A Joint Model for Normalizing
Gene and Organism Mentions in Text

Georgi Georgiev∗
georgi.georgiev@ontotext.com
Preslav Nakov†
nakov@comp.nus.edu.sg
Kuzman Ganchev‡
kuzman@cis.upenn.edu
Deyan Peychev∗
deyan.peychev@ontotext.com
Vassil Momchev∗
vassil.momtchev@ontotext.com

Abstract
The aim of gene mention normalization is to
propose an appropriate canonical name, or an iden-
tifier from a popular database, for a gene or a
gene product mentioned in a given piece of text.
The task has attracted a lot of research atten-
tion for several organisms under the assumption
that both the mention boundaries and the tar-
get organism are known. Here we extend the
task to also recognizing whether the gene men-
tion is valid and to finding the organism it is
from. We solve this extended task using a joint
model for gene and organism name normaliza-
tion which allows for instances from different or-
ganisms to share features, thus achieving sizable
performance gains with different learning meth-
ods: Naïve Bayes, Maximum Entropy, Percep-
tron and MIRA, as well as averaged versions of
the last two. The evaluation results for our joint
classifier show F1 score of over 97%, which proves
the potential of the approach.

Keywords
Gene normalization, gene mention tagging, organism recogni-
tion, identity resolution.

1 Introduction
Gene mention normalization is one of the emerg-
ing tasks in bio-medical text processing along with
gene mention tagging, protein-protein interaction, and
biomedical event extraction. The objective is to pro-
pose an appropriate canonical name, or a unique iden-
tifier from a predefined list, for each gene or gene pro-
duct name mentioned in a given piece of text. Solv-
ing this task is important for many practical application,
e.g., enriching high precision databases such as the
Protein and Interaction Knowledge Base (PIKB), part of
LinkedLifeData1, or compiling gene-related search indexes for large document collections such as
LifeSKIM2 and MEDIE3.

∗Ontotext AD, 135 Tsarigradsko Ch., Sofia 1784, Bulgaria
†Department of Computer Science, National University of
Singapore, 13 Computing Drive, Singapore 117417
‡Department of Computer and Information Science, Univer-
sity of Pennsylvania, Philadelphia, PA, USA
1 http://www.linkedlifedata.com
2 http://lifeskim.sirma.bg
3 http://www-tsujii.is.s.u-tokyo.ac.jp/medie/

In this work, we focus on the preparation of good
training data and on improving the performance of
the normalization classifier rather than on building an
integrated solution for gene mention normalization.

The remainder of the paper is organized as follows:
Section 2 gives an overview of the related work, Sec-
tion 3 present our method, Section 4 describes the
experiments and discusses the results, and Section 5
concludes and suggests directions for future work.

2 Related work
Several approaches have been proposed for gene nor-
malization including classification techniques [5], rule-
based systems [7, 19], text matching against dictionar-
ies [2], and different combinations thereof.
Systems for gene mention identification and normal-
ization typically work in three stages: (1) identifying
candidate mentions in text, (2) determining the se-
semantic intent of each mention, and (3) normalizing by
associating each mention with a unique identifier [15].
For example, Crim et al. [5] first recognize the gene
mentions in the text, then match them against a lexi-
con, and finally filter the wrongly annotated matches
using a maximum entropy classifier [1].

The problem we address in this work is closest to
Task IB in BioCreAtIvE 2004 [8] and to the Gene
Normalization task in BioCreAtIvE 2006 [16], which
provide lexicons of gene identifiers for a particular or-
ganism, e.g., human, yeast, mouse and fly, each of
which represents a separate challenge. Given a text
document and an organism, the tasks ask that a list be
produced containing the identifiers (from the lexicon)
of all genes for the target organism that are mentioned
in the document. Since the relationship between gene
names and identifiers is M:M, disambiguation is a cen-
tral issue.

Even though reported for individual organisms only,
the results from the BioCreAtIvE challenge are quite
promising. For yeast, the best F1 was 0.92 [8]. For
mouse and fly, the task was found to be more diffi-
cult, probably because of the larger numbers of genes,
the higher ambiguity in the gene naming conventions
(particularly for fly), and the complexity of mouse gene
names; for fly, the best F1 was 0.82, while for mouse
it was 0.79 [8]. For human, the best F1 was 0.81 [16].
3 Method

Our approach is most similar to that of Crim et al. [5], but there are many differences in the details. First, we do gene mention tagging using a one-best structured version of the Margin-Infused Relaxed Algorithm (MIRA) [4] in order to collect high recall gene mentions. Second, instead of using the conventional strict match, we extensively study different string matching distance metrics. Third, we represent the normalization task as a multi-class classification problem by extending it to multiple organisms (mouse and human). We train a joint statistical classifier that recognizes valid gene identifiers and the corresponding organism at the gene mention level. Finally, we allow the human and mouse examples in the joint model to share features, which yields sizable performance gains.

We try our approach with six classifiers: Naïve Bayes [11], Maximum Entropy [1], Perceptron [20], MIRA [4], and averaged versions of the last two [6].

3.1 One-best structured MIRA

In what follows, $x_i$ will denote the generic input sentence, $Y(x_i)$ will refer to the set of all possible labelings of $x_i$, and $y_i$ will be the “gold” labeling of $x_i$. For each pair of a sentence $x_i$ and a labeling $y_i \in Y(x_i)$, we will compute a vector-valued feature representation $f(x_i, y_i)$. Given a weight vector $w$, the score $w \cdot f(x, y)$ ranks the possible labelings of $x$; we will denote the top-scoring one as $y_w(x)$. As with hidden Markov models [17], for suitable feature functions, $y_w(x)$ can be computed efficiently using dynamic programming.

A linear sequence model is given by a weight vector $w$.

We started with a CRF tagger [10], which yielded a very low recall (R=73.02%). We further experimented with feature induction [12] and with a second-order CRF, but the recall remained unsatisfactory: 74.72% and 76.64%, respectively. Therefore, we abandoned CRFs altogether and adopted structured MIRA, which allows for transparent training with different loss functions.

After a number of experiments, we found that the highest recall is achieved with a loss that uses the number of false negatives, i.e., a larger loss update is made whenever the model fails to discover a gene mention, while discovering a spurious sequence of words would be penalized less severely. We experimented with some popular feature sets used previously in [14] including orthographic, POS, chunk, and presence in a variety of domain-specific lexicons, as well as different conjunctions thereof. As Table 1 shows, the final tagger achieved 83.44% recall.

3.2 Gene tagging

We experimented with the training and the testing abstracts provided by BioCreAtIV-E 2006. We tokenized, sentence split, part-of-speech (POS) tagged and chunked them using maximum entropy models trained on Genia\textsuperscript{3} corpora. We subsequently trained several sequence taggers, using the standard BIO encoding [18] and different feature sets.

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3.3 Semantic intent of gene mentions

We addressed gene normalization as a classification problem where, given a gene mention and a candidate gene identifier, a yes/no decision is to be made about whether this is the correct identifier for that mention.

\begin{table}[h]
\centering
\begin{tabular}{|l|l|}
\hline
Predicate Name & Regular Expression \\
\hline
Initial Capital & A-Z.* \\
Capital Any & A-Z, \\
Initial Capital Alpha & A-Z[a-z]* \\
All Capitals & A-Z+ \\
All Lower & a-z+ \\
Capital Mix & A-Za-z+ \\
Has Digit & [0-9]* \\
Single Digit & 0-9 \\
Double Digit & 0-9[0-9] \\
Natural Number & 0-9+ \\
Real Number & 0-9+[.][0-9]+ \\
Alpha-Numeric & A-Za-z0-9+ \\
Roman & [ivxdlcm]+[[ivxdlcm]+ \\
Has Dash & *-* \\
Initial Dash & - \\
End Dash & *- \\
Punctuation & [.,;:?!-+"""] \\
Multidots & ..+ \\
Ends with a Dot & [.]+ \\
Acronym & A-Z[A-Z][A-Z][A-Z][A-Z]+ \\
Lonely Initial & A-Z, \\
Single Character & A-Za-z \\
Quote & * \\
\hline
\end{tabular}
\caption{The orthographic predicates used in the structured MIRA gene tagger. The observation list for each token includes a predicate for each regular expression that matches it.}
\end{table}

\textsuperscript{3}www-tsujii.is.s.u-tokyo.ac.jp/GENIA/home/wiki.cgi
We prepared training data for the classifier as follows. We first created an extended lexicon that combines the lexicons for mouse and human from BioCreAtive 2004 and 2006, and we matched against it each chunk that was recognized as a potential gene mention by the gene tagger described in Section 3.2. In the process of matching, we ignored case, punctuation and numbers, and we only used maximal matching strings, i.e., sub-strings of matching strings that linked to the same ID were ignored. At the end of this stage, each gene mention was paired with a corresponding gene identifier (mouse or human), and the pair was marked as either positive or negative. Using these pairs as training data, we built a classifier, which achieved 74% recall and 9.3% precision. In order to boost the recall further, we tried different string similarity metrics within the simmetric package\(^6\), and we selected the Jaro-Winkler distance, a modification of the Jaro distance \(^9\), that represents a good compromise between specificity and speed. We thus achieved 85% recall and 1% precision.

### 3.4 Joint organism and gene normalization

While the previous step achieved a very high recall, this was at the expense of precision, which dropped to just 1%. We thus trained a classifier to filter out the bad matches as follows. For each gene mention - gene identifier pair from the previous step, we built a classification example, which includes the gene identifier, the gene name and the words from the local context of the gene mention (two words to the left/right of the mention), and a label: human-positive match, mouse-positive match or negative match. Since we aimed to create a joint classification model for gene normalization of human and mouse gene and gene product names, we represented the label tag of each gene mention subject to classification as a complex tag containing simple labels for the organism and an indication on the validity of the gene identifier. Thus, our model jointly decides whether the match is positive/negative and determines the organism it belongs to.

On training, we considered an example positive for human/mouse if the corresponding gene identifier was included in the list of identifiers for the target abstract and organism, and negative otherwise. Below are shown three examples, each containing a candidate gene match, a context of two tokens on each side of the match, and the corresponding label. In the first example, the match is calcitonin gene-related peptide, its left context is that confers, its right context is \(\text{CGRP} \rightarrow \text{human-positive}\). It is annotated as positive for human, since the abstract annotation and the match annotation agree on the Entrez Gene identifier: 27297. Similarly, the second example is positive for mouse. In the third example, p53 is a valid gene name, but it has been annotated with a wrong mouse identifier, MGI:106202, which is not included in the list of gene identifiers for the target abstract.

\[ f_i(x,y) = \begin{cases} 1 & \text{if 'WORD}_{-1} = \text{confers'} \in x, \text{y = human-positive;} \\ 0 & \text{otherwise.} \end{cases} \]

Some of the above features have been used in previous research in normalizing gene mentions \([5, 21]\), but some are novel, e.g., words/lemmata from the current sentence and presence of sequences of words from the current sentence in various lexicons.

The lexicons we used were compiled from the UniprotKB part of Uniprot\(^6\), Entrez Gene\(^7\), Entrez Taxonomy\(^8\), and various disease databases. From UniprotKB and Entrez Gene, we took the gene or gene product names, and we filtered them based on the organism: human, mouse, yeast or fly. From Entrez Organism, we compiled an organism list. From the disease databases, we compiled a list of diseases in human and mouse. The different lexicons had different matching scopes. For example, while the lexicon of gene names was used to match both against the candidate gene mention and against the rest of the sentence, organism and diseases lists were only allowed to match against the rest of the sentence.

\(^6\) http://www.uniprot.org/
\(^7\) http://www.ncbi.nlm.nih.gov/sites/entrez?db=gene
\(^8\) http://www.ncbi.nlm.nih.gov/Taxonomy/
Next, we created features from the above predicates. In the process of doing so, we allowed for some combinations of simple labels and predicates to co-appear in the feature vectors. In particular, this allowed for features to co-appear in human and mouse instances if they shared predicates: the main intuition is that positive examples for mouse and human should naturally share some positive features and should only differ in organism-specific features. We have achieved this by means of feature function decomposition as will be described below.

First, note that all machine learning algorithms used in the present work are linear models. This means that for each input example \( x \), the best output label \( \hat{y} \) can be found using an inference procedure that can be expressed by the following equation:

\[
\hat{y} = \arg \max_y [w^T f(x, y)] = \arg \max_y \sum_i w_i f_i(x, y) \tag{2}
\]

where \( f(x, y) \) is a vector of feature functions, \( w \) is a weight vector, \( f_i(x, y) \) and \( x \) are the values of the \( i \)th coordinates of those vectors, and \( y \) ranges over the possible labels.

In our joint model, \( y \) can take the following three possible values: human-positive, mouse-positive, and negative. We further decomposed human-positive and mouse-positive into three simplified labels: human, mouse and positive. In this new representation, the simplified positive label co-exists in both human-positive and mouse-positive. Therefore, it will be useful if some of the features between the two instances – one for mouse and one for human – are shared since they both represent positive gene matches. In order to achieve this, we decomposed the feature function \( f_i(x, \text{human-positive}) \) as follows:

\[
f_i(x, \text{human-positive}) = f_{i,1}(f_{i,2}(x, \text{positive}), \text{human-positive}) \tag{3}
\]

where \( f_{i,1} \) maps the input into a sparse vector, and \( f_{i,2} \) combines it with a possible output in order to generate the final sparse vector used to assess the compatibility of the label for this input. In this representation, all instances labeled human-positive and mouse-positive share some features since they use a common feature sub-function \( f_{i,2}(x, \text{positive}) \).

Note that we only allowed a subset of the predicates listed above to participate in the feature sub-function – those that are organism-independent, e.g., the number of words in the matched phrase, the total number of possible gene identifiers for the matched phrase, all character prefixes and suffixes of length up to four for the words within the phrase, etc. For example, the following feature for \( f_{i,2} \) (see Eq 3 above) can be generated both for a human-positive and for a mouse-positive instance:

\[
f_{i,2}(x, y) = \begin{cases} 1 & \text{if } \#(\text{GenesMatched}) = 5' \in x, y = \text{positive}; \\ 0 & \text{otherwise.} \end{cases}
\]

4 Experiments and evaluation

Below we describe our experiments in evaluating the joint model described in Section 3.4 on the standard test sets of BioCreAtIvE. We tried Na"ive Bayes, Maximum Entropy, Perceptron, MIRA, as well as averaged versions of the last two. Since the training data for this task were limited, we also studied the dependence of each classifier on the number of training examples from both manually annotated and noisy data sources.

Figure 1 shows the performance of our six classifiers as a function of the number of manually annotated training examples for mouse. Maximum Entropy, averaged MIRA and Perceptron outperformed the rest by 3-4% of F1, in the range of 2,000-2,600 training examples. For the case of limited training data, in the range of 100-200 examples, the best-scoring classifier was Maximum Entropy.

As Figure 2 shows, for the human training data, in the range of 2,000-3,000 manually annotated examples, the best classifiers were again Maximum Entropy and the averaged Perceptron, and for 100-200 training examples, Maximum Entropy and averaged MIRA were tied for the first place. The Na"ive Bayes classifier was the worse-performing one for both the 100-200 and 2,000-3,000 ranges.

As a second set of experiments, we combined the mouse and the human training examples, and we used a multi-class version of the learning schemata to train and evaluate the joint mouse-human statistical model that has been described above. Figure 3 shows the performance for different numbers of training examples for the joint model. Again, the Maximum Entropy and the averaged Perceptron outperformed the remaining classifiers in the full range of numbers of training examples; Perceptron scored third in this experiment.

Table 2 shows the data for Maximum Entropy, Na"ive Bayes, Perceptron and MIRA presented already in detail on Figure 3, e.g., the evaluation is presented separately for mouse and human and in terms of precision, recall and F1-measure. Note that all learning methods show well-balanced precision and recall, which is a very desirable property for a gene mention normalization system. The best performing classifier for the joint model when tested on human examples was Maximum Entropy – it outperformed the rest by more than 2% absolute difference in F1-measure. For mouse, MIRA was the best, directly followed by Maximum Entropy.

In order to boost the performance of the classifier even further, we added to the model the additional noisy training examples that were provided by the BioCreAtIvE organizers for both human and mouse. For this set of experiments, we selected the Maximum Entropy classifier, and we achieved an absolute increase in F1 score of more than 12% and 7% for mouse and human test examples respectively (see Table 3, column A).

In our last experiment, we used the feature function decomposition as described in Section 3.4, which resulted in further improvement to reach the final F1 score for the Maximum Entropy classifier of 97.09% and 97.64% for mouse and human respectively (see Table 3, Column B).
Table 2: Evaluation of the joint human-mouse model with different classifiers. Precision (P), recall (R) and $F_1$-measure are shown in %.
Fig. 2: Normalization of human gene mentions using different classifiers.

|        | Mouse | Human |
|--------|-------|-------|
| R      | P     | F₁    |
| A      | 96.64 | 96.11 | 96.37 |
| B      | 96.62 | 97.61 | 97.09 |

Table 3: Evaluation of the Maximum Entropy joint human-mouse model, with regular (A) and decomposed (B) feature functions. Precision (P), recall (R) and F₁-measure are shown in %.

5 Conclusions and future work

We have proposed an extension to the popular task of gene mention normalization to also recognize whether the target gene mention is valid and to find the organism it is from. We have addressed this extended task using a joint model for gene and organism name normalization which allows for instances from different organisms to share features. This model yielded sizable performance gains with the following six statistical classifiers: Naïve Bayes, Maximum Entropy, Perceptron and mira, as well as averaged versions of the last two. The evaluation results for our best joint classifier using Maximum Entropy and noisy training data show F₁ score of over 97%, which proves the potential of the approach.

Unlike previous work, we have focused on training examples preparation and classification – two stages that are often underestimated when designing gene name normalization systems. We have shown that by tuning the loss function of the structured mira classifier, it is possible to enhance the recall of the gene tagger significantly. We have further proposed and carefully evaluated a joint model that recognizes both the organism and the correctness of a gene mention - gene identifier pair in a particular text context. Finally, we have evaluated six classifiers, comparing them on training data of different sizes, and we have shown that the performance of several of them is very close when the number of training examples is in the range 2,000-3,000.

There are many ways in which the present work can be extended in the future. First, we would like to experiment with more training data, including noisy and unlabeled data, in order to reveal the full potential of the idea for feature function decomposition. Applying the idea to other related problems in the biomedical domain is another promising research direction. Ultimately, we will try to integrate the joint model into a fully functional system and compare its performance to that of existing gene mention normalization systems for a single organism, e.g., those that participated in BioCreAtIvE. We further plan to include other important organisms in the joint model, the most obvious candidates being yeast and fly.

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Fig. 3: Joint organism and gene normalization using different classifiers.

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