Transitive Text Mining for Information Extraction and Hypothesis Generation

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Abstract

Transitive text mining - also named Swanson Linking (SL) after its primary and principal researcher - tries to establish meaningful links between literature sets which are virtually disjoint in the sense that each does not mention the main concept of the other. If successful, SL may give rise to the development of new hypotheses.

In this communication we describe our approach to transitive text mining which employs co-occurrence analysis of the medical subject headings (MeSH), the descriptors assigned to papers indexed in PubMed. In addition, we will outline the current state of our web-based information system which will enable our users to perform literature-driven hypothesis building on their own.

Keywords: Text Mining, Swanson Linking, Hypothesis generation

1 Introduction

Transitive text mining tries to link the major themes of disjoint literature sets. Don Swanson was the first to describe the disclosure of "hidden", i.e. unpublished but implicit links between concepts not mentioning each other in their respective literature representations (Swanson (1986, 1988, 1991)). Later, the principle of his method was termed Swanson Linking (SL) which may be defined as finding disjoint literature partners by establishing meaningful links between them using information retrieval from bibliographic databases (Stegmann and Grohmann(2003)).

The published examples of SL involve basically three different sets of literature: (i) a problem-based literature - e.g. describing a disease - is referred to as "source"; (ii) a literature not being mentioned in the source literature but possibly contributing to problem solving is called "target"; (iii) a literature representing a major concept which is relevant for and occurs in both, source and target literature, is labeled "intermediate" (Swanson and Smallheiser (1999)). The discovery process might normally proceed from source to target via intermediate; however, the reverse order is naturally conceivable, and any

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coherent literature set regarded as "intermediate" may be explored for source and target concepts simultaneously.

Different approaches have been developed to detect in the investigated literature sets key terms representing possible intermediate and target or source concepts. Some authors extract title and abstract words and phrases (Swanson and Smalheiser (1999), Gordon and Lindsay (1996), Gordon and Dumais (1998), Lindsay and Gordon (1999), Weber et al. (2001)) or extract the medical subject headings (MeSH) assigned to documents indexed in PubMed (Srinivasan (2004)) and try to find relevant terms on top of ranked lists. We use the co-word analysis technique described by Callon et al. (1991) for clustering of extracted MeSH terms and for two-dimensional visualisation of the clusters according to their internal density and external centrality in so-called "strategic diagrams". We found that in some cases key concepts relevant to the discovery process can be identified on the basis of some positional and/or numerical characteristics of the respective clusters (Stegmann and Grohmann (2003), Stegmann and Grohmann (2004)).

In this communication we discuss and value these features with the following examples of transitive text mining: Raynaud’s Disease - Fish Oil (Swanson (1986)), Migraine - Magnesium (Swanson (1988)), Schizophrenia - Phospholipase A_2 (Smalheiser and Swanson (1998)).

In addition, we shortly describe our web-based information system which will enable our users to analyse the knowledge domain represented by a literature set and to perform transitive text mining on their own.

2 Methods

PubMed searches were performed as indicated at the legends. The retrieved document sets were downloaded in MEDLINE format. Extraction of MeSH terms, subsequent co-occurrence analysis, term clustering and calculation of cluster density and centrality were performed as described (Stegmann and Grohmann (2003), Stegmann and Grohmann (2004)). A brief description of the cluster process follows: co-occurrence strength of MeSH term pairs was calculated as Equivalence Index (Callon et al. (1991))

\[ E_{ij} = \frac{C_{ij}^2}{C_iC_j}, \]

where \( C_{ij} \) is the number of co-occurrences of terms \( i \) and \( j \) (i.e. the number of documents in which terms \( i \) and \( j \) co-occur), and \( C_i \) and \( C_j \) are the number of occurrences of terms \( i \) and \( j \), respectively. Multiple occurrences of a MeSH term within the MeSH fields of a document (e.g. with different subheadings) are ignored. A threshold of \( E_{ij} \geq 0.05 \) was applied. The cluster process starts with the term pair exhibiting the highest equivalence index. Of those remaining terms having links with the cluster members the term with the highest link strength is added to the cluster. Cluster size is limited to 3 – 10 terms. The clusters of a literature set are graphically displayed according to their mean internal link strength (density) and the sum of their external link strength (centrality).

The tools for MeSH term extraction, calculation of equivalence indices, cluster generation and calculation of cluster density and centrality have been programmed in PERL and JAVA. The JAVA programs are part of our web-based
information system *Charité-Mlink*. Cluster diagrams were created using the software package R (R Development Core Team (2004)).

3 Results and Discussion

The strategical diagrams have a two-fold function: (i) they should allow the identification of clusters containing terms of potential interest for the transitive discovery process; (ii) they represent knowledge domains (as far as they are comprised by the database retrieval) which can be analysed in terms of centrality indicating the importance of clusters and cluster terms for the whole domain, and in terms of density indicating the strength of the local coherence of (sub-) themes expressed by the cluster terms (Callon et al. (1991)).

Figure 1, 2, 3 show strategical diagrams of source literatures which allow the identification of intermediate terms which in turn are prerequisites for the detection of target concepts. Diagrams of intermediate literatures are displayed in Figure 4, 5, 6. They harbor both, target and source terms.

3.1 Source literature

In the diagrams of source literatures the clusters with the terms defining the literature are located in regions of high centrality and density, as one can expect (Figure 1, 2, 3). The clusters containing some of the already known (from Swanson’s work) intermediate terms are indicated (Figure 1, 2). The terms *Spreading Cortical Depression* and *Epilepsy*, being intermediate for the *Migraine - Magnesium* literature track occur in clusters located in the below-median centrality and density region of the diagram, that is in the periphery of the knowledge domain ”Migraine” (Figure 2). In contrast, the cluster containing the term *Blood Viscosity* as an intermediate for the *Raynaud’s Disease - Fish Oil* literatures has a higher centrality and about median density (Figure 1). For each cluster with a centrality > 0 a centrality/density ratio (cdr) can be calculated as the quotient of its centrality and density. Dividing the cdr of the source cluster by the cdr of an intermediate cluster gives a Source-Intermediate Ratio (SIR). SIR is around 1 for the intermediate terms *Blood Viscosity* (Figure 1) and *Epilepsy* (Figure 2). However, the SIR of the intermediate *Spreading Cortical Depression* (Figure 2) is quite different from 1. The analysis of other source literatures (not shown) also identifies some intermediate terms in clusters being located in regions of low density and centrality and/or showing a SIR of around 1 so that these characteristics may be taken as indicators where to start the screening of the clusters for terms of possible relevance for the discovery process. However, the other clusters should be screened, too. Due to the cluster method used the members of a cluster show some similarity to each other and oftenly define the different aspects of a more general theme which may be helpful in generating ideas of intermediate concepts. The diagram of the *Schizophrenia* source literature (Figure 3) may serve as an example: here, the intermediate cluster is neither located below the medians nor shows a SIR of around 1. In fact, we identified it tentatively as an intermediate because it contains the term *Platelet Aggregation* which is also an intermediate term in the *Raynaud’s Disease* and *Migraine* literature (not shown) and because that term represents some physiological property. It is generally a good idea to look for candidate
intermediate terms dealing with physiological conditions (Weeber et al. (2001)).

3.2 Intermediate literature

Figure 4, 5, 6 show the strategical diagrams of the intermediate literatures represented by the intermediate term identified in Figure 1, 2, 3. As to be expected, the clusters containing the main concept of the literature sets show high centrality. The intermediate literatures contain by definition the respective source terms because the former was chosen due to the identification of its main term from the diagrams of the source literatures. Now, in the diagrams of the intermediate literatures the clusters containing a source term may be regarded as a guide to possible target concepts. In the Blood Viscosity literature diagram (Figure 4) the cluster containing the target terms Eicosapentaenoic Acid and Fish Oils are not only located close together but also show similar centrality/density ratios which give a quotient (Source-Target Ratio, STR) of about 1. In the diagram of the intermediate Spreading Cortical Depression literature set (Figure 5) we also find source and target clusters in close vicinity, the STR, however, is well above 1. In the diagram of the intermediate Platelet Aggregation literature (Figure 6) source and target clusters are not so close together, but the STR value is around 1. All target terms are already known by Swanson’s work.

As with the source literature we can start the screening of intermediate literature clusters exhibiting similar centrality/density ratios and/or being in the neighbourhood of source clusters. However, we must also say that some target terms are found in clusters outside of this frame (not shown); the screening of other clusters is always advisable. In addition, dealing with large literature sets consisting of many thousand documents very many clusters have to be screened. We did not yet experiment with variable cluster sizes but higher number of terms per cluster might affect the cluster readability. Thus, other text mining methods should be employed. For example, Gordon and Dumais (1998) applied Latent Semantic Analysis (LSA) to the analysis of the Raynaud’s Disease literature and found relevant intermediate terms at high ranks on lists generated from title and abstract words. They failed, however, to find target terms at equally high positions on lists derived from the intermediate literature after LSA treatment. We are currently investigating the usefulness of LSA for the analysis of document-by-MeSH-term matrices (in preparation).

3.3 Charité-Mlink

Our web-based information system Charité-Mlink enables the user to upload PubMed literature sets and to navigate in the information space constituted by the MeSH term clusters generated by the system. In addition, the system makes suggestions with respect to clusters containing terms of potential relevance to a discovery process based on transitive text mining as described in the previous sections. The first version of Charité-Mlink has been released in August 2005 and can be accessed at http://mlink.charite.de/
4 Conclusion

We have described an approach to transitive text mining which is based on the co-occurrence analysis and subsequent clustering of the MeSH terms assigned to PubMed documents. Our results allow some suggestions which clusters should be screened at first in a discovery process. Future work is necessary employing other text mining methods in order to generate hypotheses which cannot derived from one knowledge domain only.

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Raynaud’s Disease

Figure 1: Strategical diagram of the Raynaud’s Disease\(^\dagger\) literature set.
\(^\dagger\)PubMed title search for ”raynaud*”, publication years 1966-1985.
No. of documents: 802, no. of distinct MeSH terms: 454, no. of clusters: 44.
Triangles: indicate cluster positions, dotted lines: indicate medians.
RD: cluster containing the source term Raynaud’s Disease.
BV: cluster containing the intermediate term Blood Viscosity.
SIR: source-intermediate ratio.
Figure 2: Strategical diagram of the Migraine\textsuperscript{†} literature set.
\textsuperscript{†}PubMed title search for "migraine", publication years 1966-1987.
No. of documents: 2583, no. of distinct MeSH terms: 1021, no. of clusters: 106.
Mi: cluster containing the source term Migraine.
Epi: cluster containing the intermediate term Epilepsy.
SCD: cluster containing the intermediate term Spreading Cortical Depression.
Other details: see Figure 1.
Figure 3: Strategical diagram of the Schizophrenia\(^\dagger\) literature set.
\(^\dagger\)PubMed title search for "schizophrenia", publication years 1966-1985.
No. of documents: 6225, no. of distinct MeSH terms: 1598, no. of clusters: 164.
Sch: cluster containing the source term Schizophrenia.
PA: cluster containing the intermediate term Platelet Aggregation.
Other details: see Figure 1.
Blood Viscosity

Figure 4: Strategical diagram of the Blood Viscosity\textsuperscript{†} literature set.
\textsuperscript{†}PubMed title search for ”blood viscosity”, publication years 1966-1987.
No. of documents: 326, no. distinct of MeSH terms: 293, no. of clusters: 39.
BV: cluster containing the intermediate term Blood Viscosity.
RD: cluster containing the source term Raynaud’s Disease.
EPA: cluster containing the target terms Eicosapentaenoic Acid and Fish Oils.
STR: source-target ratio.
Other details: see Figure 1.
Figure 5: Strategical diagram of the Spreading Cortical Depression literature set.

PubMed title search for "spreading cortical depression", publication years 1966-1985.
No. of documents: 502, no. distinct of MeSH terms: 391, no. of clusters: 30.
SCD: cluster containing the intermediate term Spreading Cortical Depression.
Mi: cluster containing the source term Migraine.
Mg: cluster containing the target terms Magnesium.
Other details: see Figure 4 and Figure 4.
Figure 6: Strategical diagram of the Platelet Aggregation\(^*\) literature set.
\(^*\)PubMed title search for "platelet aggregation", publication years 1966-1985.
No. of documents: 2638, no. distinct of MeSH terms: 1449, no. of clusters: 148.
PA: cluster containing the intermediate term Platelet Aggregation.
Sch: cluster containing the source term Schizophrenia.
PLA: cluster containing the target terms Phospholipase A.
Other details: see Figure 1 and Figure 4.