Complex Biological Event Extraction from Full Text using Signatures of Linguistic and Semantic Features

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Abstract

Building on technical advances from the BioNLP 2009 Shared Task Challenge, the 2011 challenge sets forth to generalize techniques to other complex biological event extraction tasks. In this paper, we present the implementation and evaluation of a signature-based machine-learning technique to predict events from full texts of infectious disease documents. Specifically, our approach uses novel signatures composed of traditional linguistic features and semantic knowledge to predict event triggers and their candidate arguments. Using a leave-one out analysis, we report the contribution of linguistic and shallow semantic features in the trigger prediction and candidate argument extraction. Lastly, we examine evaluations and posit causes for errors in our complex biological event extraction.

1 Introduction

The BioNLP 2009 Shared Task (Kim et al., 2009) was the first shared task to address fine-grained information extraction for the bio-molecular domain, by defining a task involving extraction of event types from the GENIA ontology. The BioNLP 2011 Shared Task (Kim et al., 2011) series generalized this defining a series of tasks involving more text types, domains and target event types. Among the tasks for the new series is the Infection Disease task, proposed and investigated by (Pyysalo et al., 2011; Pyysalo et al., 2010; Bjorne et al., 2010).

Like the other tasks for the BioNLP Shared Task series, the goal is to extract mentions of relevant events from biomedical publications. To extract an event, the event trigger and all arguments must be identified in the text by exact offset and typed according to a given set of event and argument classes (Miwa et al., 2010). Entity annotations are given for a set of entity types that fill many of the arguments.

Here we describe Pacific Northwest National Laboratory’s (PNNL) submission to the BioNLP 2011 Infectious Disease shared task. We describe the approach and then discuss results, including an analysis of errors and contribution of various features.

2 Approach

Our system uses a signature-based machine-learning approach. The system is domain-independent, using a primary task description vocabulary and training data to learn the task, but domain resources can be incorporated as additional features when available, as described here. The approach can be broken down into 4 components: an automated annotation pipeline to provide the basis for features, classification-based trigger identification and argument identification components, and a post-processing component to apply semantic constraints. The UIMA framework\(^1\) is used to integrate the components into a pipeline architecture.

2.1 Primary Tasks

A definition of the events to be extracted is used to define candidates for classification and post-process the results of the classification. First a list of domain-specific entity classes is given. Entities of

\(^1\)http://uima.apache.org/
Table 1: Summary of the target events. Type restrictions on fillers of each argument type are shown in parenthesis. Multiplicity of each argument type is also marked (+ = one-to-many, ? = zero-to-one, * = zero-to-many, otherwise = one).

| Event Class          | Arguments                                                                 |
|----------------------|---------------------------------------------------------------------------|
| Gene expression      | Theme(Protein|Regulon-operon)                                                          |
| Transcription        | Theme(Protein|Regulon-operon)                                                          |
| Protein catabolism   | Theme(Protein)                                                             |
| Phosphorylation      | Theme(Protein), Site(entity)?                                            |
| Localization         | Theme(core_entity), AtLoc(entity)?, ToLoc(entity)?                      |
| Binding              | Theme(core_entity)+, Site(entity)*                                       |
| Regulation           | Theme(core_entity|event), Cause(core_entity|event)?, Site(entity)?, CSite(entity)? |
| Positive regulation  | Theme(core_entity|event), Cause(core_entity|event)?, Site(entity)?, CSite(entity)? |
| Negative regulation  | Theme(core_entity|event), Cause(core_entity|event)?, Site(entity)?, CSite(entity)? |
| Process              | Participant(core_entity)?                                                |

these classes are assumed to be annotated in the data, as is the case for the Infectious Disease task. Then, each event class is given, with a list of argument types for each. Each argument is marked with its multiplicity, indicating how many of this argument type is valid for each event, either: one – exactly one is required, one-to-many – one or more is required, zero-to-one – one is optional, and zero-to-many – one or many are optional. Also, restrictions on the classes of entities that can fill each argument are given, by listing: one or more class names – indicating the valid domain-specific entity classes from the definition, core_entity – indicating that any domain-specific entity in the definition is valid, event – indicating that any event in the definition is valid, or entity – indicating that any span from the text is valid. Table 1 shows the summary of the event extraction tasks for the Infectious Disease track.

2.2 Annotation

Linguistic and domain annotations are automatically applied to the document to be used for trigger and argument identification in framing the tasks for classification and generating features for each instance. Linguistic annotations include sentence splits, tokens, parts of speech, tree parses, typed dependencies (deMarneffe et al., 2006; MacKinlay et al., 2009), and stems. For the Infectious Disease task, the parses from the Stanford Parser (Klein and Manning, 2003) provided by the Supporting Analysis (Stenetorp et al., 2011) was used to obtain all of these linguistic annotations, except for the stems, which were obtained from the Porter Stemmer (van Rijsbergen et al., 1980).

For the Infectious Disease task, two sets of domain specific annotations are included: known trigger words for each event class and semantic tags from the Unified Medical Language System (UMLS) (Bodenreider, 2004). Annotations for known trigger words are created using a dictionary of word-stem-event class pairs created from annotated training data. An entry is created in the dictionary every time a new stem is seen as a trigger for an event class. When a word with one of these stems is seen during processing, it is annotated as a typical trigger word for that event class.

Semantic tags are calculating using MetaMap 2010 (Aronson and Lang, 2010). MetaMap provides semantic tags for terms in a document with up to three levels of specificity, from most to least specific: concept, type and group (Torii et al., 2011). Word sense disambiguation is used to identify the best tags for each term. For example, consider the tags identified by MetaMap for the phrase *Human peripheral B cells*:

- **Human**
  - concept: Homo sapiens
  - type: Human
  - group: Living Beings

- **Peripheral**
  - type: Spatial Concept
  - group: Concepts & Ideas

- **B-Cells**
  - concept: B-Lymphocytes
  - type: Cell
In this example, semantic mappings were found for three terms: Human, Peripheral and B-Cells. Human and B-Cells were mapped to specific concepts, but Peripheral was mapped to a more general group.

Entities are also annotated at this point. For the Infectious Disease task, annotations for five entity types are given: Protein, Two-component system, Chemical, Organism, or Regulon/Operon.

2.3 Trigger Identification

Triggers are identified using an SVM classifier (Vapnik, 1995; Joachims, 1999). Candidate triggers are chosen from the words in the text by part-of-speech. Based on known triggers seen in the training data, all nouns, verbs, adjectives, prepositions and adverbs are selected as candidates. A binary model is trained for each event type, and candidate triggers are tested against each classifier.

The following features are used to classify candidate event triggers:

- **term** – the candidate trigger
- **stem** – the stem of the term
- **part of speech** – the part of speech of the term
- **capitalization** – capitalization of the term
- **punctuation** – individual features for the presence of different punctuation types
- **numerics** – the presence of a number in the term
- **ngrams** – 4-grams of characters from the term
- **known trigger types** – tags from list of known trigger terms for each event type
- **lexical context** – terms in the same sentence
- **syntactic dependencies** – the type and role (governor or dependent) of typed dependencies involving the trigger
- **semantic type** – type mapping from MetaMap
- **semantic group** – group mapping from MetaMap

For training data, both the Infectious Disease training set and the GENIA training set were used. Although the GENIA training set represents a different genre and is annotated with a slightly different vocabulary than the Infectious Disease task data, it is similar enough to provide some beneficial supervision. The Infectious Disease training data is relatively small at 154 documents so including the larger GENIA training set at 910 documents results in a much more larger training set. Testing on the Infectious Disease development data, a 1 point improvement in fscore in overall results is seen with the additional training data.

2.4 Argument Identification

Arguments are also identified using an SVM classifier. For each predicted trigger, candidate arguments are selected based on the argument types. For arguments that are restricted to being filled by some set of specific entity and event types, each annotated entity and predicted event is selected as a candidate. For arguments that can be filled by any span of text, each span corresponding to a constituent of the tree parse is selected as a candidate. Each pair of an event trigger and a candidate argument serves as an instance for the classification. A binary model is trained for each event type, and each pair is tested against each classifier.

Many of the features used are inspired by those used in semantic role labeling systems (Gildea and Jurafsky, 2002). Given an event trigger and a candidate argument, the following features are used to classify event arguments:

- **trigger type** – the predicted event type of the trigger
- **argument terms** – the text of the argument
- **argument type** – entity or event type annotation on the argument
- **argument super-type** – core entity or core argument
- **trigger and argument stems** – the stems of each
- **trigger and argument parts of speech** – the part of speech of each
- **parse tree path** – from the trigger to argument via least common ancestor in tree parse, as a list of phrase types
- **voice of sentence** – active or passive
- **trigger and argument partial paths** – from the trigger or argument to the least common ancestor in tree parse, as a list of phrase types
• **relative position of argument to trigger** – before or after
• **trigger sub-categorization** – representation of the phrase structure rule that describes the relationship between the trigger, its parent and its siblings.

The training data used is the same as for trigger identification: the Infectious Disease training set plus the Genia training set.

### 2.5 Post-processing

A post-processing component is used to turn output from the various classifiers into semantically valid output according to the target task. For each predicted trigger, the positive predictions for each argument model are collected, and the set is compared to the argument restrictions in the target task description.

For example, the types on argument predictions are compared to the argument restrictions in the target task, and non-conforming ones are dropped. Then the multiplicity of the arguments for each predicted event is checked against the task vocabulary. Where there were not sufficient positive argument predictions to make a full event, the best negative predictions from the model are tried. When a compliant set of arguments can not be created for a predicted event, it is dropped.

### 3 Results and Discussion

Results for the system on both the development data and the official test data for the task are shown in Table 2 and Table 5, respectively. For the development data, a system using gold-standard event triggers is included, to isolate the performance of argument identification. In all cases, the total f-score for non-regulation events were much higher than regulation events. On the official test data, the system performed the best in predicting Phosphorylation (fscore = 71.43), Gene Expression (fscore = 53.33) and Process events (fscore = 51.04), but was unable to find any Transcription and Regulation events. This is also evident in the results on the development data using predicted triggers; additionally, no matches were found for localization and binding events. The total f-score on the development data using gold triggers was 55.33, more than 13 points higher than when using predicted triggers. In the discussion that follows, we detail the importance of individual features and their contribution to evaluation fscores.

#### 3.1 Feature Importance

The effect of each argument and trigger feature type on the Infectious Disease development data was determined using a leave-one-out approach. The argument and trigger feature effect results are shown in Table 3 and Table 4, respectively. In a series of experiments, each feature type is left out of the full feature set one-by-one. The difference in f-score between each of these systems and the full feature set system is the effect of the feature type; a high negative effect indicates a significant contribution to the system since the removal of the feature resulted in a lower f-score.

| Features                      | fscore | effect |
|-------------------------------|--------|--------|
| all features                  | 41.66  |        |
| w/o argument terms            | 36.16  | -5.50  |
| w/o argument type             | 39.50  | -2.16  |
| w/o trigger partial path      | 40.65  | -1.01  |
| w/o argument part of speech   | 40.98  | -0.68  |
| w/o argument partial path     | 41.16  | -0.50  |
| w/o trigger sub-categorization| 41.45  | -0.21  |
| w/o argument stem             | 41.48  | -0.18  |
| w/o argument super-type       | 41.63  | -0.03  |
| w/o trigger type              | 41.63  | -0.03  |
| w/o trigger part of speech    | 41.81  | 0.15   |
| w/o trigger stem              | 41.81  | 0.15   |
| w/o voice of sentence         | 41.85  | 0.19   |
| w/o relative position         | 42.21  | 0.55   |
| w/o parse tree path           | 42.67  | 1.01   |

Table 3: Effect of each argument feature type on Infectious Disease development data.

Within the argument feature set system, the parse tree path feature had a notable positive effect of 1.01. The features providing the greatest contribution were argument terms and argument type with effects of -5.50 and -2.16, respectively. Within the trigger feature set system, the lexical context and syntactic dependencies features showed the highest negative effect signifying positive contribution to the system. The text and known trigger types features showed a negative contribution to the system.
Table 2: Results on Infectious Disease development data. The system is compared to a system using gold standard triggers to isolate performance of argument identification.

| Event Class          | Using Gold Triggers | Using Predicted Triggers |
|----------------------|---------------------|--------------------------|
| gold/ans./match      | gold/ans./match     |                          |
| recall               | recall              |                          |
| prec.                | prec.               |                          |
| fscore               | fscore              |                          |

| Event Class          | gold/ans./match      | gold/ans./match      |
|----------------------|----------------------|----------------------|
| recall               | recall               | recall               |
| prec.                | prec.                | prec.                |
| fscore               | fscore               | fscore               |

Table 4: Effect of each trigger feature type on Infectious Disease development data.

- Growth at pH 5.8 resulted in pmrD transcript levels that were approximately 3.5-fold higher than in organisms grown at pH 7.7 (Fig. 4A).

In both the development and test data evaluations, our system did not predict any transcription events, resulting in a 0.0 fscore; however, the system achieved 75.41 fscore when the gold-standard triggers were provided to the evaluation. Because argument prediction performed well, the system will benefit most by improving transcription event trigger prediction.

The following are regulation events from the document PMC1804205-02-Results-01 in the development data.

- ... we grew Salmonella cells harbouring chromosomal lacZY A transcriptional fusions to the PmrA-regulated genes pbgP, pmrC and ugd (Wosten and Groisman, 1999) in N-minimal media buffered at pH 5.8 or 7.7.

- We determined that Chelex 100 was effective at chelating iron because expression of the pmrA-independent iron-repressed iroA gene ...
in the evaluation. Hypotheses for poor performance on candidate argument prediction are addressed in the following sections.

We posit that false negative trigger identifications are due to the limited full text training data (i.e. transcription events) and the inability of our system to predict non-verb triggers (i.e. second transcription example above). The SVM classifier was unable to distinguish between true transcription event triggers and transcription-related terms and ultimately, did not predict any transcription event in the development or test evaluations. To improve transcription event prediction, immediate effort should focus on 1) providing additional training data (e.g., BioCreative\textsuperscript{citation}BioCreative) and 2) introduce a trigger word filter that defines a subset of event triggers that have the best hit rate in the corpus. The hit rate is the number of occurrences of the word in a sentence per event type, divided by the total count in the gold standard (Nguyen et al., 2010).

3.3 +/-Regulation and Binding

The following positive regulation event is from document PMC1874608-03-RESULTS-03 in the development data.

- Invasiveness for HEp-2 cells was reduced to 39.1\% of the wild-type level by mlc mutation, whereas it was increased by 1.57-fold by hilE mutation (Figure 3B).

In the preceding example, our system correctly predicted the +regulation trigger and the theme hilE; however, the correct argument was a gene expression event, not the entity. Many errors in the positive and negative regulation events were of this type; the predicted argument was a theme and not an event.

Evaluation of our system’s binding event predictions resulted in low recall (12.50 or 0.0) in the test and development evaluations. The proceeding binding events are from document PMC1874608-03-RESULTS-05 in the development data. In both of the examples, our system correctly predicted the trigger binding; however, no arguments were predicted. Evaluation on the development data with gold standard triggers also resulted in an fscore of 0.0; thus, further algorithm refinement is needed to improve binding scores.

- \textit{Mlc} directly represses \underline{hilE} by binding to the \underline{P3 promoter}.

- These results clearly demonstrate that \textit{Mlc} can regulate directly the \underline{hilE P3 promoter} by binding to the \underline{promoter}.

The following binding event is from document PMC1874608-01-INTRODUCTION in the development data and is representative of errors across many of the tasks. Here, the trigger is correctly predicted; however, the candidate arguments did not match with the reference data. Upon closer look, the arguments were drawn from the entire sentence, rather than an independent clause. The syntactic parse feature was not sufficient to prevent over-predicting arguments for the trigger, a potential solution is to add the arguments syntactic dependency.
to the trigger as a feature to the candidate argument selection.

- Using two-hybrid analysis, it has been shown that HilE interacts with HilD, which suggests that HilE represses hilA expression by inhibiting the activity of HilD through a protein-protein interaction (19,20).

4 Summary

This article reports Pacific Northwest National Laboratory’s entry to the BioNLP Shared Task 2011 Infectious Disease track competition. Our system uses a signature-based machine-learning approach incorporating traditional linguistic features and shallow semantic concepts from NIH’s METAMAP Thesaurus. We examine the contribution of each of the linguistic and semantic features to the overall Fscore for our system. This approach performs well on gene expression, process and phosphorylation event prediction. Transcription, regulation and binding events each achieve low Fscores and warrant further research to improve their effectiveness. Lastly, we present a performance analysis of the transcription, regulation and binding tasks. Future work to improve our system’s performance could include pre-processing using simple patterns (Nguyen et al., 2010), information extraction from figure captions (Kim and Yu, 2011) and text-to-text event extraction. The last suggested improvement is to add semantic features to the candidate argument prediction algorithm in addition to using rich features, such as semantic roles (Torii et al., 2011).

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