An intelligent search engine and GUI-based efficient MEDLINE search tool based on deep syntactic parsing

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Abstract

We present a practical HPSG parser for English, an intelligent search engine to retrieve MEDLINE abstracts that represent *biomedical events* and an efficient MEDLINE search tool helping users to find information about biomedical entities such as *genes*, *proteins*, and the *interactions* between them.

1 Introduction

Recently, biomedical researchers have been facing the vast repository of research papers, e.g. MEDLINE. These researchers are eager to search biomedical correlations such as protein-protein or gene-disease associations. The use of natural language processing technology is expected to reduce their burden, and various attempts of information extraction using NLP has been being made (Blaschke and Valencia, 2002; Hao et al., 2005; Chun et al., 2006). However, the framework of traditional information retrieval (IR) has difficulty with the accurate retrieval of such relational concepts. This is because relational concepts are essentially determined by semantic relations of words, and keyword-based IR techniques are insufficient to describe such relations precisely.

This paper proposes a practical HPSG parser for English, **Enju**, an intelligent search engine for the accurate retrieval of relational concepts from MEDLINE, **MEDIE**, and a GUI-based efficient MEDLINE search tool, **Info-PubMed**.

	F-Score	
	GENIA treebank	Penn Treebank
HPSG-PTB	85.10%	87.16%
HPSG-GENIA	86.87%	86.81%

Table 1: Performance for Penn Treebank and the GENIA corpus

2 Enju: An English HPSG Parser

We developed an English HPSG parser, Enju [1] (Miyao and Tsujii, 2005; Hara et al., 2005; Ninomiya et al., 2005). Table 1 shows the performance. The F-score in the table was accuracy of the predicate-argument relations output by the parser. A predicate-argument relation is defined as a tuple $\langle \sigma, w_h, a, w_a \rangle$, where σ is the predicate type (e.g., adjective, intransitive verb), w_h is the head word of the predicate, a is the argument label (**MOD, ARG1, ..., ARG4**), and w_a is the head word of the argument. Precision/recall is the ratio of tuples correctly identified by the parser. The lexicon of the grammar was extracted from Sections 02-21 of Penn Treebank (39,832 sentences). In the table, 'HPSG-PTB' means that the statistical model was trained on Penn Treebank. 'HPSG-GENIA' means that the statistical model was trained on both Penn Treebank and GENIA treebank as described in (Hara et al., 2005). The GENIA treebank (Tateisi et al., 2005) consists of 500 abstracts (4,446 sentences) extracted from MEDLINE.

Figure 1 shows a part of the parse tree and fea-

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[1] http://www-tsujii.is.s.u-tokyo.ac.jp/enju/

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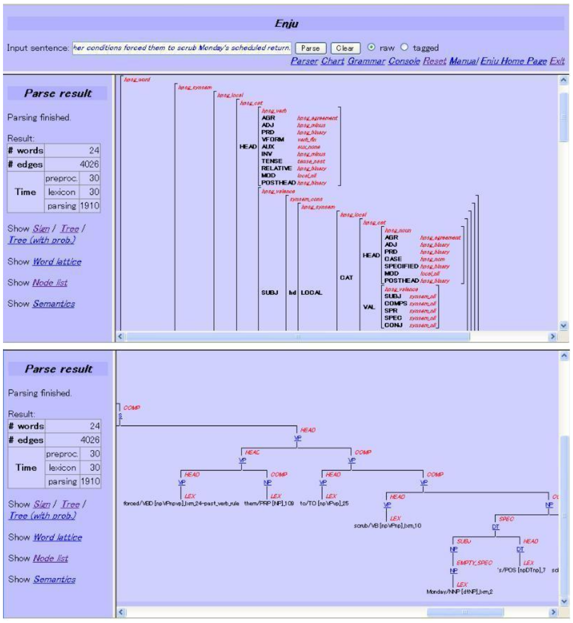


Input sentence: her conditions forced them to scrub Monday's scheduled return.

Parsing finished.

Result:

# words		24
# edges		4026
Time	preproc.	30
	lexicon	30
	parsing	1910

Figure 1: Snapshot of Enju

ture structure for the sentence “NASA officials vowed to land Discovery early Tuesday at one of three locations after weather conditions forced them to scrub Monday’s scheduled return.”

3 MEDIE: a search engine for MEDLINE

Figure 2 shows the top page of the MEDIE. MEDIE is an intelligent search engine for the accurate retrieval of relational concepts from MEDLINE [2] (Miyao et al., 2006). Prior to retrieval, all sentences are annotated with predicate argument structures and ontological identifiers by applying Enju and a term recognizer.

3.1 Automatically Annotated Corpus

First, we applied a POS analyzer and then Enju. The POS analyzer and HPSG parser are trained by using the GENIA corpus (Tsuruoka et al., 2005; Hara et al., 2005), which comprises around 2,000 MEDLINE abstracts annotated with POS and Penn Treebank style syntactic parse trees (Tateisi et al., 2005). The HPSG parser generates parse trees in a stand-off format that can be converted to XML by combining it with the original text.

We also annotated technical terms of genes and diseases in our developed corpus. Technical terms are annotated simply by exact matching of dictionary entries and the terms separated by space, tab, period, comma, hat, colon, semi-colon, brackets, square brackets and slash in MEDLINE.

The entire dictionary was generated by applying the automatic generation method of name variations (Tsuruoka and Tsujii, 2004) to the GENA dictionary for the gene names (Koike and Takagi, 2004) and the UMLS (Unified Medical Language System) meta-thesaurus for the disease names (Lindberg et al., 1993). It was generated by applying the name-variation generation method, and we obtained 4,467,855 entries of a gene and disease dictionary.

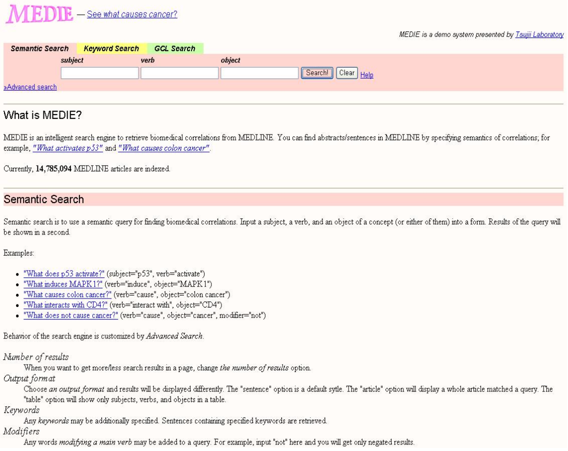
3.2 Functions of MEDIE

MEDIE provides three types of search, **semantic search**, **keyword search**, **GCL search**. GCL search provides us the most fundamental and powerful functions in which users can specify the boolean relations, linear order relation and structural relations with variables. Trained users can enjoy all functions in MEDIE by the GCL search, but it is not easy for general users to write appropriate queries for the parsed corpus. The semantic search enables us to specify an event verb with its subject and object easily. MEDIE automatically generates the GCL query from the semantic query, and runs the GCL search. Figure 3 shows the output of semantic search for the query ‘What disease does dystrophin cause?’. This example will give us the most intuitive understandings of the proximal and structural retrieval with a richly annotated parsed corpus. MEDIE retrieves sentences which include event verbs of ‘*cause*’ and noun ‘*dystrophin*’ such that ‘dystrophin’ is the subject of the event verbs. The event verb and its subject and object are highlighted with designated colors. As seen in the figure, small sentences in relative clauses, passive forms or coordination are retrieved. As the objects of the event verbs are highlighted, we can easily see what disease dystrophin caused. As the target corpus is already annotated with diseases entities, MEDIE can efficiently retrieve the disease expressions.

4 Info-PubMed: a GUI-based MEDLINE search tool

Info-PubMed is a MEDLINE search tool with GUI, helping users to find information about biomedical entities such as *genes*, *proteins*, and

[2] http://www-tsujii.is.s.u-tokyo.ac.jp/medie/



MEDIE — *See what causes cancer?*

MEDIE is a demo system presented by Tsujii Laboratory

What is MEDIE?

MEDIE is an intelligent search engine to retrieve biomedical correlations from MEDLINE. You can find abstracts/sentences in MEDLINE by specifying semantics of correlations; for example, *"What activates p53"* and *"What causes colon cancer"*.

Currently, **14,785,094** MEDLINE articles are indexed.

Semantic Search

Semantic search is to use a semantic query for finding biomedical correlations. Input a subject, a verb, and an object of a concept (or either of them) into a form. Results of the query will be shown in a second.

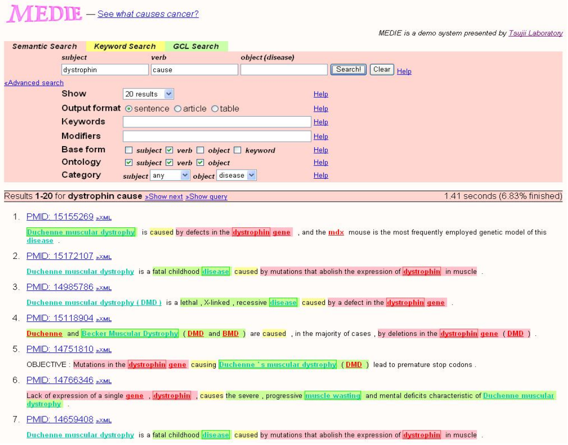
Examples:

- "What does p53 activate?" (subject="p53", verb="activate")
- "What induces MAPK1?" (verb="induce", object="MAPK1")
- "What causes colon cancer?" (verb="cause", object="colon cancer")
- "What interacts with CD4?" (verb="interact with", object="CD4")
- "What does not cause cancer?" (verb="cause", object="cancer", modifier="not")

Behavior of the search engine is customized by *Advanced Search*.

Number of results
When you want to get more/less search results in a page, change *the number of results* option.
Output format
Choose *an output format* and results will be displayed differently. The "sentence" option is a default sytle. The "article" option will display a whole article matched a query. The "table" option will show only subjects, verbs, and objects in a table.
Keywords
Any *keywords* may be additionally specified. Sentences containing specified keywords are retrieved.
Modifiers
Any words *modifying a main verb* may be added to a query. For example, input "not" here and you will get only negated results.

Figure 2: Snapshot of MEDIE: top page‘



MEDIE — *See what causes cancer?*

MEDIE is a demo system presented by Tsujii Laboratory

subject: dystrophin
verb: cause
object (disease):

Show: 20 results
Output format: ● sentence ○ article ○ table
Keywords:
Modifiers:
Base form: □ subject ☑ verb □ object □ keyword
Ontology: ☑ subject ☑ verb ☑ object
Category: subject any object disease

Results **1-20** for **dystrophin cause** »Show next »Show query 1.41 seconds (6.83% finished)

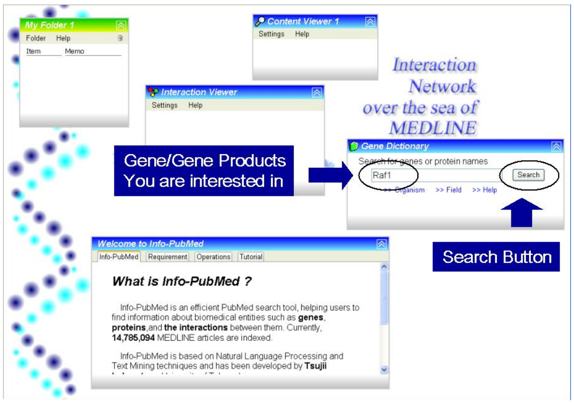
1. PMID: 15155269 »XML
   Duchenne muscular dystrophy is caused by defects in the dystrophin gene , and the mdx mouse is the most frequently employed genetic model of this disease .
2. PMID: 15172107 »XML
   Duchenne muscular dystrophy is a fatal childhood disease caused by mutations that abolish the expression of dystrophin in muscle .
3. PMID: 14985786 »XML
   Duchenne muscular dystrophy (DMD) is a lethal , X-linked , recessive disease caused by a defect in the dystrophin gene .
4. PMID: 15118904 »XML
   Duchenne and Becker Muscular Dystrophy (DMD and BMD) are caused , in the majority of cases , by deletions in the dystrophin gene (DMD) .
5. PMID: 14751810 »XML
   OBJECTIVE : Mutations in the dystrophin gene causing Duchenne 's muscular dystrophy (DMD) lead to premature stop codons .
6. PMID: 14766346 »XML
   Lack of expression of a single gene , dystrophin , causes the severe , progressive muscle wasting and mental deficits characteristic of Duchenne muscular dystrophy .
7. PMID: 14659408 »XML
   Duchenne muscular dystrophy is a fatal childhood disease caused by mutations that abolish the expression of dystrophin in muscle .

Figure 3: Snapshot of MEDIE: ‘What disease does dystrophin cause?’

the *interactions* between them [3].

Info-PubMed provides information from MEDLINE on protein-protein interactions. Given the name of a *gene* or *protein*, it shows a list of the names of other *genes/proteins* which co-occur in sentences from MEDLINE, along with the frequency of co-occurrence.

Co-occurrence of two *proteins/genes* in the same sentence does not always imply that they interact. For more accurate extraction of sentences that indicate interactions, it is necessary to identify relations between the two substances. We adopted PASs derived by Enju and constructed extraction patterns on specific verbs and their arguments based on the derived PASs (Yakusiji, 2006).



Interaction Network over the sea of MEDLINE

Gene/Gene Products You are interested in

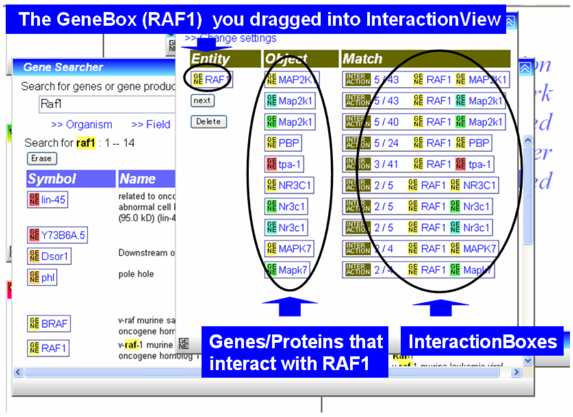
Search Button

What is Info-PubMed ?

Info-PubMed is an efficient PubMed search tool, helping users to find information about biomedical entities such as **genes**, **proteins**,and **the interactions** between them. Currently, **14,785,094** MEDLINE articles are indexed.

Info-PubMed is based on Natural Language Processing and Text Mining techniques and has been developed by **Tsujii**

Figure 4: Snapshot of Info-PubMed (1)



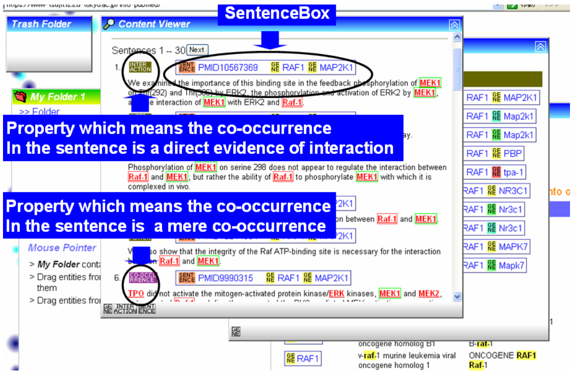
The GeneBox (RAF1) you dragged into InteractionView

Genes/Proteins that interact with RAF1

InteractionBoxes

>> Change settings
Gene Searcher
Search for genes or gene produc
Raf1
>> Organism
>> Field
Search for raf1 : 1 -- 14
Erase
Symbol
Name
lin-45
related to onc
abnormal cell
(95.0 kD) (lin-4
Y73B6A.5
Dsor1
Downstream o
phl
pole hole
BRAF
v-raf murine sa
oncogene hom
RAF1
v-raf-1 murine
oncogene homolog
Entity
Object
Match
RAF1
next
Delete
MAP2K1
Map2k1
Map2k1
PBP
tpa-1
NR3C1
Nr3c1
Nr3c1
MAPK7
Mapk7
INTERACTION 5 / 43 RAF1 MAP2K1
INTERACTION 5 / 43 RAF1 Map2k1
INTERACTION 5 / 40 RAF1 Map2k1
INTERACTION 5 / 24 RAF1 PBP
INTERACTION 3 / 41 RAF1 tpa-1
INTERACTION 2 / 5 RAF1 NR3C1
INTERACTION 2 / 5 RAF1 Nr3c1
INTERACTION 2 / 5 RAF1 Nr3c1
INTERACTION 2 / 4 RAF1 MAPK7
INTERACTION 2 / 4 RAF1 Mapk7

Figure 5: Snapshot of Info-PubMed (2)



SentenceBox

Property which means the co-occurrence In the sentence is a direct evidence of interaction

Property which means the co-occurrence In the sentence is a mere co-occurrence

Phosphorylation of MEK1 on serine 298 does not appear to regulate the interaction between Raf-1 and MEK1, but rather the ability of Raf-1 to phosphorylate MEK1 with which it is complexed in vivo.

Figure 6: Snapshot of Info-PubMed (3)

4.1 Functions of Info-PubMed

In the ‘Gene Searcher’ window, enter the name of a gene or protein that you are interested in. For example, if you are interested in Raf1, type “raf1” in the ‘Gene Searcher’ (Figure 4). You will see a list of genes whose description in our dictionary contains “raf1” (Figure 5). Then, drag

[3] http://www-tsujii.is.s.u-tokyo.ac.jp/info-pubmed/

one of the GeneBoxes from the 'Gene Searcher' to the 'Interaction Viewer.' You will see a list of genes/proteins which co-occur in the same sentences, along with co-occurrence frequency. The GeneBox in the leftmost column is the one you have moved to 'Interaction Viewer.' The GeneBoxes in the second column correspond to gene/proteins which co-occur in the same sentences, followed by the boxes in the third column, InteractionBoxes.

Drag an InteractionBox to 'ContentViewer' to see the content of the box (Figure 6). An InteractionBox is a set of SentenceBoxes. A SentenceBox corresponds to a sentence in MEDLINE in which the two gene/proteins co-occur. A SentenceBox indicates whether the co-occurrence in the sentence is direct evidence of interaction or not. If it is judged as direct evidence of interaction, it is indicated as Interaction. Otherwise, it is indicated as Co-occurrence.

5 Conclusion

We presented an English HPSG parser, **Enju**, a search engine for relational concepts from MEDLINE, **MEDIE**, and a GUI-based MEDLINE search tool, **Info-PubMed**.

MEDIE and Info-PubMed demonstrate how the results of deep parsing can be used for intelligent text mining and semantic information retrieval in the biomedical domain.

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