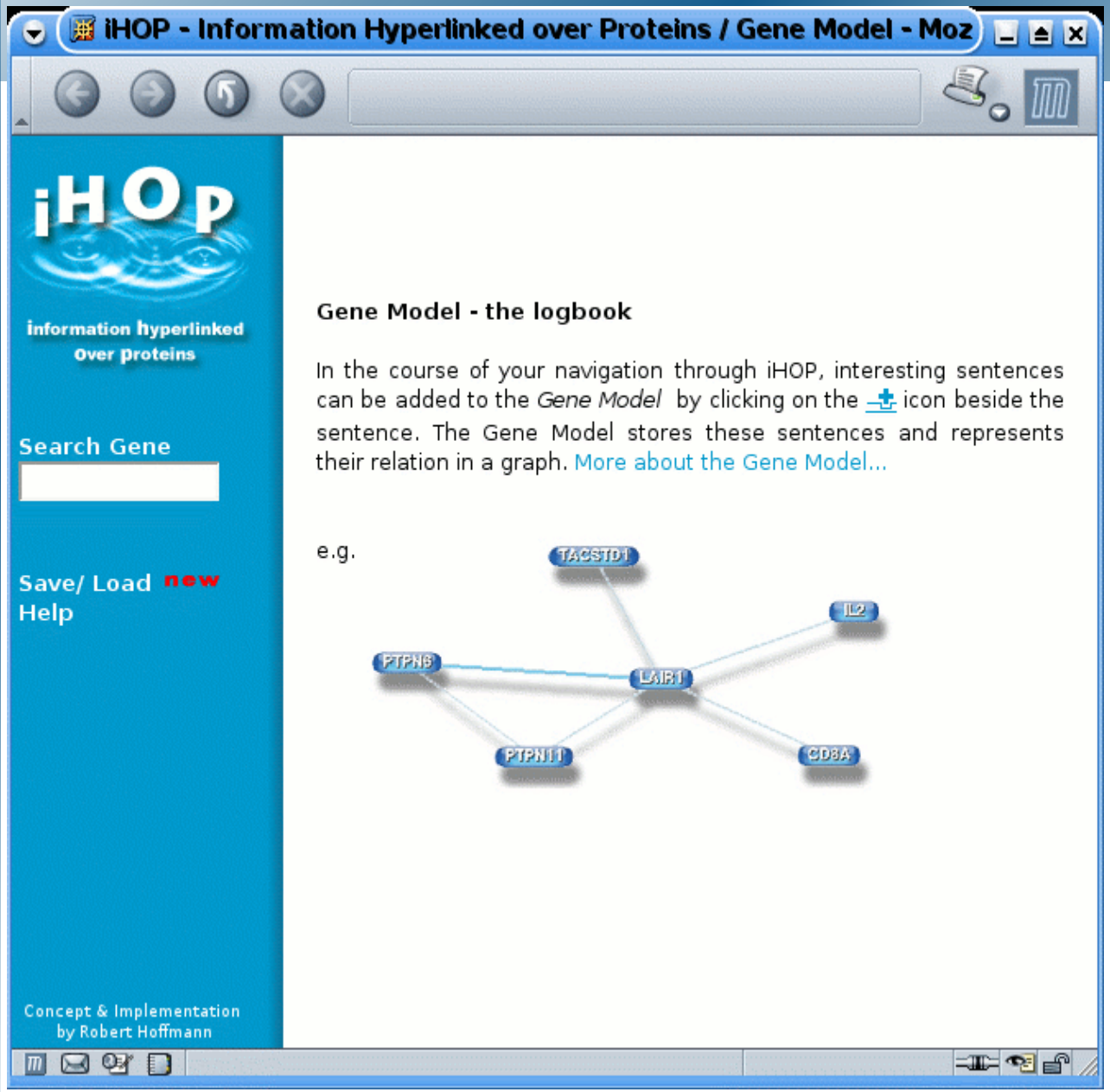
PubGene

- Use the co-occurrence of protein and gene names.
- Assumption: co-occurrence imply biological relationship
- Indexing PubMed abstracts and titles with human proteins.
- Construction of interaction networks.
- Build upon binary interactions between co-occurring proteins

Jenssen TK, Laegreid A, Komorowski J, Hovig E.A literature network of human genes for high-throughput analysis of gene expression.Nat Genet. 2001 May;28(1):21-8.

http://www.pubgene.org/

iHOP

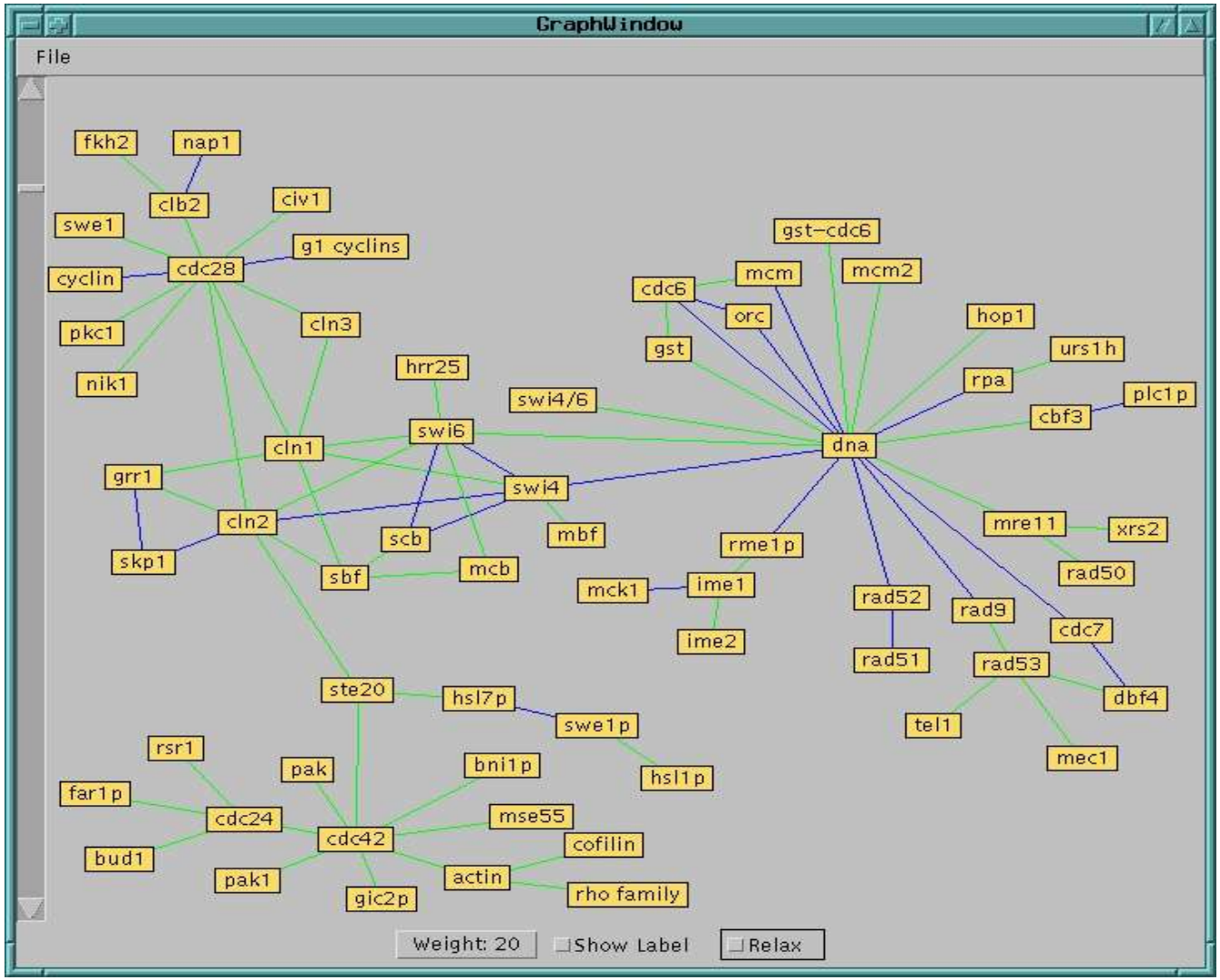


iHOP: Visualization of protein interactions using network graphs

SUISEKI

- Relationship between the co-occurring proteins using **frames**
- Frames: **textual patterns** used to express interactions
- Initial set of 14 interaction words based on domain knowledge.
- Examples: *activate*, *bind*, *suppress*
- Analysed the **order** of protein names within sentences.
- Take into account **distance** (off-set) between protein names.
- System effective for simple interaction types.
- Difficult cases: long sentences with complex grammatical structures

SUISEKI


GraphWindow
File
fkh2
nap1
clb2
civ1
swe1
g1 cyclins
cyclin
cdc28
pkc1
cln3
nik1
hrr25
swi6
swi4/6
cln1
grr1
swi4
cln2
scb
mbf
skp1
sbf
mcb
gst-cdc6
mcm
mcm2
cdc6
orc
hop1
gst
urs1h
rpa
plc1p
cbf3
dna
mre11
xrs2
rad50
rme1p
mck1
ime1
ime2
rad52
rad9
cdc7
rad51
rad53
dbf4
tel1
mec1
ste20
hsl7p
swe1p
hsl1p
rsr1
pak
bni1p
far1p
cdc24
mse55
cdc42
cofilin
bud1
pak1
actin
gic2p
rho family
Weight: 20
Show Label
Relax

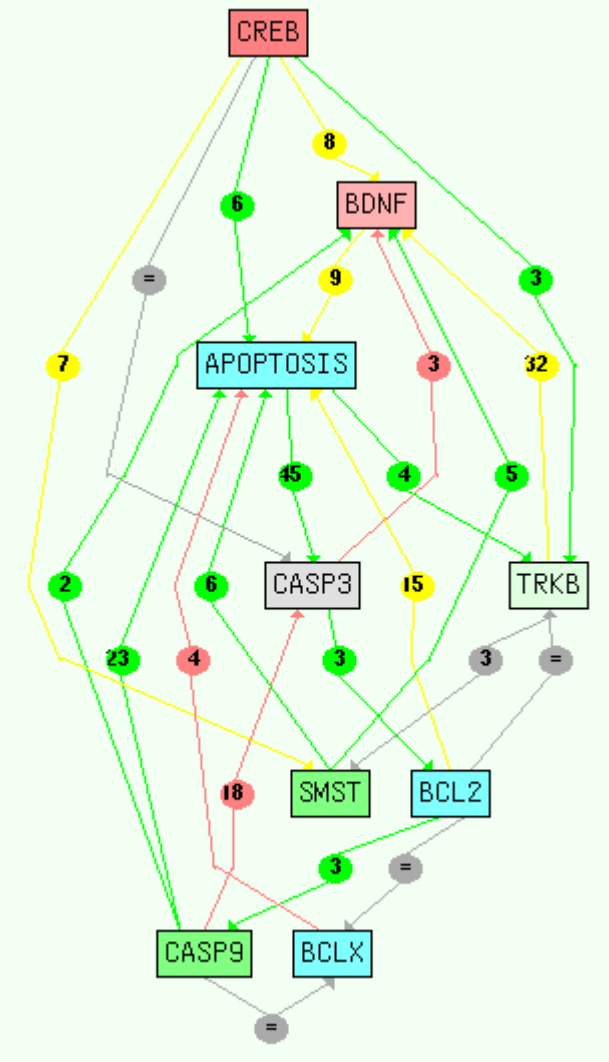
CHILIBOT

- NLP-based text mining approach.
- Content-rich relationship networks among biological
- Concepts, genes, proteins or drugs.
- Nature of the relationship: inhibitory, stimulative, neutral and simple co-occurrence.
- Internet-based application with graphical visualisation
- Sentence as unit, POS tagging, shallow parsing and rules.

Chen H, Sharp BM.Content-rich biological network constructed by mining PubMed abstracts.BMC Bioinformatics. 2004 Oct 8;5(1): 147.

http://www.chilibot.net/

CHILIBOT

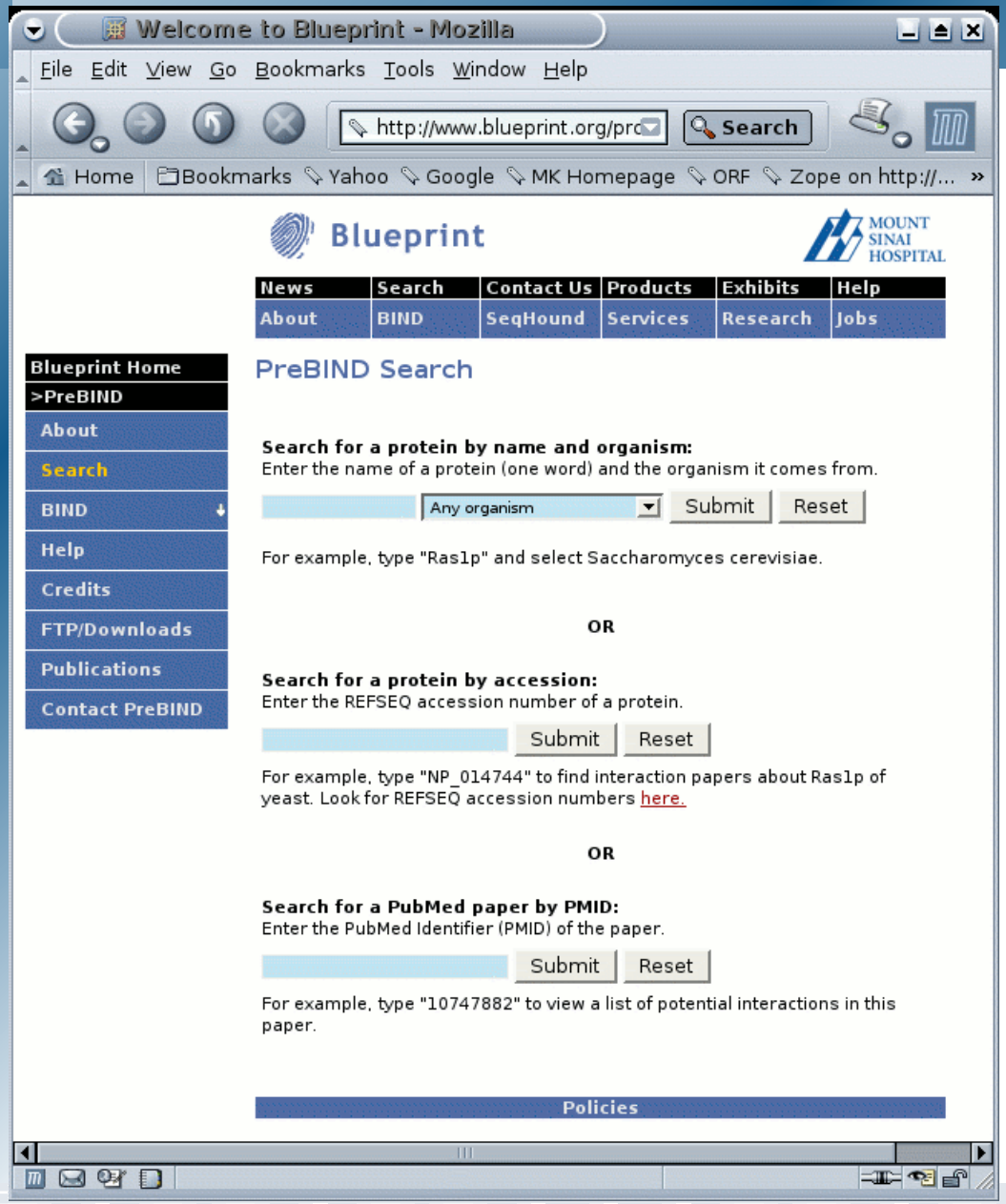


- Need registration.
- Hypothesis generation.

Chen H, Sharp BM.
Content-rich biological network constructed by mining PubMed abstracts.
BMC Bioinformatics. 2004 Oct 8;5(1):147.

http://www.chilibot.net/

PreBIND



PreBIND

- Based on SVM.
- Query protein or accession number.
- Assist the Biomolecular Interaction Network Database (BIND)

Donaldson I, Martin J, de Bruijn B, Wolting C, Lay V, Tuekam B, Zhang S, Baskin B, Bader GD, Michalickova K, Pawson T, Hogue CW.PreBIND and Textomy--mining the biomedical literature for protein-protein interactions using a support vector machine.*BMC Bioinformatics*. 2003 Mar 27;4(1):11.

http://www.blueprint.org/products/prebind

EXERCISE 6.4.: PROTEIN INTERACTIONS

- Proteins instantiate their function through interactions with other bio-molecules.
- Use different text mining tools which try to extract protein interactions for a given query protein/s (caspase, glycogenin, p53 etc...) from texts: iHOP, PreBIND, Chilibot.
- Compare your results with entries in interaction databases:
- BIND, DIP , GRID , HPID, HPRD, IntAct, MINT and STRING.
- What kind of output is produced by each tool?
- Which differences do you encounter?
- What are the difficulties encountered by those tools?
-

Microarray data analysis

- Co-ordinated expression of genes.
- Functional co-regulation within biological processes.
- Mine micro array data using the associated biomedical literature.
- Characterise groups of genes extracting functional keywords.
- Score the coherence of gene clusters.
- Group genes based on their associated literature and functional descriptions.

GEISHA

- Text mining tool for microarray analysis.
- Analyse the correlation between:
  - the increase of the level of expression patterns and
  - the significance of functional information derived from the literature.
- Extract functional information from the literature linked to the microarray genes.
- Calculates statistical significance of terms from documents associated to genes of each cluster.

GEISHA

- Text mining tool for microarray analysis.
- Analyse the correlation between:
  - the increase of the level of expression patterns and
  - the significance of functional information derived from the literature.
- Extract functional information from the literature linked to the microarray genes.
- Calculates statistical significance of terms from documents associated to genes of each cluster.

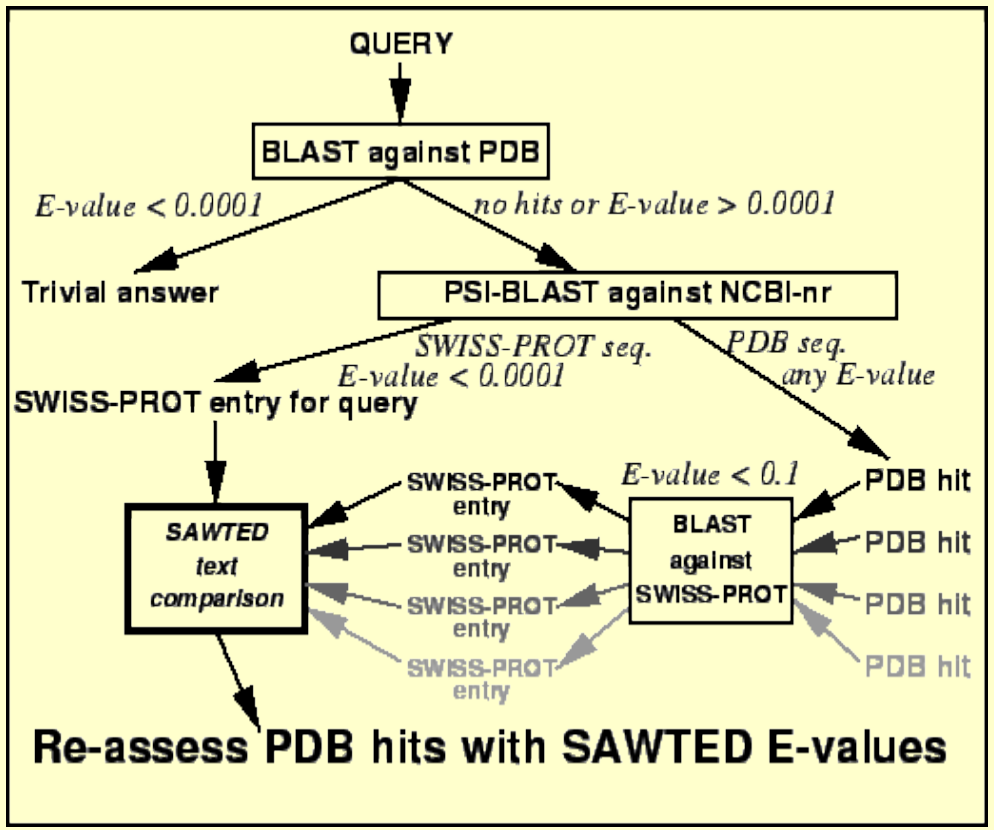
PROTEIN LOCALIZATION

- Protein activity -> specific cellular environments.
- Localisation determination:
  - Experimental techniques.
  - Bioinformatics techniques (PSORT).
  - Text mining.
- Nair and Rost: lexical information in annotation database records.
- Stapley et al: Use SVM to classify proteins according to their subcellular localisation, extracted from PubMed abstracts.

NLP AND SEQUENCE ANALYSIS: MEDBLAST

- Use NLP techniques to retrieve the related articles for a given sequence (online).
- Related articles:
  - those describing the query sequence (protein) or
  - Its redundant sequences and close homologues
- Direct search with the sequence.
- Indirect search with gene symbols.
- Use Blast against GenBank.
- Use Eutilities toolset to retrieve documents

NLP AND SEQUENCE ANALYSIS: SAWTED



Sequence similarity

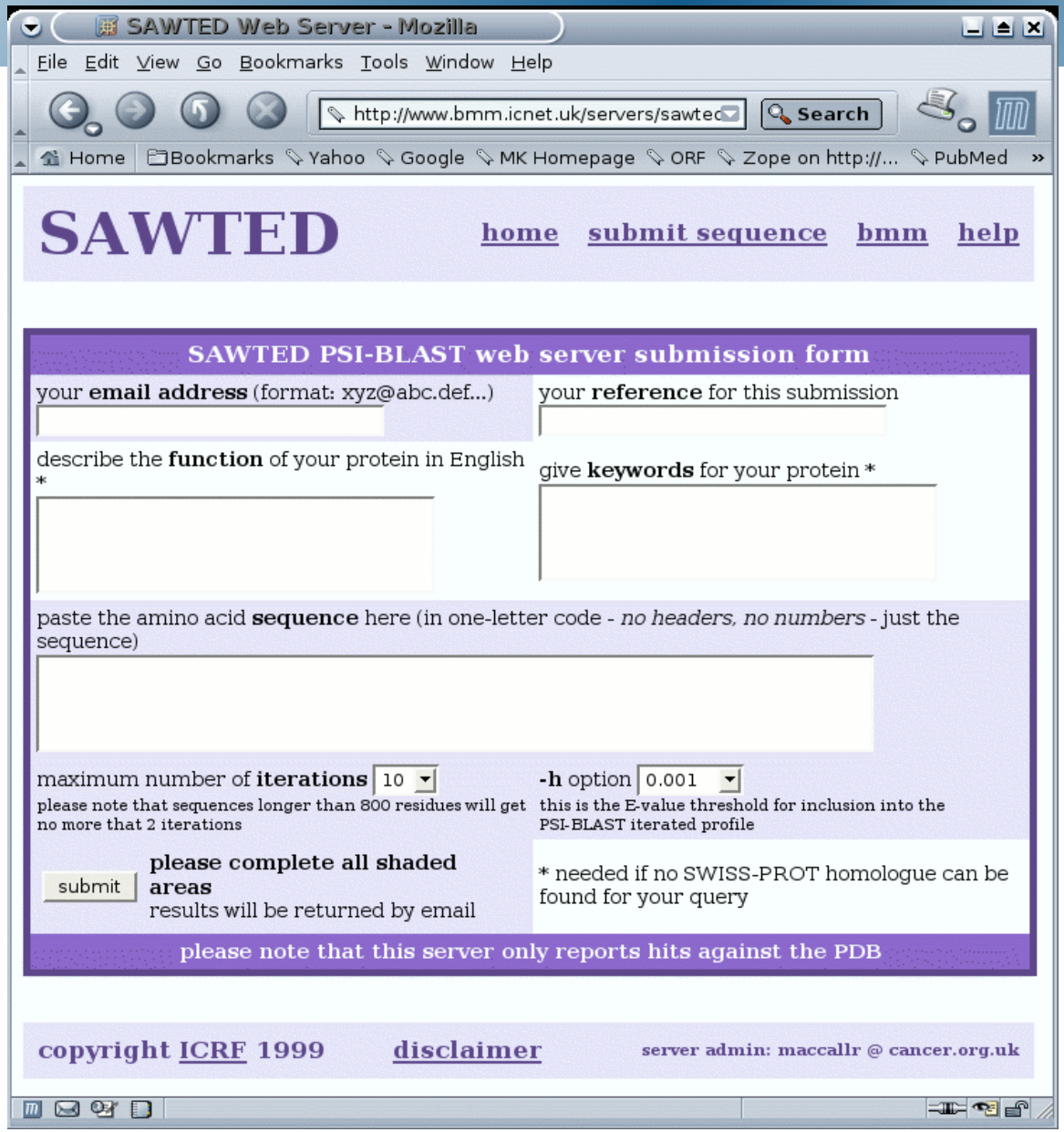
the base for identifying structure templates for query sequence

Structure Assignment With Text Description

Document comparison algorithms

http://www.bmm.icnet.uk/~sawted/

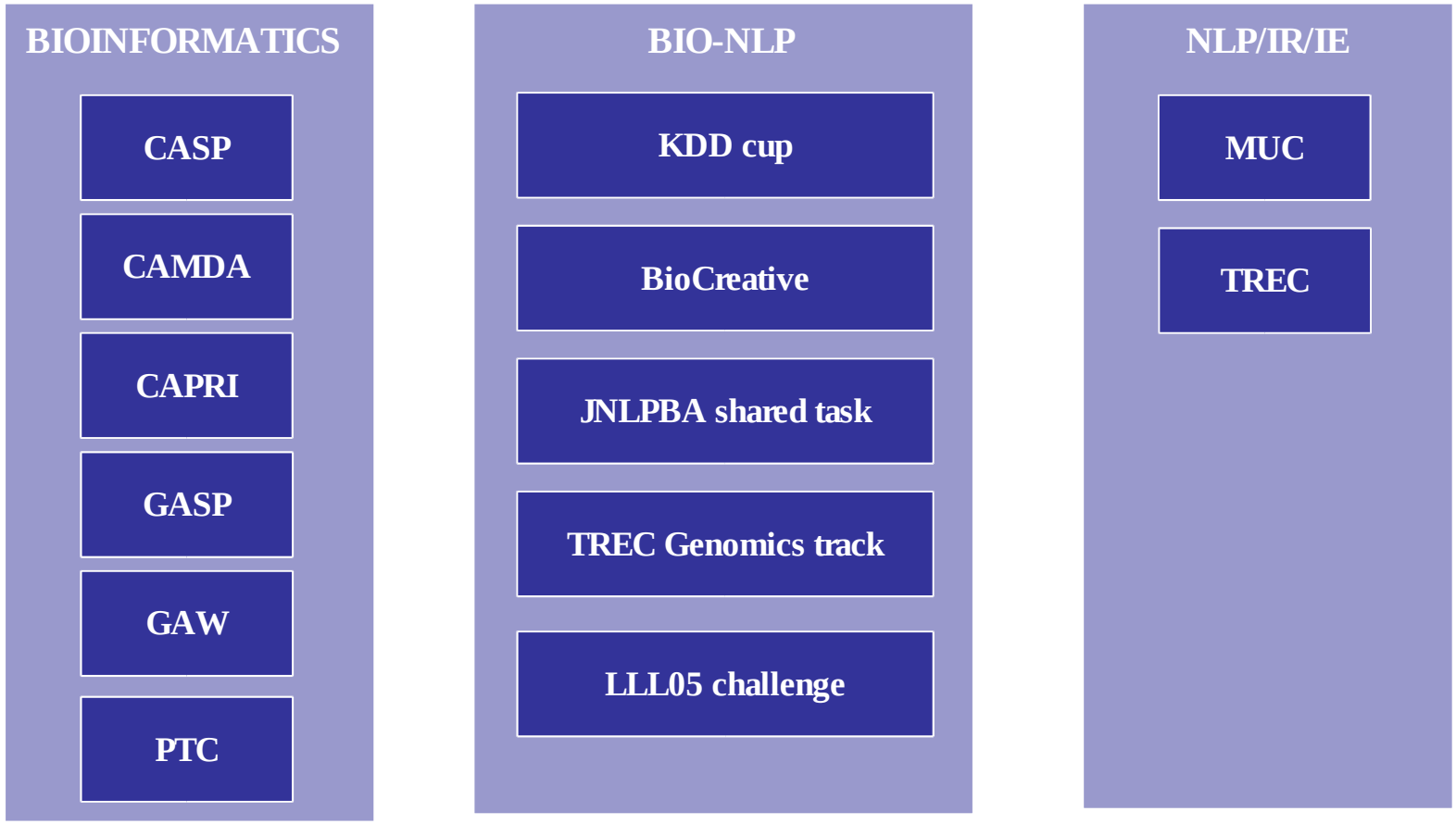
NLP AND SEQUENCE ANALYSIS: SAWTED



Use information contained in text descriptions of SwissProt annotations

identification of remote homologues

COMMUNITY WIDE EVALUATIONS



CASP: Critical asessment of Protein Structure Prediction
CAMDA: Critical Assessment of Microarray Data Analysis
CAPRI: Critical Assessment of Prediction of Interactions
GASP: Genome Annotation Assessment Project
GAW: Genome Access Workshop

PTC: Predictive Toxicology Challenge
KDD: Knowledge Discovery and Data mining
JNLPBA: Joint workshop on Natural Language Processing in Biomedicine
TREC: Text Retrieval conference
MUC: Message Understanding conference
LLL05: Genic interaction extraction challenge

CONCLUSIONS AND OUTLOOK

- BIO-NLP VERY RECENT DISCIPLINE (MAINLY 2003-TODAY).
- GROWING INTEREST
- NEW TECHNIQUES AND DATASETS
- NEED OF USER FEEDBACK AND INTERACTIVE LEARINING

SELECTED REVIEW REFERENCES

- M. Krallinger and A. Valencia. text mining and information retrievalservices for Molecular Biology. *Genome Biology*, 6 (7), 224 (2005)

- R. Hoffmann, M. Krallinger, E. Andres, J. Tamames, C. Blaschke and A. Valencia. Text Mining for Metabolic Pathways, Signaling Cascades, and Protein Networks. *Science STKE* 283, pe21 (2005).

- M. Krallinger, R. Alonso-Allende Erhadt and A. Valencia. Text-mining approaches in molecular biology and biomedicine. *Drug Discovery Today* 10, 439-445 (2005).

- M. Krallinger and A. Valencia. Applications of Text Mining in Molecular Biology, from name recognition to Protein interaction maps. In Data Analysis and Visualization in Genomics and Proteomics, chapter 4, Wiley.

SELECTED LINKS

http://www.pdg.cnb.uam.es/martink/LINKS/bionlp_tools_links.htm

http://www.pdg.cnb.uam.es/martink/links.htm

Acknowledgements

I would like to thank Alfonso Valencia for his supervisions and suggestions, the Protein Design Group at the National Biotechnology Centre (CNB) for interesting discussions.