Complex event extraction at PubMed scale
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ABSTRACT

Motivation: There has recently been a notable shift in biomedical information extraction (IE) from relation models toward the more expressive event model, facilitated by the maturation of basic tools for biomedical text analysis and the availability of manually annotated resources. The event model allows detailed representation of complex natural language statements and can support a number of advanced text mining applications ranging from semantic search to pathway extraction. A recent collaborative evaluation demonstrated the potential of event extraction systems, yet there have so far been no studies of the generalization ability of the systems nor the feasibility of large-scale extraction.

Results: This study considers event-based IE at PubMed scale.

We introduce a system combining publicly available, state-of-the-art methods for domain parsing, named entity recognition and event extraction, and test the system on a representative 1% sample of all PubMed citations. We present the first evaluation of the generalization performance of event extraction systems to this scale and show that despite its computational complexity, event extraction from the entire PubMed is feasible. We further illustrate the value of the extraction approach through a number of analyses of the extracted information.

Availability: The event detection system and extracted data are open source licensed and available at http://bionlp.utu.fi/

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1 INTRODUCTION

In response to the explosive growth of biomedical scientific literature, there has recently been significant interest in the development of automatic methods for analyzing domain texts (Chapman and Cohen, 2009). In the previous decade of work on automatic information extraction (IE) from biomedical publications, efforts have focused in particular on the basic task of recognizing entity mentions in text, such as gene, protein or disease names (Kim et al., 2004; Smith et al., 2008; Yeh et al., 2005) and on the extraction of simple relations of these entities, such as statements of protein-protein interactions (PPI; Krallinger et al., 2008; Nédellec, 2005). State-of-the-art IE methods frequently rely on a detailed analysis of sentence structure ( parsing) (Airola et al., 2008; Miwa et al., 2009), and several studies have addressed the development and adaptation of parsing methods to biomedical domain texts (Haiz et al., 2007; Lease and Charniak, 2005; McClosky, 2009; Rimell and Clark, 2009).

The research focus on biomedical text analysis has brought forth notable advances in many areas. Automatic protein and gene Named Entity Recognition (NER) with performance exceeding 90% F-score was demonstrated to be feasible in the recent BioCreative community evaluation (Smith et al., 2008). Similarly, significant improvement has been made in PPI extraction (Airola et al., 2008; Chowdhary et al., 2009; Miwa et al., 2009) and there is an active collaboration between database curators and method developers to integrate PPI methods into curation pipelines (Chatr-aryamotri et al., 2008). Finally, methods for a variety of biomedical text processing tasks ranging from sentence splitting (Tomanek et al., 2007) to full parsing (McClosky, 2009) have been introduced with performance approaching or matching the performance of similar methods on general English texts.

Building on such text analysis methods, several IE systems and services have been created for retrieving interaction information from PubMed (http://www.pubmed.com). Varying levels of parsing and other NLP methods have been used to detect biological entities of interest and their relationships. Most previous efforts have focused on pairwise PPI, with extracted pairs often represented as merged interaction networks. The MEDIHE and InfoPubmed systems (Ohta et al., 2006) offer access to deep syntactic analysis and entity relation extraction results from the entire PubMed through subject-verb-object search patterns. The Chilibot system looks for pairwise relationships based on co-occurrence and uses the presence of interaction keywords to type them (Chen and Sharp, 2004). The TextMed system, based on the LYDIA project (Lloyd et al., 2005), uses shallow parsing and co-occurrence information to generate pairwise entity relationship networks from PubMed citations. The Ali Baba system likewise visualizes relationships from PubMed abstracts as graphs (Palaga et al., 2009). HIOP hyperlinks PubMed abstracts together through shared protein and gene mentions (Hoffmann and Valencia, 2004). Finally, GoPubMed uses Gene Ontology (http://www.geneontology.org/) and medical subject headings (MeSH) (http://www.nlm.nih.gov/mesh/) to provide a knowledge-based search for relevant citations (Doms and Schroeder, 2005).

Supported in part by the maturation of basic technologies for biomedical text analysis and the availability of richly annotated text corpora (Kim et al., 2008; Pyysalo et al., 2007), there has recently been notable movement in the biomedical IE community toward more detailed and expressive representations of extracted information. In particular, event representations that can capture different types of associations of arbitrary numbers of entities and events in varying roles have been described as an alternative to the simple relation representation. While the applicability of the results produced by IE methods employing relation representations is closely tied to the specific relation type targeted (i.e. PPI or gene-disease), event representations have wider potential in supporting applications ranging from PPI to semantic search and

1 F-score is the harmonic mean of (p)recision and (r)ecall, i.e. $F = \frac{2pr}{p + r}$
pathway extraction (Kim et al., 2009). Showing wide interest in
the approach, 24 teams participated in the first community-
wide competitive evaluation of event extraction methods, the
BioNLP’09 Shared Task on Event Extraction (http://www-
tsuji.is.s.u-tokyo.ac.jp/GENIA/SharedTask/). Kim et al., 2009). The
number is comparable to the 26 teams participating in the PPI task of
the established BioCreative II community evaluation (Kral linger
et al., 2008).

In this study, building on the best performing system in the
BioNLP’09 shared task (Björne et al., 2009) and J.Björne et al.
(submitted for publication) which remains competitive with even
the most recent advances (Miwa et al., 2010), we jointly take state-
of-the-art methods for biomedical text parsing, protein/gene name
recognition and IE into a unified system capable of event extraction
from unannotated text. We apply this system to a random 1% sample
of citations from the PubMed literature database, providing the first
estimate of the results of event extraction from the entire PubMed
data. We further analyze the performance of the key components
of the system, thus providing the first evaluation of the ability of
state-of-the-art event extraction systems to generalize to PubMed
scale.

2 SYSTEM AND METHODS

The event extraction system presented in this article follows the model of
the BioNLP’09 Shared Task on event extraction in its representation of
extracted information. The BioNLP’09 Shared Task was the first large-scale
evaluation of biomedical event detection systems (Kim et al., 2009). The task
introduced an event representation and extraction task based on the GENIA
event corpus annotation (Kim et al., 2008). The primary extraction targets
in the defined task are nine fundamental biomolecular event types (Table 1)
and the participants in these events. In this article, the term event refers to
events as defined by the Shared Task annotation scheme.

Several aspects of the event representation differentiate the event
extraction task from the body of domain IE studies targeting, e.g. PPI and
gene–disease relations, including previous domain shared tasks (Kral linger
et al., 2008; Nédellec, 2005). While domain IE has largely focused on a
relation model representing extracted information as entity pairs, the event
model allows for a more expressive way of capturing statement semantics.
Events can have an arbitrary number of participants whose roles in the
event (e.g. theme or cause) are specified, making it possible to capture n-ary
associations and statements where some participants occur in varying roles
or are only occasionally mentioned. Further, events are modeled as primary
objects of annotation and bound to specific statements in text (triggers),
allowing events to participate in other events and facilitating further analysis
such as the identification of events stated in a negated or speculative context.
Finally, events following the Shared Task model are given GENIA Event
ontology types drawn from the community-standard Gene Ontology, giving
each event well-defined semantics. Using events to represent information
contained in natural language sentences, for the first time it is now possible
to accurately describe in a formal fashion the multitude of different biological
phenomena depicted in research articles.

In the rest of this section, we describe the steps of the event extraction
pipeline (Fig. 1).

2.1 Named entity recognition

NER is a fundamental requirement for IE: the analysis of IE systems normally
takes the form of associations between references to entities, and most
applications require the references to be sufficiently specific to identify
particular real-world entities, i.e. entity names. Consequently, NER is a
well-studied subtask in IE. Also in the biomedical domain NER has been

![Fig. 1. Event extraction. A multiphased system is used to generate an event graph, a formal representation for the semantic content of the sentence. Before event detection, sentences are parsed (A) to generate a suitable syntactic graph to be used in detecting semantic relationships. Event detection starts with identification of named entities (B) with BANNER (parses are not used at this step). Once named entities have been identified, the trigger detector (C) uses them and the parse for predicting triggers, words which define potential events. The edge detector (D) predicts relationship edges (event arguments) between triggers and named entities. Finally, the resulting semantic graph is divided into individual events by (E) duplicating trigger nodes and regrouping argument edges.](image-url)
Table 2. NER system performance

| System         | Corpus     | F-score | References |
|----------------|------------|---------|------------|
| JNLPA (best)   | GENIA term | 72.6%   | Kim et al. (2004) |
| BioCreative I (best)   | GENETAG | 83.2%   | Yeh et al. (2005) |
| BioCreative II (best) | GENETAG | 87.2%   | Smith et al. (2008) |
| BANNER         | GENETAG    | 86.4%   | Leaman and Gonzalez (2008) |

Performance shown for the best performing systems at various shared tasks and the BANNER system used in this work.

Note that while the GENIA term corpus used in the JNLPA task requires differentiation between, e.g., protein and gene entities, GENETAG only marks a single gene/RNA/protein type, contributing to the measured differences.

2.3 Event detection

At the core of our approach to event extraction are graph representations of sentence syntax and semantics. The syntactic graph corresponds to a dependency analysis of sentence structure, and the semantic graph represents the event structure, with nodes representing named entities and events, and edges corresponding to event arguments (Fig. 1). The syntactic graph is generated from the text by the parser and the protein/gene entities of the semantic graph are detected by the NER system. The goal of the core event extraction system, described in detail in Björne et al. (2009) and J.Björne et al. (submitted for publication) is then to generate the semantic graph given a sentence with marked named entities and syntactic analysis. The system considers the sentences independently since, based on an analysis of the BioNLP’09 Shared Task dataset, only 4.8% of events cross sentence boundaries.

The event extraction system is based on supervised machine learning, i.e. it performs predictions for unknown cases based on a supervised model automatically learned from annotated training data. Here, we present a model trained on annotated data from BioNLP’09 Shared Task. The training data consists of 31,792 examples with 295,034 unique features. The system classifies each event into one of nine event types or a negative, i.e. not corresponding to an event.

As can be seen in Figure 1, the dependency parse is very close to the semantic graph that we aim to extract, and consequently it is the most important source of features. Notable is the use of very large numbers of unique features, usually small numbers of very large features, for example, the training data for the edge detector consists of 31,792 examples with 295,034 unique features.

Our system has two key machine learning-based classification steps, trigger detection and edge detection, followed by a rule-based event construction step.

2.3.1 Trigger detection

Triggers are the words in the sentence that state the events between the named entities, and trigger detection is thus the first step in event detection. As determined from the BioNLP’09 Shared Task dataset, 92% of all triggers consist of a single word. Therefore, we represent all triggers with their head word, the syntactically most relevant word within a particular trigger, typically its syntactic head. Trigger detection is thus the task of identifying those individual words in the sentence that act as a trigger head word. In contrast with NER, where sequential models are typically applied (Smith et al., 2008), the system classifies each word in isolation as one of the nine event types, or a negative, i.e. not corresponding to an event trigger.

Triggers cannot be identified based only on the words themselves, as most potential trigger words do not uniquely correspond to a specific trigger class. For example, only 28% of the instances of the word activates are triggers for positive regulation events in the BioNLP’09 Shared Task dataset and the commonly used word overexpression is equally distributed between gene expression events, positive regulation events and the negative class. For this reason, a large number of features that aim to capture the full semantic context of a potential trigger word are used in the classification.

Features for the trigger detection are based on both the linear order of words and the dependency parse. The largest number of features comes from the dependency parse, from which undirected chains of up to three dependencies are built, starting from the potential trigger word. The words themselves are also sliced into two or three letter N-grams that aim to capture similarities between closely related words or inflected forms.

2.3.2 Edge detection

Each edge in the semantic graph corresponds to an event argument and edge detection thus follows trigger detection. Edge detection is cast as a multiclass classification task, since event arguments may
have multiple types (cause, theme). One example is defined for each possible directed pairwise combination of trigger and entity nodes, and this example will then be classified as belonging to one of the argument type classes or as negative. Each edge example is classified independently, even though the BioNLP'09 Shared Task event scheme imposes conditions on valid combinations of argument types for each type of event. These conditions are enforced in the event construction phase.

In contrast with trigger detection, the linear order of words is not considered and the features are entirely based on the dependency parse, more specifically on the shortest path of dependencies that link together the two trigger or entity nodes under consideration. To describe the path as features, it is divided into multiple dependency N-grams, each consisting of 2–4 consecutive dependencies between sentence words. Features built from previous classification steps, i.e. ones based on the named entities and triggers, are also an important part of the edge detection feature set.

2.3.3 Event construction The semantic graph created in the trigger and edge detection steps (Fig. 1D) contains strictly one event node for each trigger word. The final events are created by duplicating these nodes when necessary and separating their edges into valid combinations based on the syntax of the sentences and the conditions on argument type combinations stated in the BioNLP'09 Shared Task event scheme. This step is rule based and as such does not require training data.

2.3.4 Machine learning method As the machine learning method applied in all stages of the core event extraction system, we use the SVM*multiclass (Tsochantaridis et al., 2005) implementation (http://svmlight.joachims.org/svm_multiclass.html) of an SVM. SVMs are based on the same idea as neural networks, except that they are more general and do not require training data. The SVMs are trained using the same features, it is divided into multiple dependency N-grams, each consisting of 2–4 consecutive dependencies between sentence words. Features built from previous classification steps, i.e. ones based on the named entities and triggers, are also an important part of the edge detection feature set.

3 RESULTS

We apply the event extraction system to a 1% sample of the 2009 distribution of the PubMed literature database. The full PubMed dataset contains 17.8 million citations, which we downsampled at random to create a dataset of 177,648 citations. To assure that results are representative of the full PubMed database, we performed no document selection or filtering. Consequently, 81,516 of the citations in the sample (46%) contain only a title but no abstract, and the earliest citation in the sample is for an article published in 1867 (PMID 17230723). While many of the citations in the sample are thus likely to have limited utility for biomolecular event extraction, their inclusion assures unbiased results and a fair test of the true generalization ability of the applied methods.

In total, the system extracted 168,949 events from 29,781 citations in the PubMed sample. The number of extracted events for the nine event types is presented in Table 3. The BANNER NER system marked 363,204 gene/protein entities in 54,051 citations in the sample, averaging two mentions per citation overall and almost seven per citation for those containing at least one tagged entity. By this estimate less than a third of PubMed citations contain gene/protein mentions. When the extracted events are broken up by publication year, a strong trend for increasing number of citations containing gene/protein mentions and events is visible, with 25% of citations from the last 10 years containing at least one event (Fig. 2). Since the extracted events are of the protein/gene-specific BioNLP'09 Shared Task types, this trend can be seen to reflect the growing prominence of molecular biology. Based on the predicted named entities and events, the present release of PubMed can be estimated to contain more than 5 million citations containing gene/protein mentions, totaling over 35 million mentions overall and nearly 3 million citations containing events of the Shared Task types, totaling over 16 million such events overall. The number of citations with events has increased consistently with the growth of PubMed (Fig. 2) until the year 2000. After this the total amount of citations grows more rapidly, perhaps reflecting PubMed’s expanded coverage of life science topics since then (Benton, 1999).

Table 3. Frequency of the nine event types in the output of the system on the PubMed sample

| Event Type          | Count (% ) |
|---------------------|------------|
| Gene expression     | 48,144 (28.5) |
| Positive regulation | 43,155 (25.5) |
| Binding             | 24,159 (14.3) |
| Negative regulation | 21,833 (12.9) |
| Regulation          | 13,910 (7.9) |
| Localization        | 10,766 (6.4) |
| Phosphorylation      | 3,852 (2.3)  |
| Transcription        | 2,492 (1.5)  |
| Protein catabolism   | 1,218 (0.7)  |
| **TOTAL**            | **168,949 (100.0)** |
The event extraction system (without the NER component) achieves an event. For named entities, we consider as positives cells, cellular we extend the criteria for what is considered a named entity and of the biomolecular interactions stated in the texts as possible, so molecules such as Ca²⁺. Our aim in this work is to recover as many of signaling interactions between proteins and small inorganic only between genes and proteins, leaving out e.g. the multitude their correctness.

predicted named entities and 100 predicted events and determine precision errors is a comparatively easy task and allows us to determine the subdomain. In contrast, manually inspecting the system output for practical for this study, particularly since relevant events are very example, annotating the GENIA event corpus consisting of 9 372 entities and events. Annotating sentences for positive and negative a large enough fraction of the PubMed sample for all named system was originally trained.

In the BioNLP'09 Shared Task data events are annotated an F-score of 52.86% (precision 58.13% and recall 48.46%) on the BioNLP'09 Shared Task test set. The Shared Task data, based on the GENIA corpus, is composed of PubMed citations relevant to biological reactions concerning transcription factors in human blood cells (Kim et al., 2008). The GENIA corpus is focused on a particular subdomain and thus not a representative sample of the entire PubMed, the focus of this study. Additional analysis is, therefore, necessary to evaluate the extraction result. A particular point of interest is the ability of the system to perform on input data that, compared with the GENIA corpus, has far fewer events per sentence and thus deviates from the distribution on which the system was originally trained.

Evaluating the recall of the system would require fully annotating a large enough fraction of the PubMed sample for all named entities and events. Annotating sentences for positive and negative events is, however, a time and labor-intensive process. For example, annotating the GENIA event corpus consisting of 9 372 sentences required 1.5 years with five part-time annotators and two coordinators (Kim et al., 2008). Such an annotation is thus not practical for this study, particularly since relevant events are very rare in a random sample of PubMed not focused on any particular subdomain. In contrast, manually inspecting the system output for errors is a comparatively easy task and allows us to determine the precision of the system output. We examine a random sample of 100 predicted named entities and 100 predicted events and determine their correctness.

In the BioNLP'09 Shared Task data events are annotated only between genes and proteins, leaving out e.g. the multitude of signaling interactions between proteins and small inorganic molecules such as Ca²⁺. Our aim in this work is to recover as many of the biomolecular interactions stated in the texts as possible, so we extend the criteria for what is considered a named entity and an event. For named entities, we consider as positives cells, cellular components and molecules that take part in biochemical interactions. For events, we consider the event to be correct if all its named entity arguments are correct and the trigger word in the text is correctly detected.

In the manual evaluation of the 100 predicted named entities, we estimate the precision of the named entity detection step (the BANNER system) to be 87%. This compares well with BANNER performance on the GENETAG corpus with precision of 89% (for an F-score of 86%). The precision of the 100 predicted events was 64%, a figure close to the 58% (for F-score of 53%) established on the BioNLP'09 Shared Task data. While recall cannot be directly measured, as discussed above, considering that the event extraction system was trained on example-rich data that favors making positive predictions, it can be expected not to decrease substantially from results established on subdomain corpora.

The results of this manual analysis indicate that the performance of the named entity and event detection components does generalize from the subdomain corpus data to a representative unbiased sample of the entire PubMed. It should, however, be noted that evaluating automatically generated predictions after the fact is more prone to a positive bias than annotation of plain text with no predictions.

3.2 Event network

One of the most promising applications for large-scale event mining is the generation of interaction networks. Unlike networks constructed from binary interactions, an event network defines the types and directions of the relationships, the polarity (positive or negative) of regulatory relationships and the mechanisms involved (e.g. phosphorylation). Sufficiently accurate event graphs can be used for inferring complex regulatory relationship networks and other biologically relevant tasks.

Figure 4 illustrates a sample network constructed from events extracted by our system around interleukin-4. To build the network, we merge the individual predicted events into a single graph, loosely following the approach employed by Saey et al. (2009). We determine two protein mentions to be the same if their names match after lowercasing and removal of whitespace and hyphens. All mentions of the same protein are represented in the graph by a single node. Event argument edges connect the proteins through event trigger nodes.

The entire graph extracted from the PubMed sample has one major connected component comprising 88 477 (38%) of the total of 232 760 nodes. The remaining nodes form a large number of considerably smaller connected components, the largest of which contains a mere 95 nodes.

3.3 Topic analysis

As a final analysis of the extraction results, we studied the topics of event-containing citations. Over 90% of records in PubMed are manually indexed with a number of descriptors chosen from Medical Subject Headings (MeSH), a hierarchical thesaurus in which the descriptors are arranged primarily in general—specific hierarchy. The descriptors assigned to a PubMed citation record express the main topics discussed in the respective article and allow queries within specific subtopics, reducing the variance and sparsity of simple keyword search. In the following, we investigate the connection between MeSH descriptors and event types, establishing
Fig. 4. Extracted event network around interleukin-4. This graph shows a subset of the predicted event network, including only named entities with at least 50 extracted instances. The round event nodes are (P)ositive regulation, (N)egative regulation, (R)egulation, gene (E)xpression, (B)inding, p(H)osphorylation and (L)ocalization. For clarity, single-argument events (E, B, H and L) are displayed only when they also act as arguments of regulation events.

The topical areas in PubMed likely to contain citations relevant to event extraction.

We measured the degree of dependence between a MeSH descriptor $d$ and an event type $e$ using pointwise mutual information

$$MI(d,e) = \log \frac{P(d,e)}{P(d)P(e)}$$

where $P(d,e)$ is defined as the fraction of citations indexed by the descriptor $d$ and containing at least one event of type $e$, out of all citations that contain at least one event. Similarly, $P(d)$ (respectively $P(e)$) is the fraction of citations containing the descriptor $d$ (respectively event of type $e$) out of all citations that contain at least one event. The measure calculates the ratio of joint probability of $d$ and $e$ to the probability of their co-occurrence by chance. To deal with sparsity problems, we first expanded, for each citation, the set of its original MeSH descriptors indexed in PubMed with all descriptors that are more general in the MeSH hierarchy. This allows us to find more general descriptors, rather than the specific ones indexed in PubMed.

For each of the nine event types, we built a list of five most related descriptors, that is, descriptors with the highest pointwise MI. To avoid unnecessarily specific descriptors, we only considered those descriptors that were present in at least 10% of citations with an event of the given type, and discarded descriptors that were hyponyms (more specific) to another descriptor already in the list. The resulting lists are given in Table 4. These illustrate that the descriptors obtained are indeed relevant to the respective event types, except for the two obviously too general descriptors Technology, Industry, and Agriculture and Information Services, which we discarded in all subsequent analyses. Apart from validating the IE system, although very indirectly, these MeSH descriptor lists can be used to focus PubMed searches to citations likely containing the relevant event types.

Of the 177,648 citations in the PubMed sample, 66,227 (37.3%) are indexed by at least one of the descriptors in Table 4, or its hyponym (we will refer to these citations as MeSH-relevant). In contrast, only 12,405 (7.3%) of the 168,949 events identified by the system were extracted from the 62.7% MeSH-irrelevant citations, demonstrating that the MeSH terms in Table 4 are indeed strong predictors of citations containing relevant events. Intuitively, it can be expected that MeSH-irrelevant citations are also likely to contain a higher proportion of false positive named entities.
Top related MeSH descriptors for the nine event types

Table 5.

| Event type       | Five most related MeSH descriptors                                                                 |
|------------------|-------------------------------------------------------------------------------------------------|
| Gene expression  | Gene expression regulation; RNA; gene expression; cytokines; immunohistochemistry               |
| Positive regulation | Intracellular signaling peptides and proteins; phosphotransferases; transcription factors; cytokines; gene expression regulation |
| Negative regulation | Molecular mechanisms of pharmacological action; intracellular signaling peptides and proteins; therapeutic uses; phosphotransferases; tumor cells, cultured |
| Binding          | Protein binding; information services; physicochemical phenomena; chemistry techniques; analytical receptors; cell surface |
| Regulation       | Gene expression regulation; RNA; messenger; transcription factors; protein kinases; peptide hormones |
| Localization     | Endocrine system, protein precursors; nerve tissue proteins; hormones, hormone substitutes and hormone antagonists; organelles |
| Transcription    | RNA; gene components; gene expression; base sequence; transcription factors                      |
| Phosphorylation  | Organic chemistry phenomena; tyrosine adaptor proteins, signal transducing; phosphotransferases (alcohol group acceptor) phosphoproteins |
| Protein catabolism | Hydrolases; macromolecular substances; technology, industry and agriculture; physicochemical processes; metabolism |

Table 6. Comparison of named entity and event detection precision between MeSH-relevant and MeSH-irrelevant citations

| Citation TP FP Precision (%) | Named entities | Events |
|------------------------------|----------------|--------|
| MeSH-relevant                | 66 5 93.0       | MeSH-relevant |
| MeSH-irrelevant              | 21 8 72.4       | MeSH-irrelevant |
|                              | 58 29 66.7       |        |
|                              | 4 9 30.8        |        |

3.4 Computational requirements

The computational requirements of the system components, in terms of time and space, are detailed in Table 6. NER using BANNER is a comparatively light-weight processing step in the pipeline. Processing the entire dataset consumed <18 h on a desktop-level computer, averaging more than three citations per second. NER tagging could thus be run for the entire PubMed database in ~75 days on a single machine, or a matter of days on a modest cluster.

Full dependency parsing is the most resource-intensive step in the pipeline. The parsing time of the Charniak–Johnson parser for one sentence is in our case 0.81 s, with an additional 0.15 s taken by the SD scheme conversion. Parsing all 935 186 sentences in the PubMed sample would thus take 249 processor hours (2.84 processor years projected for the entire PubMed). However, only sentences with at least one recognized named entity, and thus a potential target for the IE system, need to be parsed, considerably decreasing the number of sentences that must be parsed to 199 941 and the parsing time to 53 h (222 days projected for the entire PubMed).

We note that the parsing process is not a straightforward technical undertaking. The Charniak–Johnson parser takes about 10 s to load the parsing model files and, in order for this fixed time penalty not to accumulate, it is necessary to divide the parsing task to large batches rather than parsing a single abstract, or even single sentence at a time. On the other hand, there were 26 sentences in the PubMed sample that caused the parser to process interminably without producing an analysis. It was necessary to detect these cases, terminate the parser and restart the process. Of the 199 915 sentences parsed by the Charniak–Johnson parser, further 37 sentences were not successfully processed by the SD conversion tools. The final number of successfully parsed sentences was thus 199 878. It must be stressed that this number represents a highly respectable 99.97% of sentences successfully parsed, demonstrating the high reliability achieved by the current state-of-the-art in syntactic parsing.

Finally, the event extraction step took 27 processor hours (114 processor days projected for the entire PubMed), thus averaging roughly one citation per 2 s for the 54 051 citations with at least one detected named entity. The total processing time of the pipeline was 98 processor hours (411 processor days projected for the entire PubMed), or, one PubMed citation per 2 s.
4 DISCUSSION AND CONCLUSIONS

We have presented to the best of our knowledge the first application of event-style biomedical interaction extraction to a large-scale real-world dataset, 1% of the PubMed citation database. We combined the event detection system of J.Björne et al. (submitted for publication), the winning system of the BioNLP’09 Shared Task, with the efficient Charniak–Johnson parser (Charniak and Johnson, 2005) equipped with the biomedical domain model of McClosky (2009) and the BANNER named entity detector (Leaman and Gonzalez, 2008), creating a system capable of extracting events from unannotated biomedical text. Successful processing of 1% of PubMed in 98 processor hours demonstrates that the computational requirements, although considerable, are well within reach of generally available computational resources.

Analysis of the 1% PubMed sample dataset produced over 160,000 biomedical events. Based on a manual analysis of a subset of these predicted events, the precision of the system was 64%, indicating that the event detection system performance generalized well to real world conditions represented by a random, unbiased sample of PubMed. Analysis of the resulting event graph showed that the generated events form a highly connected interaction network. It is especially in this regard that extraction of events, rather than n-ary relations, holds a great promise: the complexity of interaction networks can only be utilized effectively when detailed information about the type, direction and polarity of the various interactions is available.

Even though a mere 1% of PubMed was analyzed in this study, the result is a large dataset of over 160,000 events extracted by a state-of-the-art event extraction system as well as 177,000 PubMed citations processed with the essential NLP tools. In most respects, this dataset is representative of the entire PubMed and allows a number of subsequent analyses to be performed even before the entire PubMed is processed by the system. As a practical contribution to the emerging field of biomedical event detection, we publish the dataset in a flexible XML format as well as the widely adopted BioNLP’09 Shared Task format. The event detection system used in this study and described in more detail in Björne et al. (2009) and J.Björne et al. (submitted for publication) is published under an open source license. Both are available at http://bionlp.utu.uta.fi/.

Having shown its feasibility, the future work will focus on processing the entire PubMed and, as with this study, making the results available for analysis to the community.

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