Extraction of Adverse Drug Events from Medical Case Reports

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Definitions

A side-effect is an unintended effect of a medicine. Normally it is undesirable but it could be beneficial.

An adverse drug reaction (ADR) is an unintended and noxious effect that is attributable to a medicine when it has been given within the normal range of doses used in man.

An adverse event (AE) is an undesirable occurrence that occurs in the context of drug treatment but which may or may not be causally related to a medicine.

• Use ‘ADR’ to mean that it is now generally accepted that drug x may cause effect y rather than in relation to individual cases. Qualify the term with ‘possible’ if there is doubt.

• Use ‘suspected ADR’ when a health professional or investigator indicates that a drug may have been responsible for an event in an individual case. A valid case submitted as a spontaneous report to a company or regulatory authority is a suspected ADR by definition.

• Use ‘AE’ only in the context of systematic data collection when no element of judgement is involved in determining whether or not a case is counted.
A 60 year-old woman with chronic renal failure developed acute proximal muscle weakness after receiving a regular dosage of colchicine. [PMID:10904571]

colchicine $\rightarrow$ acute proximal muscle weakness (True)
colchicine $\rightarrow$ chronic renal failure (False)

**Fig. 1.** Example of a sentence annotated with drug, conditions, and relations between them. *True* indicates presence of adverse effect relation and *False* indicates absence of adverse effect relation.
Can we automatically detect intra-sentence adverse drug events?
Our approach

Presented in (Giuliano et al. EACL 2006)
  – State-of-the-art in protein-protein interaction

Supervised machine learning
  – Kernel-based

Two information sources
  – Global context
  – Local context

Shallow linguistic Information:
  – tokenization
  – lemmatization/stemming
  – sentence splitting
  – PoS tagging
Modularity of Kernel Methods

Data $\rightarrow$ Kernel Function $\rightarrow$ Learning Algorithm $\rightarrow$ Classification Function $\rightarrow$ $f(x) = \sum \alpha_i K(x_i, x)$
Kernel methods for RE

Lee Mitgang has covered education for the AP since 1981

former CBS News commentator Eric Severeid.

Eric has covered sports for ESPN since 2001

(0,1,1, ..., 1, 0)^T

Slide from Giuliano et al. 23.11.2006, LCT Colloquia, Rovereto, Italy
Shallow Linguistic Kernel

\[ K_{SL}(R_1, R_2) = K_{GC}(R_1, R_2) + K_{LC}(R_1, R_2) \]

Global context kernel

\[ K_{GC}(R_1, R_2) = K_{FB}(R_1, R_2) + K_B(R_1, R_2) + K_{BA}(R_1, R_2) \]

Local context kernel

\[ K_{LC}(R_1, R_2) = K_{left}(R_1, R_2) + K_{right}(R_1, R_2) \]

Slide from Giuliano et al. 23.11.2006, LCT Colloquia, Rovereto, Italy
Global Context Kernel (1)

**Fore-Between**

Expression of the $\sigma(K)$-dependent $cwlH$ gene depended on $\text{gerE}$.

**Between**

Expression of the $\sigma(K)$-dependent $cwlH$ gene depended on $\text{gerE}$.

**Between-After**

Expression of the $\sigma(K)$-dependent $cwlH$ gene depended on $\text{gerE}$.

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Global Context Kernel (2)

- Based on the Bag-of-Words approach
- Context representation:

\[ \phi_{FB}(\text{Expression of the } \sigma(K)\text{-dependent } cwlH \text{ gene depended on } \text{gerE}) \]

\[ (t_f(t_1, P), t_f(t_2, P), \ldots, t_f(t_l, P)) \in \mathbb{R}^l \]

- N-gram Kernel:

\[ K_{N-gram}(R_1, R_2) = \langle \phi(R_1), \phi(R_2) \rangle \]

- Global Context Kernel:

\[ K_{GC}(R_1, R_2) = K_{FB}(R_1, R_2) + K_B(R_1, R_2) + K_{BA}(R_1, R_2) \]
Local Context Kernel (1)

- Local contexts provide useful clues for detecting roles

![Diagram](slide)

- Two local Contexts

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Local Context Kernel (2)

- Local Context Representation:

\[ \phi_{Left}(\text{\texttt{GerE stimulates cotD transcription and inhibits cotA transcription...}}) \]

\[ (f_1(L), f_2(L), \ldots, f_m(L)) \in \{0, 1\}^m \]

- Feature functions \( f_i \)
  - Token
  - Lemma
  - PoS tag
  - Orthographic: Capitalization, Punctuation, Numeral, …

- Local Context Kernel:

\[ K_{LC}(R_1, R_2) = K_{left}(R_1, R_2) + K_{right}(R_1, R_2) \]
The first case concerns a 70-year-old man who developed severe aplastic anemia 7 weeks after treatment with 500mg of ticlopidine daily.
Effect of corpus size on classification performance
Fig. 2. Ontologies discussed in this work (from (Roberts et al., 2009) and (Yongqun et al., 2011)).
Next steps

• Assessment of real impact on pharmacovigilance processes
• Ontology Driven Information Extraction
• Inter-sentence ADE
• Social Media
• Electronic Health Records
• Chinese …