Medication and Adverse Event Extraction from Noisy Text

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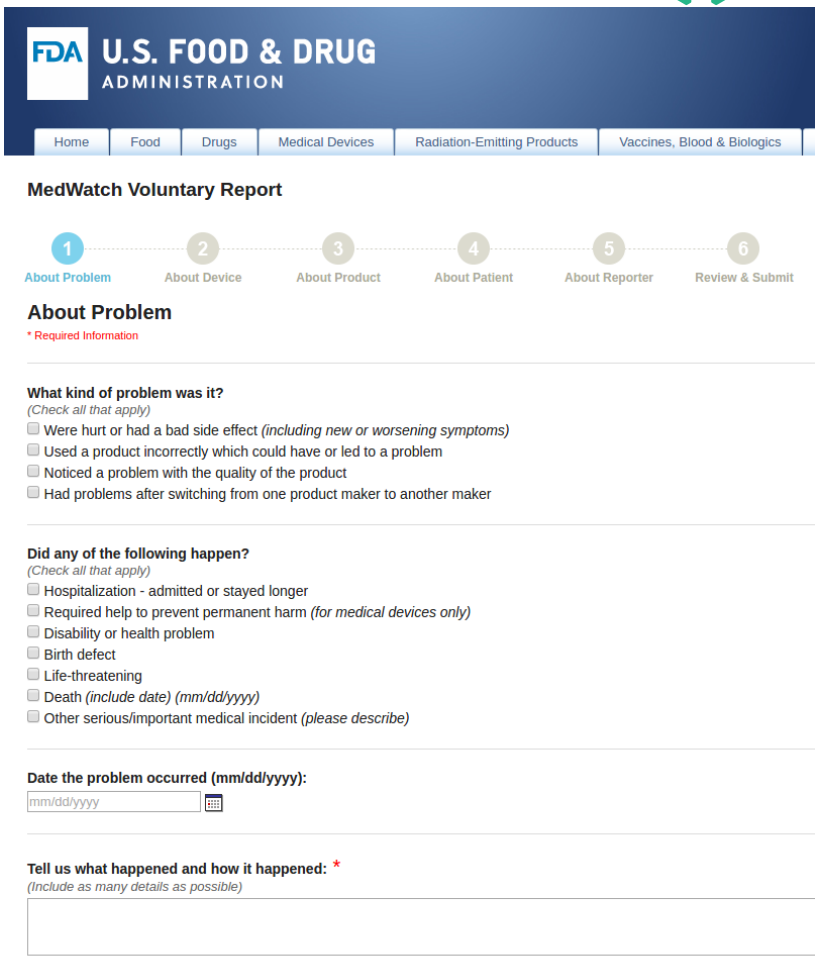
Pharmacovigilance: for safer drugs

- Pharmacovigilance relates to monitoring Adverse Drug Reactions (ADR), especially previously unreported reactions.
- An ADR is an injury occuring after a medication is used at the recommended dosage, for recommended symptoms.
- When causality between an ADR and a medication is not known, it is referred to as Adverse Drug Event (ADE).

Where is raw data from?

Official Channels have the issue of under-reporting (less than 10% of ADRs are reported [1]).

Unstructured data, such as medical reports or social network data, are becoming the primary data source.



[1] Hazell and Shakir, 2006. Under-reporting of adverse drug reactions. Drug Safety.

Given a sentence, we want to identify drugs and ADEs

Example sentence

i was put on this medication because i was taking such high doses of Advil to quell the inflammation in my neck and back muscles that it caused me to have a GI bleed.

We solve this as an NER problem.

Concept Extraction for Pharmacovigilance

- Methods
  - Lexicon-based and rule-based methods.
  - Machine learning methods
    - Classification: whether a text contains an ADE.
    - NER: extract ADEs from free-text
- Challenges
  - Distinguish between ADEs and symptoms which are supposed to be cured by drugs.
    - I am only taking 75 mg a day and it is wonderful for relieving all of my aches and pains.
  - ADEs consist of complex spans.

Our focus: complex entities

Complexity of Entity	Samples from CADEC dataset
Continuous, non-overlapping	Disorentatation, trouble brathing, extreme hot, readness and sweeling, itching, later abominal cramps.
Continuous, overlapping	pain in knee and foot.
Discontinuous, non-overlapping	My Liver blood test are also mildly elevated.
Discontinuous, overlapping	pain in knee and foot.

Our contribution

- We evaluate three NER methods for their capabilities in extracting the complex entities.
  - Sequence labeling approaches
    - CRF
    - BiLSTM [1]
  - Non-sequence labeling approach [2]
- Our aim is to identify which of these methods more accurately extracts these entities, and whether the differences in complexity or type of entities guide what method to choose.

[1] Dernoncourt et al., 2017. De-identification of patient notes with recurrent neural networks. JAMIA

[2] Xu et al., 2017. A local detection approach for named entity recognition and mention detection. ACL

Overall statistics of entities in datasets

	CADEC				i2b2	
Text	**Patient post**				**Discharge summary**	
Entity	Drug		ADE		Drug	
All	1800		6318		8850	
Discontinuous, non-overlapping	1	(0.05)	82	(1.30)	0	(0.00)
Discontinuous, overlapping	1	(0.05)	593	(9.38)	0	(0.00)
Continuous, non-overlapping	1797	(99.83)	5311	(84.06)	8850	(100.00)
Continuous, overlapping	1	(0.05)	332	(5.25)	0	(0.00)
Multiword	141	(7.83)	4574	(72.40)	2181	(24.64)
Single word	1659	(92.17)	1744	(27.60)	6669	(75.36)

- In both datasets, drug names rarely have overlapping or discontinuous properties. In contrast, it is common for ADEs to be discontinuous or overlapped.

Segment representations

BIO or BIOES[1] schemas can not be used in discontinuous or overlapping scenarios. Here is a simple example with two entities: *pain in knee* and *pain in foot*.

- BIO

pain	in	knee	and	foot
B	I	I?O?	O	O?I?

- BIOES

pain	in	knee	and	foot
B	I	E?O?	O	O?E?

[1] B: Beginning; I: Inside; O: Outside; E: Ending; S: Single

Extended BIO representation

DB-/DI- Begin/continuation of concept, for discontinuous and non-overlapping spans.

every	joint	in	my	body	is	in	pain
O	DB	O	O	O	O	O	DI

One entity: *joint pain*.

HB-/HI- Begin/continuation of concept, for discontinuous and overlapping spans.

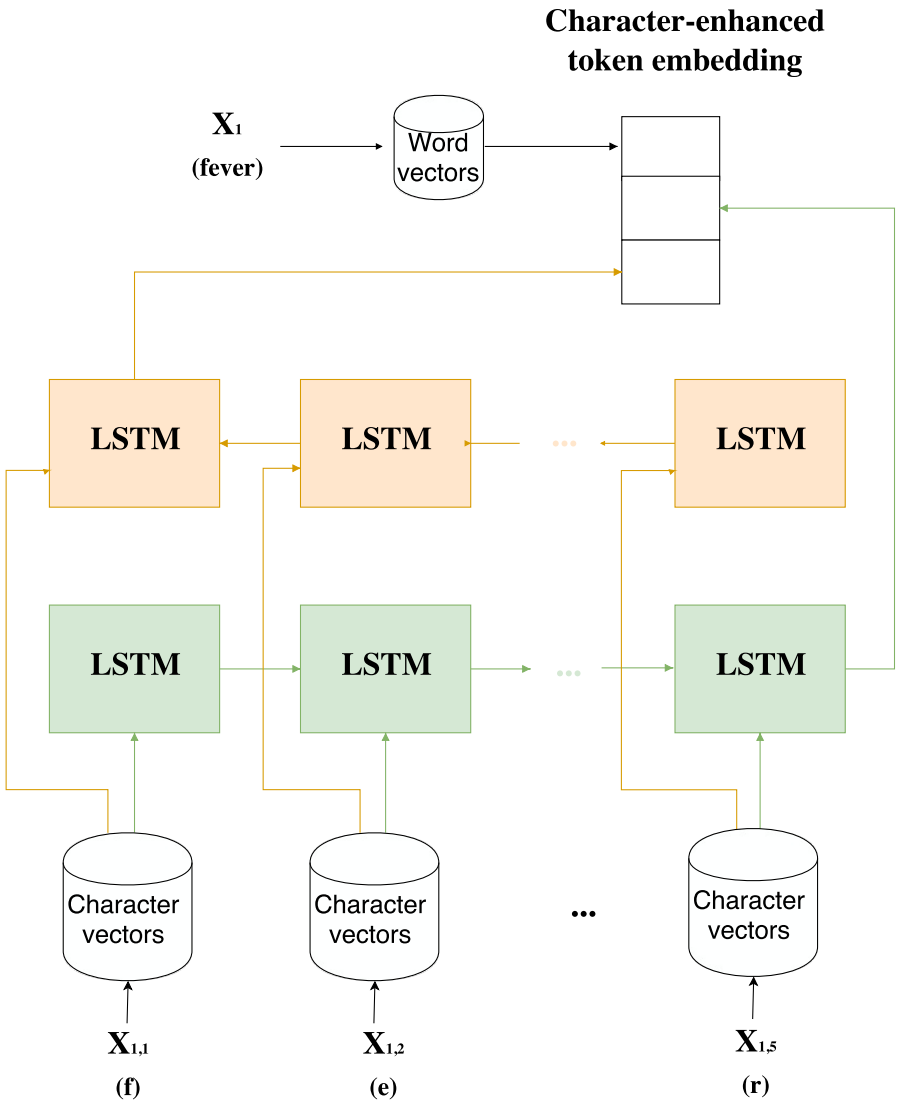
it	has	left	me	feeling	exausted	,	and	depressed
O	O	O	O	HB	HI	O	O	HI

Two entities: *feeling exausted* and *feeling depressed*.

Sequence labeling methods

1. Conditional random field (CRF)
2. Neural network based method
   - Character-enhanced token embedding layer
   - Label prediction layer: BiLSTM
   - Label sequence optimisation layer

Embedding layer

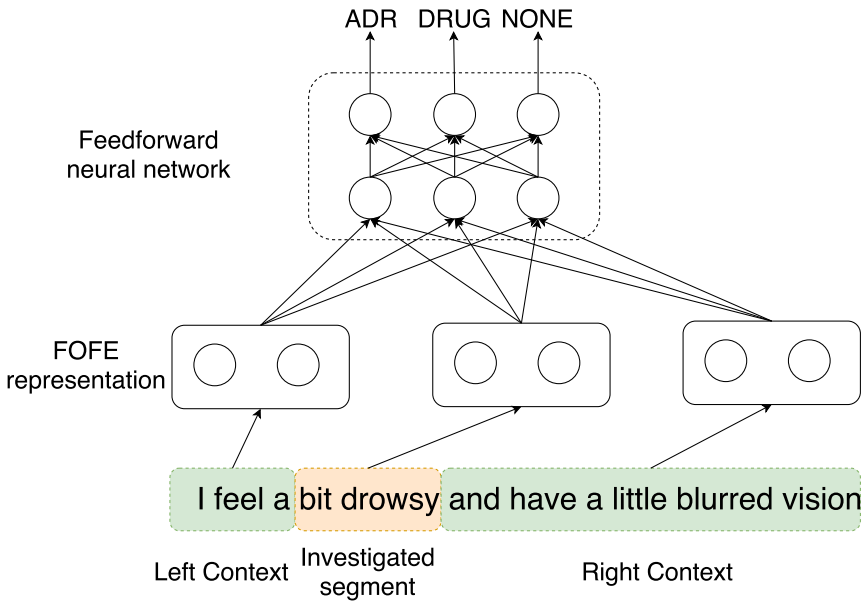


Prediction and optimisation layers

- The prediction BiLSTM layer takes as input the sequence of vectors, and outputs the probabilities for each token belonging to particular labels.
- Instead of selecting the label that has the highest probability for each token, optimisation layer models the dependencies between two subsequent labels through a transition probability matrix.

Non-sequence labeling approach

- Given a sentence $[t_1, t_2, t_3, \cdots, t_n]$, all segments whose lengths are between 1 and k will be investigated.
- Apply a feedforward neural network on top of FOFE-based features [1].



[1] Zhang et al., 2015. The Fixed-Size Ordinally-Forgetting Encoding Method for Neural Network Language Models. ACL & IJCNLP

Overall effectiveness of different methods

Dataset	Entity	Method	Precision	Recall	F-Score
CADEC	Drug	CRF	**95.1 ± 2.5**	79.1 ± 16.1	85.5 ± 11.4
		Bi-LSTM	92.9 ± 2.0	**92.2 ± 1.5**	**92.5 ± 0.7**
		Non-sequence Labeling	88.6 ± 4.9	89.8 ± 1.8	89.1 ± 2.1
	ADE	CRF	67.5 ± 5.1	57.7 ± 2.9	62.1 ± 3.6
		Bi-LSTM	**73.4 ± 3.9**	**64.9 ± 4.4**	**68.7 ± 2.1**
		Non-sequence Labeling	62.9 ± 3.8	61.6 ± 1.8	62.1 ± 1.0
i2b2	Drug	CRF	**93.5 ± 1.0**	85.7 ± 2.5	89.4 ± 1.7
		Bi-LSTM	93.2 ± 1.2	89.7 ± 1.3	**91.4 ± 0.6**
		Non-sequence Labeling	84.4 ± 4.2	**90.2 ± 2.4**	87.1 ± 2.7

- On both datasets, Bi-LSTMs perform better than two other methods.

Effectiveness of different methods based on entity complexity

Dataset	Complexity	Method	Precision	Recall	F-Score
CADEC	Overlapping	CRF	21.4	15.3	**17.8**
		Bi-LSTM	–	3.5	–
		Non-Seq.	–	0.0	–
	Discountinuous	CRF	21.4	1.5	2.8
		Bi-LSTM	13.8	2.3	3.9
		Non-Seq.	–	0.0	–
	Multiword	CRF	57.4	46.4	51.4
		Bi-LSTM	60.9	62.6	61.7
		Non-Seq.	62.3	66.5	**64.3**
	Simple	CRF	78.0	63	69.7
		Bi-LSTM	79.6	68.5	**73.6**
		Non-Seq.	61.9	51.8	56.4
i2b2	Multiword	CRF	91.1	82.6	**86.7**
		Bi-LSTM	85.0	86.8	85.9
		Non-Seq.	82.8	81.5	82.1
	Simple	CRF	94.4	86.8	90.4
		Bi-LSTM	94.9	89.6	**92.2**
		Non-Seq.	91.1	92.4	91.7

Conclusion

- A comparison of three NER methods for extraction of medications and ADEs.
  - BiLSTM: an overall effective model, but fails to directly extract discontinuous and overlapping entities.
  - CRF: more successful for discontinuous entities.
  - Non-sequence labeling method: tends to extract long strings as one entity due to its natural mechanism.
- Future work
  - Other methods to utilise syntactic structure
  - Other biomedical datasets
  - Nested entities