CONCEPT BAG: A NEW METHOD FOR COMPUTING SIMILARITY

by

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ABSTRACT

Biomedical data are a rich source of information and knowledge. Not only are they useful for direct patient care, but they may also offer answers to important population-based questions. Creating an environment where advanced analytics can be performed against biomedical data is nontrivial, however. Biomedical data are currently scattered across multiple systems with heterogeneous data, and integrating these data is a bigger task than humans can realistically do by hand; therefore, automatic biomedical data integration is highly desirable but has never been fully achieved. This dissertation introduces new algorithms that were devised to support automatic and semiautomatic integration of heterogeneous biomedical data. The new algorithms incorporate both data mining and biomedical informatics techniques to create "concept bags" that are used to compute similarity between data elements in the same way that "word bags" are compared in data mining. Concept bags are composed of controlled medical vocabulary concept codes that are extracted from text using named-entity recognition software. To test the new algorithm, three biomedical text similarity use cases were examined: automatically aligning data elements between heterogeneous data sets, determining degrees of similarity between medical terms using a published benchmark, and determining similarity between ICU discharge summaries. The method is highly configurable and 5 different versions were tested. The concept bag method performed particularly well aligning data elements and outperformed the compared algorithms by more than 5%. Another configuration that included hierarchical semantics performed particularly well at matching medical terms, meeting or exceeding 30 of 31 other published results using the same benchmark. Results for the third scenario of computing ICU discharge summary similarity were less successful. Correlations between multiple methods were low, including between terminologists. The concept bag algorithms performed consistently and comparatively well and appear to be viable options for multiple scenarios. New applications of the method and ideas for improving the algorithm are being discussed for future work, including several performance enhancements, configuration-based enhancements, and concept vector weighting using the TF-IDF formulas.

Simplicity is the ultimate sophistication.

Leonardo da Vinci, 1452 to 1512 AD

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF EQUATIONS

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CHAPTER 1

INTRODUCTION

1.1 Importance of Data Reuse in Biomedical Informatics

Biomedical data are a potentially rich source for information and knowledge discovery. Biomedical data that are collected for patient care and stored in electronic health records (EHR) are often reused to support clinical research [1-3], translational research [4], comparative effectiveness research (CER) [5, 6], population health [7], public health [8], quality improvement [9, 10], and for measuring healthcare practices in general [11-13]. There are far too many publications to list them all. Both the “bio” and “medical” aspects of biomedical data are deep and wide in both scope and breadth, with countless opportunities for study and discovery.

Data reuse is also referred to as “secondary use,” and has been a popular topic in the literature for decades, but has been especially popular since the National Institute of Health (NIH) started supporting reuse directly. The NIH granted Clinical and Translational Science Awards (CTSA) to over 60 academic medical centers across the U.S. starting in 2006, with the mission to facilitate more efficient translational research. Multiple awards were granted to research and build innovative solutions that would enable biomedical data sharing. The CTSA program recognized that innovative solutions are required to enable both “sharing” and “reusing” biomedical data and dedicated resources via awards to institutions to break down barriers. Multiple policies deliberately prevent or restrict sharing, and technical barriers prevent the efficient reuse of biomedical data after sharing has occurred.

More recently, in 2009 the U.S. Government passed legislation that invests heavily in interoperable EHR technologies supportive of instantaneous biomedical data sharing and reuse by third parties. The HITECH Act allocated $19.2 billion for healthcare delivery organizations that implement certified EHR technology that meets "Meaningful Use" criteria [14]. Healthcare organizations across the U.S. now have an opportunity to adopt interoperable EHR solutions at a much lower cost due to these incentives. Just to be clear, interoperable EHRs facilitate instantaneous data sharing and reuse, and this is exactly what this legislation was intended to achieve.

All of the discoveries that have been made reusing biomedical data as well as the substantial U.S. government efforts to support sharing underscore how valuable biomedical data are. Biomedical data are at the heart of multibillion-dollar healthcare and biomedical research industries such as clinical research, pharmaceutical research, translational research, and public health. The considerable efforts to improve the sharing and reuse of biomedical data are also indicative of the surrounding complex issues and challenges.

1.2 Issues with Biomedical Data Reuse

1.2.1 Privacy

The initial barriers for reusing human biomedical data (more so than other species) are typically privacy issues. Clinicians or healthcare staff with proper "need to know [to provide or support patient care]" are the only people who have access to EHR data due to privacy laws such as HIPAA, the U.S. Government's official health information privacy regulations [15].

Access and reuse of fully identifiable data for the purpose of research typically requires human subject research training, a significant affiliation with the data provider, and an IRB approval from that provider. IRBs are routinely granted in one's local institution, but having a significant affiliation with a remote provider to obtain an IRB may be a barrier. There is an exception. IRB may not be necessary when biomedical data are deidentified [16, 17]. In this case researchers may need to provide verification of human subject research training before deidentified data are released, but this is much more straightforward than completing and passing an IRB review. Automated methods are being developed to streamline the approval processes but have not been adopted at this point in time.

Working with deidentified data has a new list of challenges. While they are easier to access, the deidentification process strips out variables that would normally be used to link data sets. This implies that a deidentified breast cancer data set cannot be linked to diagnostic data from an EHR to identify comorbidities, for example. There are tradeoffs between time to data access and what information or knowledge the data are capable of providing.

Privacy also plays a crucial role when data sharing agreements need to be established between potential competitors. Business privacy between large healthcare organizations that compete for patient business or for research dollars may prevent sharing. Sharing business data with a competitor is risky; it could be used to identify business opportunities and/or to disadvantage the competition. Biomedical data have the potential to contain business-related information, and organizations are interested in protecting it.

Biomedical data privacy laws protect patients from improper use of their personal information, but also make it difficult to reuse valuable data for valid research. Methods are being developed to overcome these barriers such as automated approval processes [18] and data deidentification. Deidentification has become mainstream but the automated approval processes have not. Easy access to some data is better than no access and no data.

1.2.2 Unknown Data Quality

When biomedical data are reused for research, unknown data quality may invalidate important study findings. Comparative effectiveness research (CER) studies, for example, attempt to associate clinical practice variations with clinical outcomes, and in these studies, multisite study findings are more likely to be generalizable than single-site findings. Site-level findings have different prediction variables, disease incidence, and outcomes, and these differences may represent true variation in outcomes and practice patterns, or they may represent artificial variation due to data collection method variability across sites. A quality framework created to distinguish between true and false variation found that when true variation was present, CER studies could deliver important information regarding treatment safety and effectiveness between sites and populations. Conversely, the framework found artificial variation between sites could invalidate study findings altogether [19].

Another cause of unknown data quality originates from undocumented, inadequately documented, or otherwise misunderstood metadata and data [20]. When explicit dictionaries or access to data providers who can define and describe the details of how and when data were collected do not exist, improper assumptions may lead to improper interpretations of results [21]. Variables may be misunderstood and utilized inappropriately. Systems may turn on and off for periods of time. New buildings with new services may be added to an organization that then start feeding new data spikes into the collective data, and so on. Imagine a new breast cancer facility is erected, breast cancer treatment begins, and suddenly the number of breast cancer cases appears to skyrocket in the patient data warehouse. When cases like this go undetected, new spikes may be viewed as problematic increases when they are not. Numerous anomalies like these can occur from lack of documentation and/or understanding of the data, especially when there are a large number of heterogeneous data providers and sophisticated data integration processes are involved.

1.2.3 Heterogeneity

Biomedical data are modeled and represented using various formats, syntaxes, and values to represent clinical statements or facts. While several significant clinical data modeling efforts have been designed to reduce heterogeneity and to improve clinical data consistency and interoperability [22-25], the market remains slow to adopt and implement such models. Healthcare and research communities are decentralized and continue to produce heterogeneous data sets. When the goal is to reuse multiple heterogeneous data sets, they typically require aggregation and/or integration involving several forms of heterogeneity resolution [26, 27]. Resolution of heterogeneity is essentially the resolution of the differences between data sets. The next sections review the data set differences that cause data heterogeneity.

1.2.3.1 Structural differences

Structural heterogeneity occurs when data model constructs, constraints, and data are modeled differently [27]. Data may require "vertical integration" (integrating semantically similar data) or "horizontal integration" (integrating data from different domains) with information distributed and expressed differently across data structures. Hierarchical relationships between data in relational models are structurally different than they are when represented using XML, for example. Structural differences may also result from diverse data types and conceptual granularities. A "Clinician type," for example, may be modeled with one data element with a value such as "critical care nurse," or it may be modeled with two, one for "specialty" and another for "role," with values such as "critical care" and "nurse," respectively. When one data set implements the single-element strategy and another data set implements the two-data-element strategy, we have both a structural difference (one versus two data elements) and conceptual difference (one versus two concepts). Both the single-element and double-element versions represent semantically identical information but are managed differently according to how data are structured. Additionally, there may be dependency conflicts (different cardinalities) or key conflicts (unresolved identifiers) that occur due to structural differences.

1.2.3.2 Naming differences

In reference to the semiotic triangle [28], naming differences occur when different symbols (words in this case) are used to represent the same referents (concepts). Different words that have the same conceptual meaning may be in the form of synonyms or abbreviations and may manifest in the metadata or in the data—“Doctor” versus “physician” or “MRN” versus “Patient ID,” for example. These kinds of naming differences are typically managed by “terminologists” using a “terminology” and/or an “ontology” that are used to model “concepts,” “terms” (linguistic labels), “codes” (a unique identifier that designates a single concept), and lexical or semantic “relationships” [29, 30].

1.2.3.3 Semantic differences

Semantic differences occur between data sets when the meanings of metadata or data are similar but are not equivalent [27]. For example, a data set with data element “Blood culture growth” with possible values 0, 1+, 2+, 3+, and 4+, and another data set with the same data element and possible values of “no growth,” “moderate growth,” or “significant growth” are possible to align semantically by mapping to the least granular set (the categorical values) as follows:

0 = no growth

1+, 2+ = moderate growth

3+, 4+ = significant growth

Imagine another data set is added that stores the answer as “no growth” or “growth.” Then the semantic mappings are as follows:

0 = no growth

1+, 2+, 3+, 4+, moderate growth, significant growth = growth.

In both cases the integrated form of the data loses meaning. The only values that can be queried across the integrated set are “growth” or “no growth.”

The previous two examples are both resolvable using semantic mappings, but not all semantic differences are logically resolvable. Consider another example similar to the previous, where data element A’s value set is “light or no growth,” “moderate or significant growth,” and data element B’s value set contains “no growth,” “light or moderate growth,” and “significant growth.” There is simply not a mapping solution between these value sets that guarantees an accurate result [27]. Querying for “no growth” for example, is not an option because data element B’s value set does not support this level of granularity. Querying for A’s “light or no growth” is not an option since data element B’s value set does not have a logistically equivalent value. None of the values between these two sets can be logically mapped.

Semantic differences that occur at the conceptual level may be by design to suit clinical contexts or it may occur from a difference of modeling style or opinion [29]. One clinical specialist may require a different level of detail that is not necessary helpful for other specialists— “myocardial infarction” may be sufficient for a general practitioner, but a cardiologist benefits from the more detailed “left ventricular infarction,” for example. Similarly, semantic differences may be due to precoordination versus postcoordination disparities. Is there one concept for “right” and another for “lung” or a single concept for “right lung?” Or how many concepts are there in “nonsmall cell lung carcinoma stage III of the right upper lobe?” Should there be one concept for laterality, one for body site, one for the problem, and one for the stage? Or is there one precoordinated concept that means, “nonsmall cell carcinoma stage III,” and a single concept for “right upper lobe?” There are valid reasons for the different options [31, 32]. One might be more suitable for analysis while another might require less data entry.

1.2.3.4 Content differences

The most extreme content difference occurs when one attempts to perform a horizontal integration and there is no semantic overlap [33]; there is nothing in common to link or share. A set of patient demographics will not intersect with a set of DNA sequences that have no common patient identifiers that can be used to link them together. Each data set is essentially an orphan in this case. In less extreme cases content differences occur when a portion of data is not represented in a data set [27]. Facts may be implied or not straightforward to interpret. A “Diabetes patient cohort” data set may not contain computable facts that indicate that subjects have diabetes directly in the name of an object, attribute, or in the data; data are implied but are not explicit. The existence of the subject in the data set implies they have met the diabetes criteria.

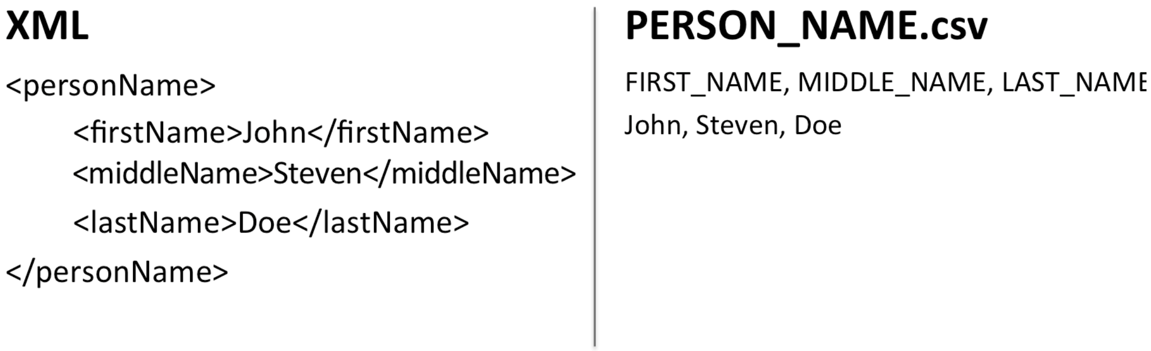
Empty or NULL data values without explicit specifications are ambiguous. An empty value may indicate “normal,” “not evaluated,” or “unavailable.” Not knowing what the implied meaning is may lead to erroneous assumptions.

Content differences may occur due to different assumptions about what should be derived from existing data and what should be stored in the database. Data integration interventions may be required to derive “age” from “birth date” or “birth year” from the “current age” because of different assumptions about what is stored in what is derived.

The other common example is storing only a “ZIP code” and not the “state” or the “city” since the ZIP Code can be used to derive states and cities.

1.2.3.5 Syntactic differences

Syntactic differences are related to structural heterogeneity, in that syntax relates to the data structure but involves additional nuances. Syntactic heterogeneity occurs when data sets are not expressed using the same syntax or technical language [27], implying interpretation and translation must occur when interoperability or data integration is desired. Figure 1.1 shows an example of two types of syntax that contain semantically homogeneous and syntactically heterogeneous data, where the syntax of one is XML and the other is a comma-delimited text file (CSV). There are no structurally- induced inconsistencies in these data, only syntactic differences that are simple to manage, but this is not to imply that managing syntactic heterogeneity is simple. A less trivial and common scenario is translating between XML and JSON [34]. They are both very popular syntaxes supportive of not only the HL7 service-oriented architecture [35],



XML

```
<personName>
	<firstName>John</firstName>
	<middleName>Steven</middleName>
	<lastName>Doe</lastName>
</personName>
```

PERSON_NAME.csv

```
FIRST_NAME, MIDDLE_NAME, LAST_NAME
John, Steven, Doe
```

Figure 1.1 Example of syntactic heterogeneity; two data sets with the same data and different syntax, a snippet of XML and CSV.

but service-oriented architecture and web-based technologies in general. Syntax-related issues that occur when translating between XML and JSON [36] include the following:

- XML namespaces do not exist in JSON.
- XML supports repeating elements, JSON does not.
- Base data types are different, as are class/data type definitions.
- Element arrays are handled differently.
- XML supports mixed data types with tags embedded in natural language, JSON does not.
- Special characters are handled differently.

There are more, but these are the primary issues. Many of the issues in this specific case are recoverable by adopting agreed upon translation patterns [36], but syntactic heterogeneity can be associated with complex translation issues. There are many software tools that can assist with syntactic translation issues.

1.2.4 Lossy Data Conversions

"Lossy" data conversions are discussed in the context of data compression for various kinds of media, such as images or videos, where the original format is compressed and only the most important data are kept while the less significant data are "lost." The same concept applies to biomedical data. When biomedical data are interpreted and translated, sometimes only the most important data are kept to comply with a specific data model or coding scheme while other unsupported data are lost in translation. The previous examples describing semantic difference mappings in section 1.2.3.3 illustrate how the loss of data also potentially implies the loss of semantics. To avoid misinterpretation, losses must be accounted for and presented to data analysts. This is another significant research topic: representing and communicating “data provenance” [37, 38]. Understanding the origin and pedigree of data is critical to maintain high-quality analysis and reproducibility of integrated biomedical data.

Losing semantics of data due to heterogeneity is a reality that occurs when biomedical data sets are integrated. All the forms of heterogeneity are common and often occur together. Tools that have been specifically designed for integrating heterogeneous biomedical data sets are discussed next.

1.3 Biomedical Data Integration Software

Biomedical data are typically integrated using one of two basic architectures, 1) the centralized data warehouse architecture where all data are copied and resolved into a common data model and database [39, 40], or 2) the federated database architecture where data are left in their original databases and are queried across networks using a federated query engine [41-44] to analyze data. Two software products that integrate biomedical data are described: one that uses a centralized data warehouse and one that uses federated data architecture.

1.3.1 i2b2

The Informatics for Integrating Biology and the Bedside (i2b2) software suite is based on the centralized data warehouse architecture and was designed to give researchers direct access to existing biomedical data sets [45] that have been previously merged and integrated into an i2b2 data warehouse. The i2b2 software supports diverse forms of biomedical data, including natural language clinical texts and genomic data documents via the i2b2 “cells” and “hive” [45, 46]. The software is open source and freely available but requires a highly skilled staff to set up and maintain.

The i2b2 software should be installed and configured by information technology (IT) experts capable of setting up secure database servers, web servers, and application servers. Setting up, preparing, and loading biomedical data requires both data architecture experience and clinical terminology experience. The terminologist must learn the i2b2 ontology model and infrastructure, and then must design and load the i2b2 ontology to match the local site’s metadata and data. This requires in-depth knowledge and expertise of modeling clinical events and facts, such as “serum creatinine is a laboratory measurement used to evaluate kidney function with normal healthy values between 0.6 to 1.3 milligrams per deciliter (mL/dL).” This knowledge is required to perform semantic integration [47] and involves recognizing the semantic differences and similarities between observations such as “BUN,” “serum creatinine” and “creatinine clearance,” in terms of how they are represented in each data source and how they relate to each other in medicine. The terminologist semantically harmonizes the data by mapping each semantic alignment using the i2b2 ontology. The terminologist’s semantic alignments must be coordinated with the organization of the “observation fact” database that is typically populated by the data architect. This requires in-depth knowledge of i2b2’s data model and data extract, transform, and loading (ETL) procedures. ETL processes are responsible for maintaining privacy, data quality, patient record linking [47], managing structural differences, syntactic differences, and for maintaining integrity between the semantic alignments contained in the i2b2 ontology. The integration process requires careful and tedious cooperation between the data architect and terminologist.

The time required for i2b2 setup depends entirely on how much work is required to resolve data integration issues. When patient identity has been well maintained and data heterogeneity is low, this process may be straightforward. When thousands of data elements need to be semantically aligned, months of tedious semantic integration work may be required. It is important to recognize that the time to perform and complete the ETL process is not a shortcoming of i2b2; the amount of work required is largely a platform-independent consequence of integrating biomedical data. Once completed, however, the work left to configure the i2b2 software is straightforward. New users must have user accounts created and require a light amount of training, but training is pre-recorded and available online for free (https://www.youtube.com/results?search_query=i2b2).

A federated version of i2b2 is also available. Sites that have i2b2 can add the SHRINE extension [48] and participate in research networks. Participation in a SHRINE network allows researchers access to query for cohort counts across the network of participants. When researchers find subjects who meet specific cohort criteria at another site, they must then work out the details of sharing the biomedical data based on the site's policies. SHRINE does not support automated sharing.

Participation in a SHRINE requires additional setup and configuration. The physical network must be set up securely and connected to the i2b2 SHRINE extension and network, and local data must be semantically aligned to the SHRINE ontology. Mapping to the SHRINE ontology requires additional work by the terminologist at each site, and again, the amount of time depends completely on how similar the local site's ontology is with the SHRINE ontology. By design, a considerable portion of the SHRINE ontology is based on the use of common coding systems, such as ICD-9 billing codes, that many sites already support to ease the burden of complicated semantic mappings.

The i2b2 software has a proven track record of delivering translational features. Forty-nine CTSA sites, 34 additional academic medical institutions, and 20 international organizations use i2b2 [49]. In terms of publications, “i2b2” was contained in the PubMed title attribute property of 44 publications, and an additional 158 times searching all other attributes. Most importantly, researchers have been successful using i2b2 to make important clinical discoveries [50-52].

1.3.2 OpenFurther

OpenFurther [41] is an example of the federated database architecture and was originally designed as a statewide informatics platform housed in the Center for Clinical and Translational Science at the University of Utah [53]. The objective of OpenFurther is to deliver innovative and practical software tools and services that can directly support data and knowledge access, integration, and discovery more efficiently than has previously been possible. The software is open source and is available [54-56] for use by other organizations.

In the past, obtaining simple counts from a collection of distributed biomedical databases owned and managed by a list of institutions would have involved months of processes requiring individual sponsors from each institution, IRB approvals, communications with multiple IT staff members from each organization, project data integration and data management for each data set, and so on. OpenFurther however, allows researchers to construct queries [57] and find specific cohorts without requiring all of these time-consuming processes. The OpenFurther data integration process replaces the manual processes by performing the following technical steps:

1. When the researcher logs into OpenFurther, data access is determined by the user's roles and privileges.
2. The researcher builds and submits a query to data they have access to.
3. The query is sent to the query translator that constructs a platform-specific data query for each of the state's databases.
4. The query distributor distributes each platform-specific query to its respective data service.
5. The query is executed and returns a data set result.
6. Each result from each database is then translated into a common data model and stored in an intermediate database.
7. When all results have been received and translated, they are intersected or aggregated to compute the final results.
8. The final result set is reported to the researcher.

Step 1 occurs once for each query session. Steps 2-7 are performed each time a query request is received. Steps 3, 4, 6, 7 and 8 are unique to the federated query process and are required to support on-the-fly data integration for each query request. By comparison, data warehouse systems execute step 1 for each query session, steps 2 and 5 when a query is performed, and step 6 needs to be run once prior for the whole data set (the ETL process to load all the data must be performed before the data may be queried). Five of the 8 steps are unique to the federated data architecture.

The benefits of a federated architecture may be attractive, but the cost of setup is also high in terms of time and the required expertise. OpenFurther setup requires skilled IT professionals, including software engineers, data architects, and biomedical terminology experts. A custom semantic framework was designed for OpenFurther that utilizes an open source terminology system and tools supporting the terminologist's work of performing semantic alignments [58] and integration [47]. The framework additionally includes a metadata management system that was designed to augment the terminology system's capabilities to support more sophisticated semantic alignments, data element (DE) alignments that involve multiple DEs, values, and conditional logic [59]. The data architect and terminologist perform semantic alignments by loading and aligning metadata for each data source. Alignments have properties that indicate the nature and specific conditional logic. This work is very similar to the work that is performed using off-the-shelf ETL tools, but ETL tools are designed to support large batch processes rather than very specialized query-specific transformations. Additionally, the added work of the federated approach specified in step 2 (query translation) requires on-the-fly interpretation and translation of query logic for each data source, a significant challenge. A detailed explanation of the data architecture-specific details are contained in [42], software implementation details are described in [43], and an overview of the semantic frameworks that the query translation framework utilizes is described in [58, 59]. While there are similarities with data warehousing, the federated approach adds more complexity.

OpenFurther has a track record of supporting translational research efforts in Utah and a large CER study conducted at six pediatric hospitals across the U.S. [5, 6]. The pediatric data integration project produced three journal papers with clinically significant findings that are in the process of publication. OpenFurther produced 10 informatics-based journal papers, 25 conference posters, and 7 professional presentations that have been presented at informatics conferences.

1.3.3 Issues with Biomedical Data Integration Software

Many of the issues of integrating biomedical data are primarily the same between the two described technical architectures. The semantic alignment work is primarily the same. One who understands clinical concepts must resolve the naming and semantic differences between the heterogeneous data sources into computable semantic alignments. The data architecture work is also primarily the same. Structural and syntactic differences must be reconciled and addressed and the semantic alignments must be incorporated into the data integration operations to support data aggregation and analysis.

OpenFurther and i2b2 are representative of current state-of-the-art biomedical data integration tools. With both tools, the integration of heterogeneous biomedical data sets is a prerequisite. Of the issues that have been identified, most biomedical data integration experts agree that semantic integration (resolution of naming and semantic differences) of heterogeneous data is the most challenging aspect of integration [27, 60, 61], requiring costly terminologists and/or highly trained knowledge engineers to perform the work [62-64]. Specific costs have not been formally reported, but salaries for "Clinical Terminologist" jobs currently range from $120,000 to $130,000/year online (www.glassdoor.com), and consulting rates are approximately double that. Complexity, time, and costs of semantic integration underscore the need for continued research on automated, or at the very least semiautomatic semantic integration to help reduce these burdens.

1.4 Preventing or Resolving Heterogeneous Biomedical Data

The most desirable strategy for resolving heterogeneous biomedical data is to prevent it from happening in the first place. There has always been a tricky balance between "allowing" clinicians to express themselves using free-text versus "forcing" them to encode all observations such that data are computable [65]. Whether data are free-text or coded, heterogeneous data integration is nearly always required when combining data from biomedical data sets, and the chosen strategy should be specific to the goal of integration. The goal may be well defined where the questions and data needs are known, or the goal may involve data mining where the goal is to discover knowledge, find correlations, determine reliability, or discover anomalies [66]. When the goal is the former and the needed data is well defined, the strategy is to collect exactly what is needed. When the goal is the former, the strategy is to collect as much data as possible to expand the opportunity for discovery. In both cases the goal of integration is to disambiguate and resolve heterogeneity between data sets such that they can be analyzed harmoniously together. This goal can be reached in multiple ways. See Figure 1.2 for a graphical representation that summarizes approaches used to prevent or resolve data heterogeneity.

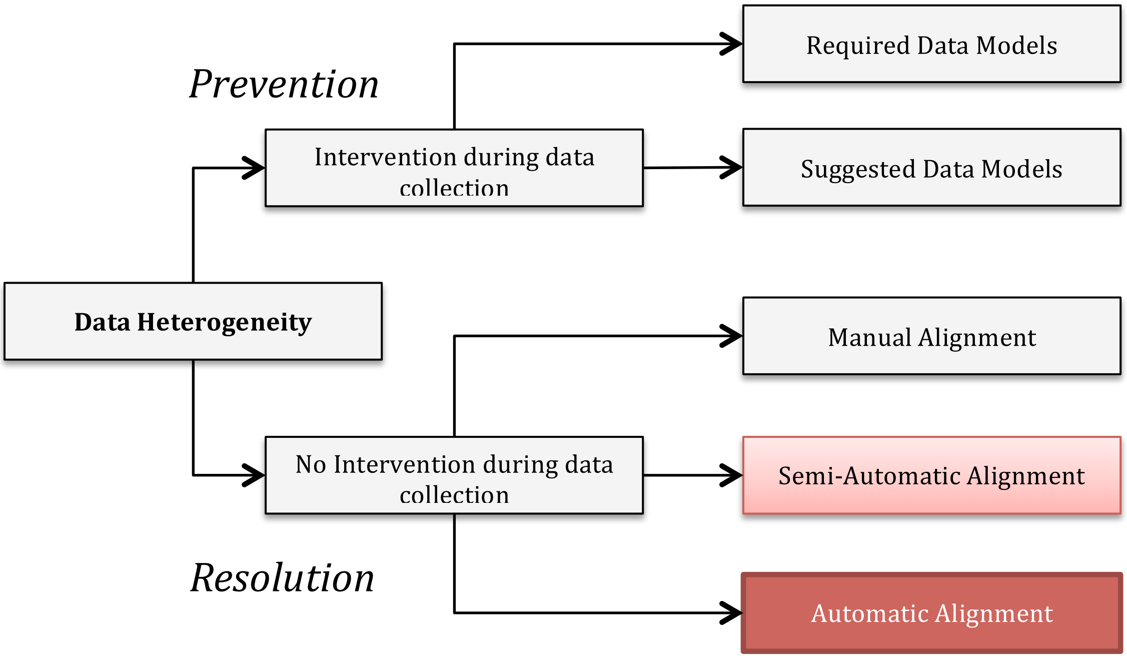


Figure 1.2 Strategies for preventing or resolving data heterogeneity. Automatic and semiautomatic data integration strategies are research topics of this dissertation.

1.4.1 Required Data Models

Data models define the organization of DEs required to represent a domain of discourse. Biomedical systems that do not offer content customization essentially require conformance to a data model and domain of discourse, and then every party that uses the same models will ideally be able to share data much more easily, since most of the heterogeneity issues do not occur; each data set will have the same syntax, same structure, same names, same codes, and therefore the same semantics.

In terms of data models, not all data models provide adequate structure or detail to maximize their value for reuse. A data set with a "diagnosis" DE that has a free-text data type where humans type in a diagnosis, does not contain optimally computable diagnosis data [65, 67]. Amplifying this simple example by modeling a large number of data domains this way equates to sharable data, but these types of data are much less computable and are unsuitable for highly accurate analysis.

Within the biomedical domain, Detailed Clinical Models (DCM) are the basis for clinical data consistency, interoperability, and highly accurate analysis. They are rigorously defined such that they retain computable meaning [68]. Sharable, computable meaning is the basis of shared computable logic [69] for applications such as clinical decision support, clinical trial eligibility criterion, or for computational analysis in general. DCMs make computations possible by providing formal specifications of the logical structure of clinical data, including their terminological specifications for value sets and forms of coded values.

“Required Data Models” is one of the U.S. government’s primary intentions of the HITECH act. The government has incentivized healthcare organizations to support consistent data models such that computable data can be shared between organizations, applications, and systems [14, 35, 70-72]. The potential benefit of embracing and supporting DCMs is significant and there are several ongoing efforts that continue to develop and support DCM-based technologies [73, 74] (http://www.openehr.org), but wide dissemination and utilization of DCMs [22] has never been achieved, despite significant efforts to do so [75]. Utilization of DCMs requires very highly specialized skills that are expensive and hard to find. This, paired with the fact that standards-based approaches often do not cover specialized clinical workflows and practices [76, 77], makes adoption an expensive and time-consuming option; adoption does not guarantee adequate coverage in all domains.

1.4.2 Suggested Data Models

The “Suggested Data Models” strategy is popular with vendor-based EHR systems such as Cerner (Cerner.com) and Epic (www.epic.com) because it has the potential benefits of the “Required Data Models” and also supports flexibility. Implementers can select from the vendor’s data dictionary or they can create new dictionary entries when necessary. This is particularly attractive for organizations with diverse data requirements, but leaves the interoperability issues that DCMs address unresolved since these vendors are not yet supporting DCMs at this point in time. Custom site-specific data will not inherently interoperate between different organizations; the degree of interoperability depends on the degree of customization.

1.4.3 Manual Alignment

Manual alignment implies that experts manually perform the work of heterogeneous data integration, as described for i2b2 in section 1.3.1 and OpenFurther in section 1.3.2. These processes were manual, involving human professionals (versus computer algorithms) who evaluate individual DEs one by one, remembering, classifying, and comparing DEs with other DEs they have encountered. Based on their decisions they must align and move data into their proper slots.

Trained professionals develop data integration skills that may involve any number of technologies or they may utilize off-the-shelf ETL tools, but tools that automatically or semiautomatically resolve the naming and semantic differences are not typically packaged with ETL tools. In the cases of OpenFurther and i2b2, both are designed to support heterogeneous data integration, but neither provides automatic nor semiautomatic data alignment tools.

1.4.4 Semi-automatic Alignment

Semiautomatic alignment occurs when data integration experts use software that identifies and suggests DE alignments. The experts then review the suggested alignments and make alignment decisions. This is highly beneficial since human experts manage complexity more accurately, especially when they have alignment visualization tools. Semiautomatic systems are designed to reduce the amount of time it takes an expert to perform integration tasks, and also improve alignment accuracy over manual approaches. Most “real” algorithm-aided alignment systems are semiautomatic since high alignment accuracy is usually a top requirement and is difficult to achieve with purely automatic methods [78, 79]. The challenges of the “automatic” portion of semiautomatic alignment are outlined in the next section.

1.4.5 Automatic Alignment

Automatic alignment algorithms attempt to align heterogeneous data without human intervention [78-80] and are particularly complex and challenging. The documented reasons are directly related to the data reuse issues described in section 1.2, and especially the data heterogeneity issues previously discussed in section 1.2.3 [27, 61, 78, 79, 81]. The primary topics are as follows:

- Data sets are developed independently for different purposes, resulting in different data structures with overlapping concepts.
- The same elements of a dataset schema may be named differently.

- Semantics are not consistently modeled; they are defined inconsistently using both data model metadata and instance data; ambiguity in semantics and language can be very difficult or even impossible to resolve.
- Metadata and data contain different levels of conceptual granularity.
- Data sets may not contain overlapping concepts.
- Alignment requires both technical expertise and domain-level expertise.
- Metadata is not typically modeled to support computable semantics.
- Lack of documentation and/or domain knowledge makes it difficult to interpret metadata and data [47].

Generally, computing semantic alignments between biomedical data sets relies on metadata, data structures, or language-based strings that are typically not consistent or precise.

Requirements, budgets, and specific technologies dictate the rigor with which biomedical data sets are created and maintained. Data viewed to be of importance for longer periods of time naturally require more documentation and organization. EHR retention requirements are typically based on state laws, but generally require retention for at least 10 years. Data sets created for a single purpose and immediate need may lack the same amount of organization, documentation, or features, such as rich metadata, that assist with data integration. Even for EHR data with the strictest requirements, semantic models have not been widely adopted and significant efforts have been deprecated in some cases due to overly complex and/or misunderstood semantic models [75].

Investing heavily in an implementation-specific data model and/or technology at this point in time is risky. Adopting specific models does not guarantee interoperability until there are others who have adopted the same strategy. This constitutes a lack of incentive and implies that we are left with the reality that computing data set alignments will likely continue to rely on imperfect data models and data for the foreseeable future. Meaningful Use and HITECH will hopefully start to change this direction, but in all likelihood, it will take decades to penetrate the entire market.

1.5 Advancing Methods for Computing Semantic Similarity

Advancing automated methods to semantically align both today's and yesterday's biomedical data sets is currently an important research topic that has the potential for significant returns. Large volumes of heterogeneous biomedical data are growing at an exponential rate that exceeds human abilities to integrate by hand; yet integrating these data contains information that unlocks important unanswered questions of healthcare, such as which treatments are the most effective at curing cancer.

1.5.1 Current Automatic Alignment Approaches

Automatic data integration techniques are based on computing "alignments" between data sets. Data sets are also referred to as "schemas" although there can be subtle differences, depending on the context of the discussion. "Data set" is very generic and does not necessarily imply a specific structure, but in the context of popular spreadsheet software, a data set is a table with columns and rows. "Schema" has a stronger implication of an underlying structure beyond a single table. This distinction is important when deciding on an alignment approach. Approaches vary based on the data and data structure that need to be integrated, the purpose of the integration, and the tools that are available. Figure 1.3 shows the taxonomy of automatic schema matching approaches. This taxonomy not only helps to classify solutions, it also helps to select an approach that is based on the schema/data set parameters of the matching problem.

1.5.2 Contribution of the Dissertation

As we look for opportunities to make a contribution that improves on existing methods, we must also consider what an accomplishable nontrivial contribution is. Upon examination of the matching taxonomy and assuming that the bulk of the market uses relational databases, we decided to focus on solutions that are conducive to DEs as defined by ISO 11179 [82], an abstraction that works well with the relational meta-model and with other common meta-models. These decisions also led to a decision to work at the "Schema-only/Element-level/Linguistic/Name" similarity level of the taxonomy in Figure 1.3. DEs do not include instance data and are not constraint-based models. This also fits the requirement of being nontrivial, because biomedical data linguistics are nontrivial. Moreover, one of the most challenging aspects of the automatic

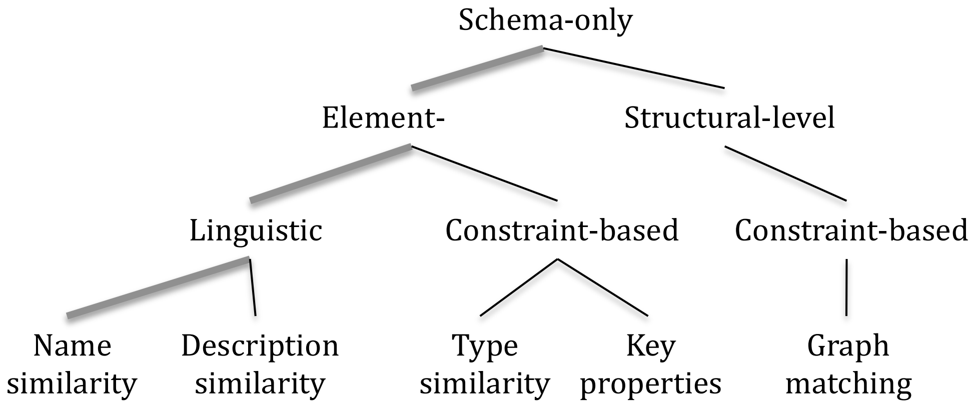


Figure 1.3 Taxonomy of automatic schema-matching schema-only approaches [80]. The bolded lines indicate the automatic matching strategy pursued.

alignment process is computationally solving the semantic "impedance mismatch" [78, 79, 81].

The underlying methods that address semantic impedance mismatches between DEs at the "Schema-only/Element-level/Linguistic/Name" level are algorithms that compute semantic similarity between language-based entities [83]. This is the primary topic and contribution of this dissertation, describing and contributing a new semantic similarity algorithm that computes the semantic similarity between language-based entities.

1.5.3 Dissertation Aims

The aims of this dissertation are as follows:

Aim 1: Introduce a new method for measuring semantic similarity that offers significant advances in biomedical data integration research.

Aim 2: Operationalize aim 1 by eliminating and/or reducing the amount of work required to semantically align heterogeneous biomedical data sets.

Aim 3: Expand, generalize, and measure the new algorithm's ability to compute

a. semantic similarity between medical terms,
b. semantic similarity between clinical notes.

Aims one and two are based on the introduction and explanation of the need for continued research on semiautomatic and automatic data integration research. The two use cases introduced in aim three were added to test the algorithm's boundaries. Measuring degrees of semantic similarity between medical terms tests the algorithm's similarity measurement range more specifically than data set alignment (details in section

4.3). Measuring similarity between clinical notes tests the algorithm on much larger and sophisticated clinical texts (details in Section 4.4).

Each of the 3 applications, performing data set alignments, calculating medical term similarity, and calculating clinical note similarity, are tested using the newly introduced methods as well as with other leading methods that are suitable for each application. This allows us to evaluate how well the new algorithm performs in a variety of scenarios. We also recognize the importance of scalability. To be highly relevant in the biomedical domain, data processing methods need to be highly scalable. Large data set alignment applications require significant computational resources and performance will therefore be addressed and discussed in the study.

1.6 Introduction Summary

In this chapter we have described how important and valuable biomedical data are. We described the primary challenges of reusing and integrating heterogeneous biomedical data. We described two architectural approaches and state-of-the-art tools for integrating and managing heterogeneous data sets. We described and illustrated approaches for integrating heterogeneous data and recognized the need for continued research. And finally, we described the aims of the dissertation and the applications of a new method that will be formally described within.

The rest of the dissertation is organized as follows: Chapter 2 defines semantic measures and describes existing best-of-breed semantic similarity algorithms for each of the 3 applications. Chapter 3 introduces the new algorithms for computing semantic similarity. Chapter 4 is the methods chapter, with a methods section-style description for each application. Chapter 5 contains the results and discussion of application-specific results. And customarily following the results, Chapter 6 contains a general discussion of the concept bag and for all the applications as a whole, followed by the future directions and conclusions of the study.

CHAPTER 2

COMPUTING SEMANTIC SIMILARITY

This chapter reviews the literature on semantic matching algorithms to give context to the research reported here, with emphasis in describing state-of-the-art algorithms used for computing the semantic similarity between biomedical text strings (short texts), controlled vocabulary concepts, text documents (longer texts), and methods that support each of these cases. All methods considered were either unsupervised or semisupervised to support the aim of eliminating or reducing human labor. Supervised methods were considered out-of-scope.

2.1 Semantics

The following definitions are part literal and part interpreted to fit the context of this dissertation. The intention is to disambiguate concepts with varying meanings in the literature. The definitions that help define semantics are as follows:

- Concept – an embodiment of a particular meaning [29]; unit of thought [30].
- Term – linguistic labels used to designate a concept [30].
- Code – a unique identifier used to designate a concept [30].
- Philological relationships – ontological relations between concepts [30].

- Taxonomy – a classification scheme dealing with the description, identification, naming, and organization of biomedical concepts [84].
- Ontology – comprised of concepts, philological relationships, and functions used to describe a domain of knowledge at the semantic level [30, 85]. A taxonomy can be represented in an ontology, but an ontology has the capability to express more sophisticated relationships between entities in a taxonomy.
- Semantic knowledge base – computable semantic networks modeled in controlled vocabularies, taxonomies, ontologies, and/or graphs.
- Semantic relatedness – concepts that are related by semantic interactions without regard for the specific type of semantic link. Example: the concepts for the terms "surgeon" and "scalpel" are related because they are frequently used together, but their meanings are not similar. The measure indicates closeness (versus far) where a high value means close and low value is not close [86].
- Concept similarity - within a semantic knowledge base concepts that are close together in the graph are considered similar [86]. Concepts for "delusion" and "schizophrenia" are close in the SNOMED CT is-a hierarchy, but are not as close as the concepts for the terms "heart" and "myocardium." The concepts for "renal failure" and "kidney failure" are closer together even still; they are synonyms of the same concept and therefore considered semantically equivalent [87]. Methods are discussed more formally in section 2.3.
- Lexical similarity – a measure that indicates lexical unit similarity.

- Lexical units - language-based text entities such as words, sentences, or paragraphs.
- Semantic similarity – a measure implicating a quantity of shared meaning between two compared entities. For the purposes of this work, the similarity of meaning is extrapolated from lexical similarity methods and/or concept similarity methods.
- Semantic distance – a measure indicating how semantically far apart two words, expressions, or documents are without restriction on the actual semantic relationship type; this is the opposite of semantic relatedness [86].

Based on these definitions, the primary focus of this work was to computationally measure semantic similarity between biomedical concept sets. How concept sets are composed is an essential consideration. In the context of biomedical texts, we explore the idea of converting lexical units into sets of concept codes using named-entity recognition software and semantic knowledge bases, and then we measure similarity between these sets using similarity algorithms.

2.1.1 Similarity Algorithms

Similarity algorithms typically employ some kind of systematic strategy for comparing candidate matches where the output of the comparison is a quantitative measurement indicating how similar or dissimilar the match is. Similarity is central to pattern recognition, categorization, memory retrieval, problem solving, and reasoning, and is also the basis of a similarity measurement (SM). SM is formally defined as follows [86]:

$$\sigma_k : E_k \times E_k \rightarrow \mathcal{R}$$

E_k = the set of elements of type $k \in K$

$$K = \{characers, words, concepts, sentences, paragraphs, texts\}$$

$$\mathcal{R} = \{[0,1], \mathbb{R}^+, \{a, b, c \ldots\}\}$$

The basic idea is that two entities of the same type can be compared for similarity (word-to-word, concept code-to-concept code, sentence-to-sentence, etc.) to produce a SM with a value between 0 and 1.

SMs can be normalized to be “dissimilarity measures” such that 0 is “no dissimilarity” and 1 is “complete dissimilarity,” but the “normal” assumption is generally that 0 is “no semantic similarity” and 1 is “perfect” semantic similarity [88]. The reader can refer to additional mathematical definitions of distance and similarity in [86, 88], including comments about the Triangle Inequality [89] and whether or not it must be satisfied to be considered a distance metric. For the purposes of this work, the Triangle Inequality is not a requirement of a SM, based on the argument that many algorithms that do not satisfy the Triangle Equality perform well in practice.

2.2 String Similarity

In the technical community a “string” is an ordered sequence of characters. A word is a string of characters. A sentence is a string of characters. A paragraph is also a string of characters. There are no specific rules or standard size limitations, but database restrictions generally support up to several gigabytes for a single string. Character strings are not specific to language. The information in a DNA sequence can be represented in a string of characters, for example. String similarity algorithms compare character sequences to measure character pattern similarity. When one is interested in computing semantic similarity between biomedical language-based character strings, lexical and concept similarity methods can be used independently or in conjunction [90].

The n-gram method is frequently used to measure string similarity and is described in detail first, since it is the basis for many of the string similarity algorithms that follow.

2.2.1 The n-gram Method

The n-gram method is a foundational text-mining method. The method applies to many applications, including mining biomedical words and language [91-94]. It is a generic method for decomposing strings into smaller units of text. It is not a measurement, but its output is used as the basis for measurement. The "n" in n-gram represents a number and "grams" represent textual units. Textual units or "chunks" may be defined in character-based units as single-character "unigrams," or two-character "bigrams," or three-character "trigrams," and so on. Or, units may be represented in words, sentences, paragraphs, and so forth. In the case where n > 1, a sliding window approach is used. The "window" is made up of n chunks and slides from left to right one chunk at a time to create each gram of text. Figure 2.1 illustrates the sliding window for character and word-based n-grams in 6 different n-gram patterns.

The n-gram patterns shown in Figure 2.1 appear to be ordered but sets do not inherently maintain order. Interestingly, the method responds to the order of things due to the way the sliding window works. See Figure 2.2 and notice how two sentences with exactly the same words and different word orders do not have any trigrams in

Text:	"John Doe has a history of pneumonia"
Character unigram:	j, o, h, n, d, e, a, s, i, t, r, y, f, p, u, m
Character bigram:	jo, oh, hn, do, oe, ha, as, a, hi, is, st, to, or, ry, of, pn, ne, eu, um, mo, on, ni, ia
Character trigram:	joh, ohn, doe, has, a, his, ist, sto, tor, ory, of, pne, neu, eum, umo, mon, oni, nia
Word unigram:	John, Doe, has, a, history, of, pneumonia
Word bigram:	John Doe, Doe has, has a, a history, history of, of pneumonia
Word trigram:	John Doe has, Doe has a, has a history, a history of, history of pneumonia

Figure 2.1 Example character and word-based n-grams. Note that each set of n-grams is a set in the mathematical sense where set elements are not duplicated when there are multiple occurrences, e.g., it is correct that there is only one 'o' in the character unigram example when there were four in the original text.

Text 1:	"John Doe has a history of pneumonia"
Text 2:	"pneumonia of history a has Doe John"
Trigram 1:	John Doe has, Doe has a, has a history, a history of, history of pneumonia
Trigram 2:	pneumonia of history, of history a, history a has, a has Doe, has Doe John

Figure 2.2 Compare two word-based trigrams containing exactly the same words except that words in Text 2 are in reverse order of Text 1. None of the trigram set elements match, illustrating how the method is sensitive to word order when n > 1; "history a has" is not equal to "has a history," for example.

common. If character-based unigrams were selected, transposing words would have no effect. In the case of unigrams order is completely lost, but in all other cases both character and word order do impact n-grams, illustrating how they are sensitive to order.

2.2.1.1 Strengths of n-grams

Character-based n-grams are useful for detecting words that are spelled similarly. This makes it a good strategy for detecting slight misspellings and/or slight word variations (see Figure 2.3).

As previously mentioned, n-grams are not language-specific. Strings of any type can be split apart into more granular chunks and analyzed at a more granular level for subpattern comparison and analysis using a similarity formula such as the Jaccard Similarity algorithm [95]. The Jaccard Similarity formula is as follows:

$$\text{Jaccard Similarity } (S1,S2) = |S1 \cap S2| \,/\, |S1 \cup S2| \qquad [2.1]$$

The n-gram method, for example, applies to comparing biological sequence strands [96-100]. See examples in [101] to observe how n-grams of different configurations can be used to compare genetic sequences to identify DNA-binding proteins where example formulas are presented to compute the optimal "n."

There are many options for analyzing n-grams. Algorithms such as the Jaccard Similarity algorithm (equation 1) can be applied to compute the ratio of matching elements, or more sophisticated, vector-based approaches may be used such as the bag-of-words method [102-107]. Prediction algorithms use n-gram corpora to establish

Comparing “brain” and “brainy”

Character bigram S1 = br,ra,ai,in
Character bigram S2 = br,ra,ai,in,ny
Jaccard(S1,S2) = 4/5 = .80

Character trigram S3 = bra, rai, ain
Character trigram S4 = bra, rai, ain, iny
Jaccard(S3,S4) = 3/4 = .75

Word unigram S5 = brain
Word unigram S6 = brainy
Jaccard(S5,S6) = 0/2 = 0

Figure 2.3 Example unigrams, bigrams, and trigrams and how they are used to decompose strings that are then compared using the Jaccard Similarity algorithm to compute similarity between two similar words; each n-gram method yields a different result.

probabilities that are used for predicting character-occurrence and word-occurrence patterns [93, 108]. Character pattern prediction may be used for suggesting error corrections [107] and for determining word senses [109]. Whatever the case may be, the point is, the method used to analyze the output of n-grams is an implementation-specific choice, and there are many options.

2.2.1.2 Limitations of n-grams

The different types of n-grams have different limitations performing approximate matching. Character-based grams, such as bigrams, are good at detecting words that have similar character sequences, but do not detect semantic similarity between words that are not spelled similarly, dissimilarly spelled synonyms like “doctor” and “physician,” for example. Neither do they detect the difference in meanings between homonyms like the word “cold” as in “I have a cold” versus “It is cold outside.” Character-based n-grams can only detect similarity when character sequences are similar.

Word-based n-grams are sensitive to word spellings. A single letter difference between word-based unigrams, bigrams, or larger, and comparisons will not match. This is a limitation when approximate word matching is desired. When n > 1, word-based n-grams are also sensitive to word order (see Figure 2.3 for a concrete example). Generally speaking, recognizing word order is a positive feature, but from a purely logical viewpoint, cases exist where strict adherence to word order eliminates or reduces the possibility of valid approximate matches.

As has been described and demonstrated, the n-gram method is the basis of many different text-mining applications, including for mining semantics via string-similarity and document-similarity algorithms. Several techniques that use the n-gram method to compute semantic similarity are described in the following sections.

2.2.2 Dice

The Dice coefficient, also referred to as the Sorenson Index [95, 110], computes lexical similarity between language-based entities . The Dice method is similar to the bigram version of the n-gram method paired with the Jaccard similarity formula, but Dice's similarity formula is slightly different. The Dice coefficient is twice the intersection of bigrams divided by the sum of the bigram set cardinalities, as follows:

$$\text{Dice Similarity} = 2|X \cap Y| \,/\, (|X| + |Y|) \qquad [2.2]$$

The Jaccard Similarity formula does not double the intersection in the numerator, and the denominator is a sum of the union of the bigram sets. Dice is a semimetric variant of Jaccard since it obeys all of the mathematical "axioms of metrics" except for the Triangle Inequality. The Dice method essentially adds extra weight to the similarity measure when grams match.

The Dice algorithm has been used in bioinformatics for medical term matching [94] and is often a top performer for DE matching [111-113].

2.2.3 Levenshtein

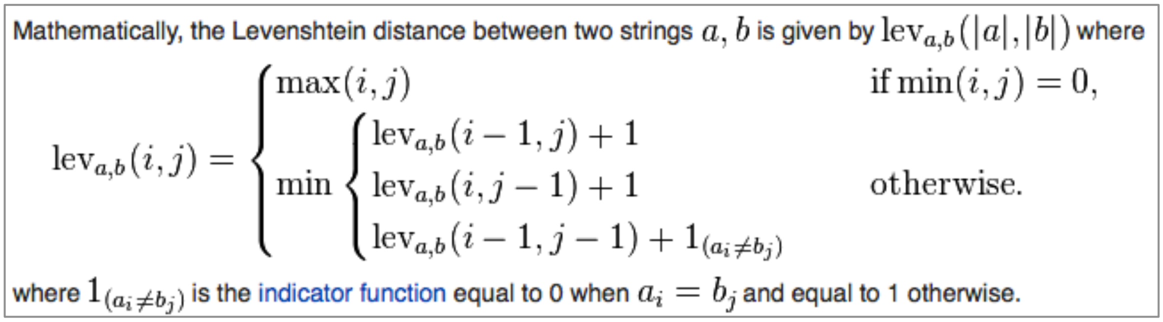
The Levenshtein string distance algorithm, also known as the "edit distance," is also a lexical similarity method. The Levenshtein method calculates the number of single-character substitutions, deletions, or insertions it would take to change one string into the other [114, 115]. Zero edits indicate that strings are exactly the same. The edit distance is converted to a similarity score between 0 and 1 as follows:

Levenshtein Similarity = 1 – number of edits/lowest possible edits.

The full algorithm is shown in Figure 2.4. The algorithm is not complex but is computationally expensive and therefore is generally recommended for short string comparisons.

2.2.4 Jaro-Winkler

The Jaro-Winkler string distance and lexical similarity measure, shown in Figure 2.5, is generally used to compare short strings and has been successfully applied to automated person-record linkage [116]. As the name implies, Jaro published a portion [117] and Winkler published an add-on [118]. The Jaro portion calculates the weighted

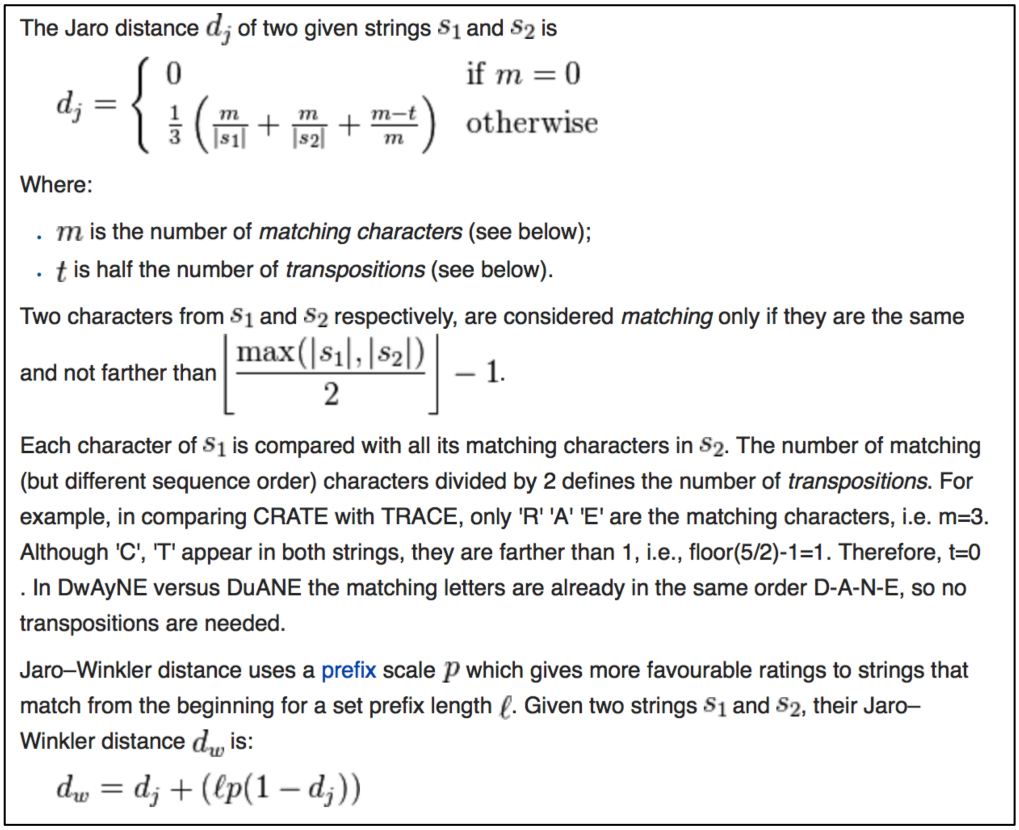


Mathematically, the Levenshtein distance between two strings a, b is given by $\operatorname{lev}_{a,b}(|a|,|b|)$ where

$$\operatorname{lev}_{a,b}(i,j) = \begin{cases} \max(i,j) & \text{if } \min(i,j) = 0, \\ \min \begin{cases} \operatorname{lev}_{a,b}(i-1,j)+1 \\ \operatorname{lev}_{a,b}(i,j-1)+1 \\ \operatorname{lev}_{a,b}(i-1,j-1)+1_{(a_i \neq b_j)} \end{cases} & \text{otherwise.} \end{cases}$$

where $1_{(a_i \neq b_j)}$ is the indicator function equal to 0 when $a_i = b_j$ and equal to 1 otherwise.

Figure 2.4 Levenshtein string distance algorithm. Taken from [115], with permission.



The Jaro distance d_j of two given strings s_1 and s_2 is

$$d_j = \begin{cases} 0 & \text{if } m = 0 \\ \frac{1}{3}\left(\frac{m}{|s_1|} + \frac{m}{|s_2|} + \frac{m-t}{m}\right) & \text{otherwise} \end{cases}$$

Where:

- m is the number of *matching characters* (see below);
- t is half the number of *transpositions* (see below).

Two characters from s_1 and s_2 respectively, are considered *matching* only if they are the same and not farther than $\left\lfloor \frac{\max(|s_1|,|s_2|)}{2} \right\rfloor - 1$.

Each character of s_1 is compared with all its matching characters in s_2. The number of matching (but different sequence order) characters divided by 2 defines the number of *transpositions*. For example, in comparing CRATE with TRACE, only 'R' 'A' 'E' are the matching characters, i.e. m=3. Although 'C', 'T' appear in both strings, they are farther than 1, i.e., floor(5/2)-1=1. Therefore, t=0 . In DwAyNE versus DuANE the matching letters are already in the same order D-A-N-E, so no transpositions are needed.

Jaro–Winkler distance uses a prefix scale p which gives more favourable ratings to strings that match from the beginning for a set prefix length ℓ. Given two strings s_1 and s_2, their Jaro–Winkler distance d_w is:

$$d_w = d_j + (\ell p(1 - d_j))$$

Figure 2.5 Jaro-Winkler algorithms. Taken from [119], with permission.

sum of the percentage of matched characters between each text and transposed characters. The Winkler portion then increases the similarity value when initial characters match and rescales the value by a piecewise function with configurable intervals and weights. These configurations make the algorithm tunable and able to support strings with different characteristics.

2.3 Concept Similarity

Concept similarity is different than the word-based lexical similarity methods. “Concept” implies that a semantic knowledge base is involved with the similarity computation, a semantic graph, for example, that is utilized to measure similarity. Path-based measures (PBM) evaluate the paths between two concepts where paths are based on conceptual nodes and edges of a semantic knowledge base graph structure. A short path implies concepts are very similar and conversely a long path implies concepts are far apart and less similar. Several variations are explored in the following sections.

Many concept similarity algorithms also incorporate different kinds of measures based on information content (IC). IC can be obtained from semantic knowledge base structures (intrinsic IC) or from existing text corpora (corpus IC) [120]. Intrinsic IC measures may use additional information from concepts in the path, such as how many nodes a given concept is related to [121], whereas a PBM alone does not, it only considers the number of nodes between two concepts. Corpus IC measures use information gained from a corpus such as the probability a given word occurs near another word [87]. Such probabilities can be used as weights of PBM. Examples and variations of IC measures and PBMs follow in the next sections.

2.3.1 Pedersen: Path

The most basic PBM is simply called "Path" [87], as it defines similarity between two concepts, c_1 and c_2, as the inverse of the shortest path length, p, as follows:

$$sim_{Path}(c_1, c_2) = \frac{1}{p} \qquad [2.3]$$

This measure gives equal weight to each node transition in the path, no matter where it exists in the graph, and does not consider IC of the nodes.

2.3.2 Leacock and Chadorow: LC

Leacock and Chadorow (LC) proposed a PBM that asserts deeper concepts in the semantic knowledge base graph are more specific, contain more IC, and should carry more semantic weight. To add weight to deeper nodes, the ratio of path length, p, to the depth, d, of the concept in the graph is computed [122] as follows:

$$sim_{LC}(c_1, c_2) = \log(2d) - \log(p) \qquad [2.4]$$

2.3.3 Wu and Palmer: WP

Wu and Palmer (WP) [123] is also a PBM that adds to the Path measure by weighing the depth of the least common subsumer (LCS) rather than the total depth. The LCS is the lowest level node both concepts have in common. The WP method scales the LCS by the length of the path between the two concepts as follows:

$$sim_{WP}(c_1, c_2) = \frac{2 * depth(LCS(c_1, c_2))}{p - 1 + 2 * depth(LCS(c_1, c_2))} \qquad [2.5]$$

2.3.4 Resnik: Concept Frequency

Resnik proposed another method that incorporated both IC and path-based information. His method incorporated concept frequency weights obtained from an existing corpus [124] with structured semantic knowledge. The IC of a concept, c, is as follows:

$$IC(c) = -\log\left(\frac{frequency(c)}{frequency(root)}\right) \qquad [2.6]$$

Corpus concept frequent weight is essentially the concept specificity that becomes the weight of each semantic concept or node in the graph. This assures a concept with high IC is very specific, while lower IC values are associated with more general concepts. The similarity function for IC is as follows:

$$sim_{Resnik}(c_1, c_2) = IC(LCS(c_1, c_2)) \qquad [2.7]$$

This equation implies the IC of the shared LCS of the evaluated concepts represents the similarity of the two concepts. One of the criticisms of this approach is that it does not consider the depth of the compared children under the LCS [87].

2.3.5 Lin Similarity

Lin goes a step further and adds IC based on individual concepts [88] rather than for the shared LCS of both concepts, as Resnik proposed to consider the depth of the concepts under the LCS. Lin's similarity calculation was as follows:

$$sim_{Lin}(c_1, c_2) = \frac{2 \cdot IC(LCS(c_1,c_2))}{IC(c_1)+IC(c_2)} \qquad [2.8]$$

For the sake of fitting it into a category, the Lin similarity measure is a PBM combined with intrinsic IC.

2.3.6 Caviedes and Cimino: CDist

The concept distance (CDist) algorithm is a PBM that uses relationships in the UMLS to find the shortest path between two concepts in the UMLS [125]. The UMLS manages multiple semantic knowledge bases in a relationship table (MRREL) where specific terminology relationships are queried to determine all possible path lengths between concepts. The shortest path length between two concepts determines the similarity score. CDist utilizes both the hierarchical structure of UMLS and IC contained within UMLS to compute path lengths and is therefore considered a PBM and IC-based method.

2.3.7 Personalized PageRank: PPR

The PageRank algorithm is a published portion of the Google Search engine [126] and was created by one of Google's founders, Larry Page. The algorithm estimates the importance of a website based on the idea that important websites are linked to by other websites. A probability vector (probability distribution) contains nodes (websites) and each has a score representing the portion of time a random visitor will stay. The Personalized PageRank (PPR) algorithm adds probability mass to specific websites to artificially direct traffic. Website advertisers, for example, pay Google to add weight to their website (node in the graph) so they are ranked very highly in Google searches.

The same principles apply to conceptual graphs represented in biomedical vocabularies. Graphs are created where vertices are concepts and edges are semantic relationships. A probability vector is computed for each concept using PPR, where random jumps are weighted toward the modeled concept. Semantic similarity is computed using the cosine of the angle between two concept probability vectors [121].

Both intrinsic and corpus IC techniques can be used to create probability vectors. Intrinsic IC can be calculated using SNOMED CT. Concepts that have more links are weighted more than those that do not since they have a higher probability of being "visited." Corpus IC can also be used to calculate probability vectors based on corpus co-occurrence probabilities.

2.3.8 Pedersen: Context Vector

The Concept Vector strategy is a corpus IC measure based on the idea that words that are frequently near each other are also semantically related. To identify words that are often together, co-occurrence word vectors are created from a corpus of text. Co-occurrence between two words occurs when a word is within a specified window of another word. Using a controlled vocabulary and thesaurus, additional terms are identified and concept mappings are added to word vectors. UMLS concept terms are then added to the word vectors to create context vectors. The similarity between a pair of concepts is defined as the cosine of the angle between their context vectors [87].

2.4 Document Similarity

Document similarity methods became particularly popular and relevant in the early 1990s, when the Internet started to grow at a rapid pace and search engines became big business. The main use case was to match a user's search to the most relevant documents, a 2 or 3-word search phrase to a collection of documents, each containing hundreds or thousands of words. Today the use case is still the same, except that scalability requirements have changed. Big Data document collections contain Petabytes or even Exabytes of data, emphasizing the importance of algorithm specificity and scalability [127]. Searching sophisticated biomedical texts adds to the challenge.

Outside of searching for relevant documents, the operational use cases for document similarity algorithms are limited. The most common unsupervised methods that are utilized for document similarity use cases follow in the next sections.

2.4.1 Shingling

The Shingling method is a lexical similarity method that compares documents for similarity using the n-gram method and Jaccard similarity [128]. "Shingles" are word-based unigrams, bigrams, or trigrams and are the typical units of comparison. Whole documents are shredded into n-grams and n-grams are compared as sets to determine similarity. It is very simple to understand and implement but is not as scalable as vector-based methods. It is slightly different than the Bag-of-words approach [129]. The Shingling method is more flexible. The Bag-of-words approach is the same as when Shingles are unigrams, but Shingles can be configured as bigrams or trigrams, for example.

2.4.2 TF-IDF

TF-IDF, or “term-frequency inverse document frequency,” is based on the Vector space model [130] and the Bag-of-words model [129] and is based on lexical similarity methods. Words from a body of text are each assigned a position in a vector. The value of any given word’s position in the vector is the inverse-document frequency (IDF) value for that word in the document. Documents that have been converted to vectors are compared for similarity by assessing the angle between the two document’s vectors using the cosine similarity function. When the angle between the two vectors is small, the compared texts are similar. Conversely, the documents are dissimilar according to larger angles.

TF-IDF is a very popular “Google-like” strategy that scales very highly into the Big Data realm. It is also the basis for the “Lucene” document indexing software [131]. Document queries are very fast and accurate even with huge volumes of document data.

2.4.3 LSA

Latent Semantic Analysis (LSA) is a technique used to analyze relationships between documents based on their lexical patterns. LSA is also based on the Vector space model and Bag-of-words model, but uses dimension-reduction techniques (singular value decomposition) to create a reduced space. Similarities are computed in the reduced space where document vectors and term vectors are both in the same vector space, implying more sophisticated searching capabilities. Not only can document term vectors be compared (as with TF-IDF), but document vectors can also be compared with other document vectors, term vectors with other term vectors, and term vectors with document vectors. Additionally, new combined term-document vectors can be "folded in" or added to the vector space to augment the space [132].

In practical terms, LSA adds the ability to search for "cardiac" and find documents that have the word "heart" or other related terms instead. This is a result of LSA's term-to-term vector composition that would relate "cardiac" and "heart" (assuming they occurred frequently together in the text). Then, comparing these highly similar term vectors with document vectors, all documents similar to the term vectors are retrieved. This example demonstrates a term-term and term-document vector similarity comparison, and more sophisticated utilization of the vector space is also possible. Document-document similarity comparisons are utilized for clustering, for example [133].

2.5 Named Entity Recognition

Named entity recognition (NER) software mines language-based text and identifies concepts from ontologies that contain additional computable semantic knowledge; therefore, biomedical text-mining applications use NER software to extract and enhance biomedical texts. For example, the concept "Oxycodone" mined from a text document could be part of an ontology that asserts "Oxycodone is-a pain medication" and "Oxycodone is-a controlled substance." After making these associations, searches for "pain medications" and "controlled substances" would return this document. Associating concepts to texts has a wide variety of useful applications [134-136] for text mining applications.

2.5.1 Open Source NER Tools

2.5.1.1 MetaMap

The NLM has developed MetaMap [137, 138] for NER and offers it for free. MetaMap is backed by the UMLS [139] and the UMLS' USAbase default vocabulary set. The USABase is made up of freely available vocabularies that do not have license restrictions in the USA. See categories 0, 4, and 9 online in the MetaMap UMLS Source Vocabulary instructions [140].

2.5.1.2 cTAKES

The clinical Text Analysis and Knowledge Extraction System (cTAKES) is an open source text-processing tool that utilizes the Unstructured Information Management Architecture framework and OpenNLP to generate linguistic and semantic annotations. As the name indicates, cTAKES is tuned for clinical text and the generated annotations are useful for higher-level semantic processing [141].

2.5.1.3 Sophia

Sophia software has been recently released (in 2014) [142]. It was developed for Veteran Affairs and the famous VINCI database with over 2.8 billion clinical notes that would theoretically take years to process using MetaMap or CTakes. Authors claim their solution is state-of-the-art based on its highly scalable architecture, faster throughput, and improved precision over MetaMap. The precision of cTAKES is barely higher (+ 0.04 F-score), but Sophia is 18 times faster.

The described set of similarity measures in this chapter represents a set of primary strategies used to compute semantic similarity between biomedical texts with different size and length characteristics. Additionally, biomedical semantic knowledge base utilization techniques and NER tools were briefly described since they play a significant role in the methods that are described in following chapters, where the new method for computing concept bag similarity is introduced and methods for testing the algorithms are described.

CHAPTER 3

THE NEW CONCEPT BAG ALGORITHMS

In a graduate-level data-mining course at the University of Utah, the professor, Dr. Jeff Philips, challenged the students to do a real data-mining project for the final project. With recent exposure to a particularly challenging biomedical data integration project and newly acquired data-mining skills, the new Concept Bag (CB) algorithm was composed based on the recognition that n-grams and named-entity recognition (NER) software could be used together to create comparable concept bags rather than word or character-based bags. This chapter describes the idea, the CB and Hierarchical Concept Bag (HCB) algorithms, and provides examples.

3.1 Concept Bag Conception

The CB method, like the n-gram, was designed to be multipurposed. The original use case was to perform automatic data integration between highly heterogeneous biomedical datasets collected from 5 large academic medical centers across the U.S.A.; in all, the combined datasets contained 899,649 unique DEs from 20,724 research datasets (see section 4.2.7.1).

Further inspection and analysis of the large number of DEs and datasets revealed DEs were in the form of variable-length biomedical expressions where synonyms, abbreviations, and other textual anomalies appeared frequently. Existing matching solutions all had something to offer, string matching, concept matching, and document matching, but the problem appeared to require a combination of techniques, techniques that would disambiguate synonyms and common abbreviations used by medical professionals.

Disambiguating synonyms and abbreviated terms such as “SBP” and “systolic BP” to a common concept code is a specialty of biomedical NER tools and was therefore one of the first recognized components of the solution. The second realization came shortly thereafter during a pilot study that was conducted to study if NER was a feasible method for processing metadata. The pilot study revealed that NER essentially produced a bag of concept codes for each text. What could be done with a bag of concept codes? Recognizing the parallel with the n-gram method and how it produced bags of things that could be compared many ways, we recognized CBs could be compared using the same methods. Further research and analysis of computable similarity methods confirmed its uniqueness and the study of the new method began.

3.1.1 Creating Concept Bags

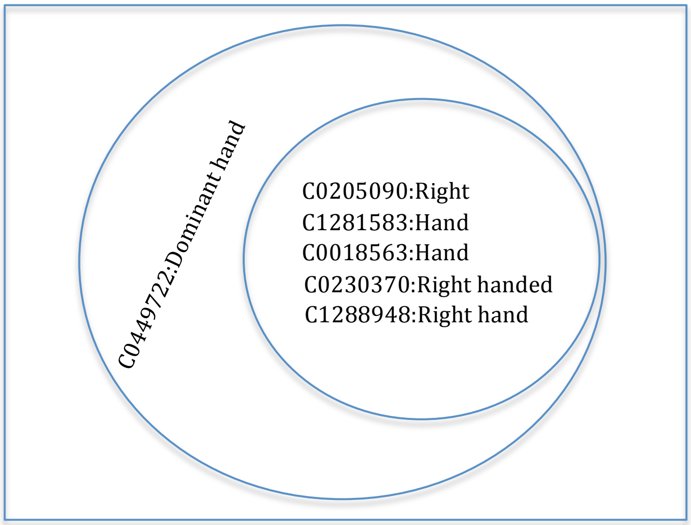
To operationalize and test the CB method, MetaMap [137, 138] was the NER tool utilized for experimentation. MetaMap fulfilled the requirements and supported a rich set of biomedical vocabularies and ontologies with literally millions of computational semantic relationships, is free, is supported by the NLM, and is well understood by the biomedical text mining research community. Using MetaMap as the NER tool, the stepwise process used to create CBs was as follows:

1. Textual elements were organized and saved in a comma-delimited (CSV) file where each row contained one textual element and a unique identifier (primary key for the text).
2. Each textual element was processed using MetaMap's default dictionaries and parameter settings, with the exception of the output flag that directs MetaMap to output XML, because XML is conducive for automated concept code extraction [138].
3. Capture the XML output from step 2 for each row and extract each of the distinct concept codes (CUIs) from the XML file.
4. Write the distinct concept codes from step 3 to a new row in another CSV file with the same unique identifier used in step 1.
5. Each row in the file created in step 4 contains the CB for a textual element.

To compare CBs for similarity, the Jaccard Similarity formula (Equation 1 in section 2.2.1.1) was selected for the initial experiments. The Jaccard formula computes a decimal value between 0 and 1 where 0 represents no similarity, and 1 represents a perfect match. Values between 0 and 1 represent the ratio of the matching concept codes. Interpretation of the similarity score is left to the application and its purpose. Figure 3.1 demonstrates the idea visually with an example.

3.2 Hierarchical Concept Bags

The CB's NER method resolves strings such as “SBP” and “systolic BP” to the same concept, recognizing synonymy between the two strings, but the method does not consider similarity between words such as “abortion” and “miscarriage” where they are



S_1 = MetaMap("right handed")
= [C1281583, C0018563, C0205090, C0230370, C1288948]

S_2 = MetaMap("dominant right hand")
= [C1281583, C0018563, C0205090, C0230370, C1288948, C0449722]

Jaccard(S_1,S_2) = $|S_1 \cap S_2|/|S_1 \cup S_2|$
= |C1281583, C0018563, C0205090, C0230370, C1288948| /
|C1281583, C0018563, C0205090, C0230370, C1288948, C0449722|
= 5/6 = 0.83

Figure 3.1 Venn diagram illustrating Concept Bag code sets for "right handed" and "dominant right hand. " The concept bags are compared using the Jaccard Similarity formula (equation 1 in section 2.2.1.1). The alphanumeric concepts (UMLS CUIs) were extracted using MetaMap and the SNOMEDCT_US dictionary.

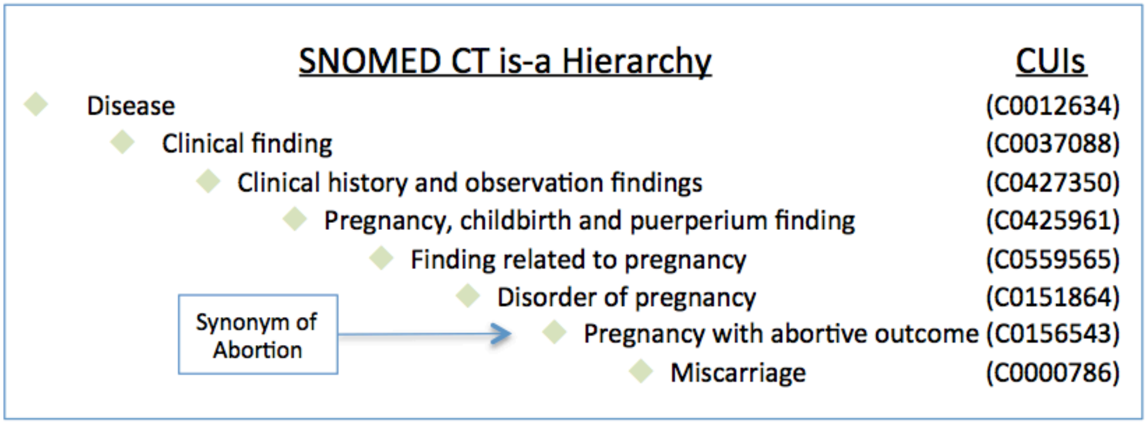
spelled very differently, are not synonyms, and are semantically similar according to terminology experts [87]. Recognizing the flexibility of the CB method, we could see that CBs could be enhanced with additional concept codes by using relationships from the semantic knowledge base that MetaMap's output CUIs are a part of. MetaMap discovers concept codes (CUIs) in the texts that are associated with a variety of semantic relationships contained in the UMLS and source vocabularies. This presents the opportunity to utilize these added semantics to further expand CBs. HCBs are CBs that have been enhanced with hierarchical semantic concept codes that have been obtained from the UMLS' semantic knowledge base.

To demonstrate the HCBs, the SNOMED CT "is-a" relationships were selected as the knowledge resource to extract hierarchical concepts for this work, but nothing precludes using other philological relationships (although the name of the method might need to be reconsidered if nonhierarchical relationships were selected). SNOMED CT contains well over 100 different relationships [143, 144]. UMLS version 2015AA contains 153 different relationships that could be utilized in a similar fashion. We chose the "is-a" relationship for practical reasons. The "is-a" relationship conceptually implies similarity and every SMOMED CT concept is included in the hierarchy (an acyclic directed graph), which is not true for any of the other relationships. Some of the next most frequently used SNOMED CT philological relationships are "episodicity," "clinical-course-of," "has-severity," "has-finding-site," "causative-agent," and "has-active-ingredient." These relationships have between 5% and 25% coverage; each could add to the sophistication of a similarity measure, especially for specific use cases, but each added relationship requires analysis and would require additional research to fully understand. For example, adding "episodicity" concept codes for every concept in a given bag may add noise in some cases, whereas adding "clinical-course-of" concept codes may add specificity in others. To expand, one might consider forming composite codes between the codes and relationships to retain the semantics in the bag of codes (composing codes for "causative-agent" and "streptococcus pneumonia" such that problems having "causative-agent streptococcus pneumonia" are similar). The possibilities of what could be done are endless. As with the other CB methods, the idea of enhancing CBs using externally defined philological relationships is intentionally left as a generic strategy, leaving the implementation-specific details to the implementer such that the method could apply to other use cases or domains of knowledge. The UMLS contains literally hundreds of controlled medical vocabularies, domain topics, and knowledge structures, and each can vary drastically. Plus, there is a plethora of other sources that UMLS does not contain, WordNet [145], for example, is another popular option that does not specialize in biomedical vocabulary but is a rich source, nevertheless.

3.2.1 Adding Hierarchical Semantics to Concept Bags

Using the CB method previously described, controlled vocabulary concepts are extracted from the text using NER tools first. Then the next and new step is to select and insert the conceptual hypernym hierarchy (demonstrated using an is-a hierarchy) into the HCBs for each text analyzed. The very top level of the hierarchy, the SNOMED CT root concept code, in this case, was left out, as it did not add information. If multiple vocabulary sources were being utilized, the root concept code may have been useful. Figure 3.2 illustrates how the CB is used to build the HCB with visual aids.

Creating HCBs from CBs adds new dimensions and possibilities, and like the NER tool implementation, does require a specific method of analysis. The next section provides diagrams and a specific example to illustrate this point.



SNOMED CT is-a Hierarchy — CUIs

- Disease (C0012634)
  - Clinical finding (C0037088)
    - Clinical history and observation findings (C0427350)
      - Pregnancy, childbirth and puerperium finding (C0425961)
        - Finding related to pregnancy (C0559565)
          - Disorder of pregnancy (C0151864)
            - Pregnancy with abortive outcome (C0156543)
              - Miscarriage (C0000786)

CB_1 = ConceptBag(“abortion”) = C0156543
CB_2 = ConceptBag(“miscarriage”) = C0000786

HCB_1 = HierarchicalConceptBag(“abortion”)
= C0037088, C0012634, C0427350, C0425961, C0559565, C0151864, C0156543

HCB_2 = HierarchicalConceptBag(“miscarriage”)

= C0037088, C0012634, C0427350, C0425961, C0559565, C0151864, C0156543, C0000786

Jaccard(CB_1, CB_2) = 0
Jaccard(HCB_1, HCB_2) = 8/9 = 0.89

Figure 3.2 Examples of the CB and HCB with hierarchical concept codes (CUIs) from the SNOMED CT is-a hierarchy comparing “miscarriage” and “abortion.” The “Parents” figure shows the hierarchies (SNOMED CT is-a hierarchy is poly-hierarchical) and all of the UMLS clinical concepts for both “miscarriage” and “abortion.” The Jaccard Similarity (equation 1 in section 2.2.1.1) scores illustrate the differences between the two methods.

3.2.2 Method Diagrams

The CB and subsequent HCB are intended to be generic alternatives to the n-gram method that can similarly be configured in many different ways to support a variety of use cases. In this section we diagram the idea to illustrate this point, see Figure 3.3. Figure 3.4 illustrates two different similarity implementations using the previous example from Figure 3.2.

Additional drawings based on Figure 3.3 are illustrated in the following section for each of the implementations tested. They are all based on comparing medical texts of

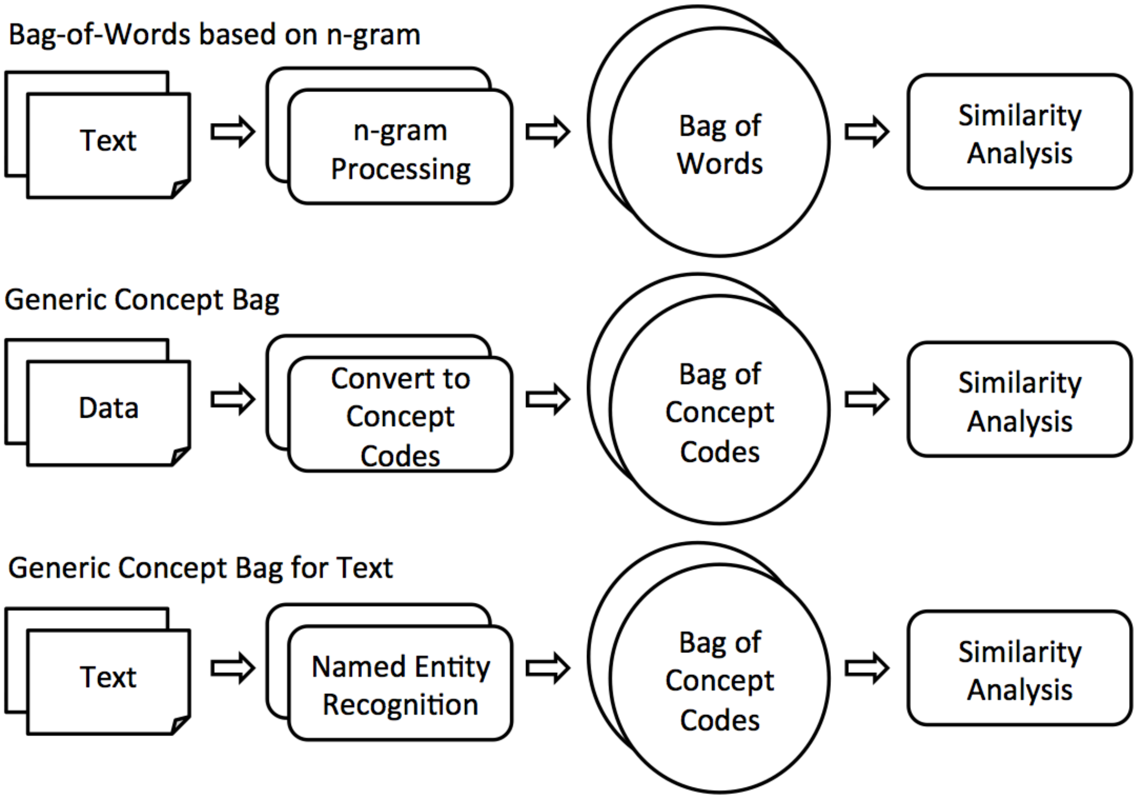


Figure 3.3 Concept Bag method comparison diagrams illustrating how a bag-of-words (or character strings) produced by the n-gram method compares to the Generic Concept Bag method. The Named-Entity Recognition component is added to derive bags of concept codes from text.

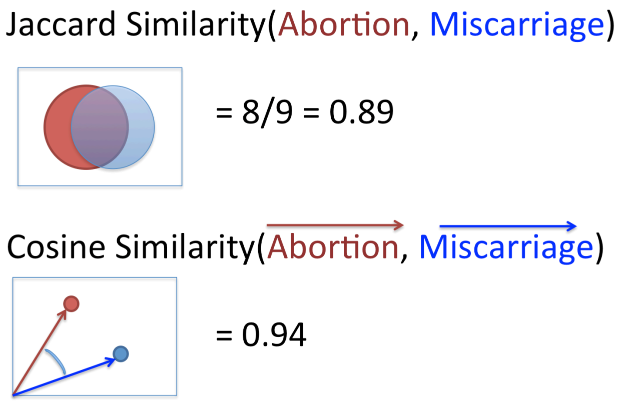

Jaccard Similarity(Abortion, Miscarriage)
= 8/9 = 0.89
Cosine Similarity($\overrightarrow{\text{Abortion}}$, $\overrightarrow{\text{Miscarriage}}$)
= 0.94

Figure 3.4 Demonstrating two different similarity implementations comparing the same Hierarchical Concept Bag codes.

different types, but as the middle diagram in Figure 3.3 implies, the "Convert to Concept Code" method could be based on nontextual processes, as well, such as billing or procedure codes derived by human coders.

As the figures and diagrams show, HCBs and CBs can be analyzed in nearly all the same ways text-based n-grams are analyzed, using any of the methods available in the literature.

CHAPTER 4

APPLICATIONS OF THE CONCEPT BAG

A new method needs to be tested rigorously in a variety of use cases. The three use cases chosen here to meet this goal were, 1) the application of aligning heterogeneous data elements (DE), 2) measuring degrees of similarity between medical terms, and 3) measuring patient case similarity between intensive care unit (ICU) discharge instructions. Four data sets were used to test the three use cases as follows:

1. DEs from a controlled vocabulary (see section 4.2.5),
2. DEs from an uncontrolled vocabulary (see section 4.2.7),
3. A medical term pair similarity benchmark (see section 4.3),
4. Deidentified ICU discharge instructions (see section 4.4).

4.1 Descriptive Analysis

A descriptive analysis was performed on each of the four data sets to describe their characteristics and to facilitate comparisons between data sets. The following textual features were tabulated and reported:

- Textual element counts - the individual DEs, medical terms, and ICU discharge summaries,
- Character count means,

- Word count means,
- Concepts per element means,
- Concepts per word means.

Each of the data sets was managed in a relational database and structured query language (SQL) queries were utilized to compute these statistics.

4.2 Application: Aligning Data Elements

4.2.1 Semantic Alignment of Data Elements

Integrating heterogeneous data sets involves semantically aligning DEs between data sets. The goal was to test the new algorithm on the task of semantically auto-aligning DEs. Optimally no humans would be required; suboptimally, human intervention would be required, but less than without assistance with other existing methods. The decision to focus on the automatic mapping challenge had implications on the chosen matching strategies. There are literally an unlimited number of possible kinds of data alignments required to map data sets, and the possibilities are specific to the purpose of the alignment, the alignment language, and the capabilities of the alignment interpreter. We chose to focus this portion of the study on the most universally supported and well-understood alignment, "equals," or more specifically, "is semantically equivalent," and focus on the semantic matching component rather than specific alignment implementations.

Identifying semantically equivalent matches does not imply that only perfect similarity scores were acceptable and that there is not an acceptable amount of fuzziness; it implies that the goal of interpreting fuzziness is to identify semantically equivalent matches; aligning DEs that have different names but exactly the same semantic meanings, such as “first name” and “given name,” was the goal. We did not attempt to automatically align partial matches that require specific functional interpretations, such as “patient name” and “first name.” This may not seem complicated for a human who is mapping familiar names (versus names from another country or language), but the alignment operation for this use case is quite complicated since it requires specific knowledge about the data that is rarely in computational form. The algorithm must consider the direction of the alignment, mapping “patient name” to “first name,” or vice versa, “first name” to “patient name,” or possibly the direction is known and specified. The algorithm must determine whether the first word of “patient name” is the first name, last name, middle name, first part of the first name, first part of the last name, etc. Moreover, neither did we attempt to automatically align semantically related (see definition in section 2.1) DEs, such as “scalpel” and “surgical procedure,” for similar reasons. This level of functional interpretation was considered out-of-scope for this work. Determining that DEs are semantically related is one problem, auto-aligning them in a computationally “meaningful” way is a different problem that is very use-case specific.

The taxonomy of automatic alignment techniques outlined in Section 1.5.1 can be summarized into 4 types, 1) “name-based techniques” where the focus is aligning entity names; 2) “structural techniques” where the focus is matching data structures and data types; 3) “extensional techniques” where the focus is matching instance data; 4) “semantic techniques” where intermediate ontologies are used as entity “anchors” to merge others entities [33]. Two of these alignment techniques were utilized for this portion of the study, the name-based technique and the semantic technique. The name-based technique was the primary strategy used for each of the tested algorithms, including the CB, but the CB also used the semantic technique by utilizing intermediate ontology concept codes to anchor concepts based on existing semantic relationships. The other two methods were not used. As is often the case, neither of the DE data sets (described below) contained rich structural information; therefore, structural techniques were left for future study. Extensional techniques did not apply either; they were simply not an option since instance data (containing patient/subject data) were not available.

Additional preparation techniques were used to normalize the DE names before they were compared. Exact string matches were counted and removed to avoid duplicate comparisons. Also, strings were duplicated and converted to uppercase to support case-insensitive comparisons, i.e., duplicate DEs and letter cases did not influence the results.

4.2.2 Aligning Data Elements with Similarity Algorithms

Recalling that similarity algorithms return a real value score between 0 and 1 that indicates how similar two given DEs are (1 = perfect similarity, 0 = no similarity), to make the alignment decision, a cutoff score must be selected. Cutoff scores determining the alignment decisions are algorithm-specific. Each similarity algorithm's score distribution can be very different. One algorithm's score of 0.5 might represent a very high probability of equivalence, while it might represent a very low probability using a different algorithm.

Cutoff scores were computed using decision analysis. Using a reference standard, scores that maximized the specificity and sensitivity of the decision were chosen for each algorithm. This strategy is called the "Youden" method [146].

4.2.3 Measuring Alignment Compliance

The alignment compliance measures how well alignment strategies agree. DE alignments are essentially decisions, and alignment compliance is a form of decision analysis. The reference alignment is a gold standard set of alignments typically curated by experts and is intended to be compared with algorithm-generated alignments. The decision analysis in this case was performed using standard confusion matrix statistics.

Confusion matrix decision analysis statistics were computed using R statistics software with the “ROCR” [147] and “Optimal Cutpoints” [146] packages. The ROCR package specializes in building Receiver Operator Curves (ROC) for viewing classifier performance. The Optimal Cutpoints package computes optimum cutoff points and reports confusion matrix statistics. Using these R packages, the following alignment compliance results were reported: optimal cut-points, sensitivity, specificity, true positive (TP), false positive (FP), false negative (FN), positive predictive value (PPV), negative predictive value (NPV), area under the curve (AUC). The F-measure was also computed using the recall (sensitivity) and precision (PPV) values for each algorithm.

4.2.4 Alignment Algorithms Tested

A total of five unsupervised string similarity algorithms were applied to the task of aligning DEs, the CB, the HCB, and three well-known unsupervised string similarity algorithms, Dice [95, 110] (see Section 2.2.1), Levenshtein [114] (see Section 2.2.3), and Jaro-Winkler [117] (see Section 2.2.4). Each of these latter three algorithms has an established string-matching track record matching biomedical concepts and DEs [94, 111, 148]. The CB and HCB method implementations are diagramed in Figure 4.1. These

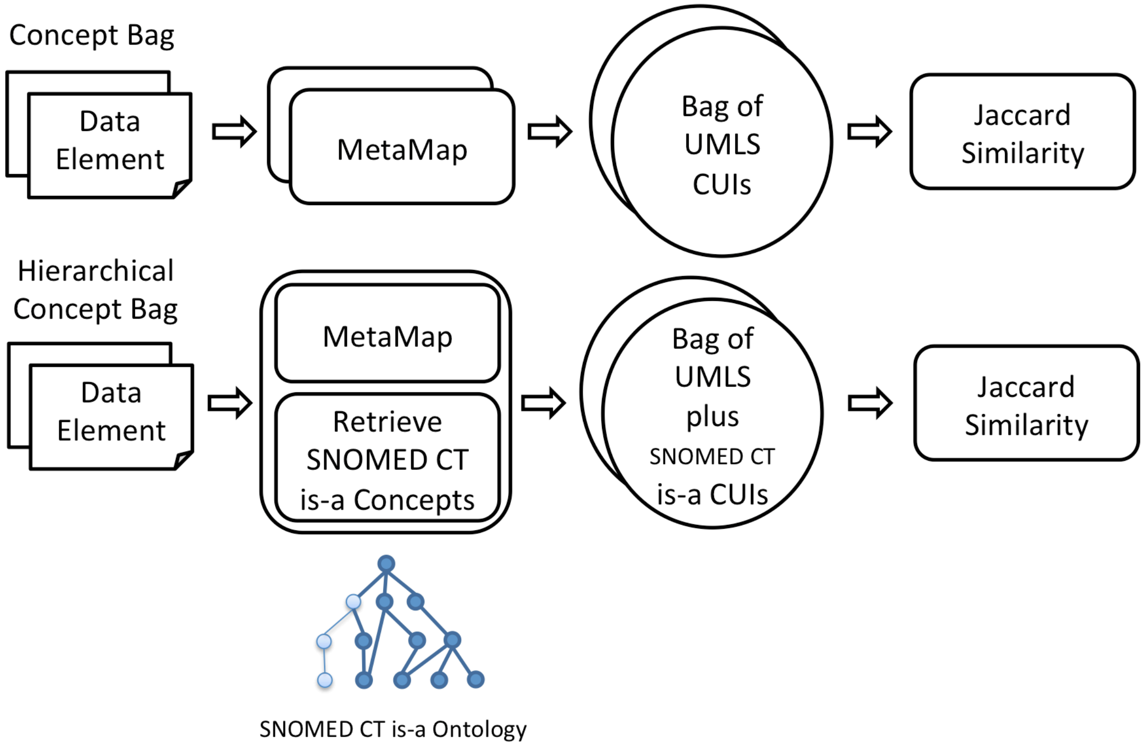


Figure 4.1 Concept Bag and Hierarchical Concept Bag implementations used for the Data Element alignment use case.

diagrams are extensions of the diagrams previously shown in Figure 3.3. Alignment compliance statistics were measured and reported for all five algorithms on two DE data sets. A description of each DE set is given in detail below.

4.2.5 Data Set: UMLS Data Elements

Seventeen DEs from three domains were selected for the study, seven demographics, five vital signs, and five echocardiogram measures. All 17 DEs were found in the UMLS by searching for their common names. Then, using existing semantic relationships in the UMLS, all distinct English synonyms were extracted, adding an additional 298 semantically matching DE names. This process generated an additional

298 DE names stemming from the original 17 totaling 315 distinct DEs by name (298+17). The selected DEs and small sample of synonyms and abbreviations were included in Table 4.1.

4.2.6 Reference Alignment: UMLS Data Elements

Reference alignments were identified using UMLS synonym relationships for all of the DE names selected and identified in UMLS. UMLS synonym relationships were curated by the original terminology contributors and by UMLS experts. For example, the DE name “SBP” and “systolic blood pressure” were synonyms mapped by terminology experts and were counted as an exact semantic match with an alignment score equal to 1. DE names that were not synonyms within the UMLS were considered nonmatching and were assigned alignment scores equal to 0. The reference alignment was a complete list of all DE pairs with alignment scores of 0 or 1. There were a total of 49,455 pairs (315*(314)/2) in the reference alignment.

4.2.7 Data Set: REDCap Data Elements

Aim two of the study is to improve upon previous methods that semantically align heterogeneous biomedical data sets. To obtain a representative set of heterogeneous data sets we utilized datasets created using REDCap [149]. REDCap, or Research Electronic Data Capture, is software developed at Vanderbilt for managing research projects and data capture. It is free and has become very popular, with over 1500 installations worldwide at this point in time. REDCap uses the “Suggested Data Models” strategy and

Table 4.1 Seventeen common data elements including example synonym terms extracted from UMLS.

Data Elements and UMLS Terms			
Topic	**Data element**	**Term count**	**Example terms**
Demographics	Date of birth	15	birth date, date of birth of person cared for, DOB
	Sex	7	gender, sex of individual
	Ethnicity	26	ethnic background, ethnic group
	Race	14	human race, racial stock
	Address	13	address, physical address, addresses
	Primary language	2	language primary
	Education level	43	education, academic achievement
Vital Signs	Body temperature	28	temp, temperature, body temperature
	Pulse rate (beats/minute)	14	pulse, heart rate
	Blood pressure	50	arterial blood pressure, arterial tension
	Respiratory rate	25	breathing rate,0 breath rate
	Oxygen saturation	21	O2 saturation, oximetry
Echo Cardiogram Measures	LVEF (%)	5	left ventricular ejection fraction, left ventricular ejection fraction (finding)
	LVIDd (cm)	2	diastolic left ventricular internal diameter
	LVH (y/n)	43	ECG LVH, electrocardiogram left ventricular hypertrophy
	Septum thickness (mm)	4	atrial septum thickness, echocardiography: thickness of atrial septum
	echoPASP (mmHg)	3	pulmonary artery main branch systolic pressure

it was suspected that the data models suggested were rarely used. A pilot study confirmed this suspicion. The REDCap installation at the University of Utah was analyzed, and less than 1% of the projects used one or more of the recommended models, none of which had been operationalized beyond a few records that appeared to be for testing.

Beyond recognizing the potential for heterogeneous data, the other reason we chose REDCap was for its large and unpredictable domain of discourse. In the pilot study we also discovered that the U had collected over 313 data sets and 39,129 DEs in 18 months of use. As this work originated as a data-mining exercise, the goal was to collect as many data sets as possible from more than one site to discover potential relationships and test the algorithm's scalability [66]. A highly scalable and accurate DE alignment algorithm would provide potentially useful enhancements for projects such as dbGap [150] or other large collections of scientific data (http://www.nature.com/sdata/).

REDCap sites that were engaged in clinical and translational research were contacted via email and asked to contribute DEs from their sites. No patient or subject-sensitive data were required or requested, only the defining elements of their data sets, the DEs. Five collaborating institutions responded to the email request and submitted 899,649 DEs, 1) University of Utah School of Medicine, 2) Einstein College of Medicine, 3) Duke University, 4) University of Colorado Denver, 5) Children's National Medical Center.

REDCap data sets followed a key-value-pair data pattern, where keys were synonymous with column names and values were synonymous with data cells in a table row. REDCap's alphanumeric column keys (somewhat cryptic) were linked to additional DE metadata, including informal data types and display-formatting information. In particular, the “element label” was an attribute used to label columns and field names on data-entry forms and reports. For example, “q1_rbc” was the alphanumeric key name for an element labeled “Red blood cell count.” Element labels contained human readable language with complete words and expressions and were chosen to represent DE names from REDCap.

All DE properties were hand-authored for each REDCap project. Specific user identifiers were not collected for the study, but it is important to recognize this set represents the number of researchers that it took to author 899,649 DEs; it must have at least been in the order of a few thousand individuals.

4.2.7.1 Preprocessing REDCap Data Elements

The contributed DEs were loaded into a relational database for the initial analysis. A total of 899,649 unique DEs were contributed from the five sites. Letter cases were removed for case insensitive comparisons, but all other textual features were left in their original form. DEs were then processed using MetaMap and the extracted concepts were stored and associated to each DE.

4.2.7.2 Aligning Data Elements via the Concept Bag

Concept bags were compared for similarity using the Jaccard Similarity formula. This process required n(n-1)/2 comparisons, or approximately half a trillion comparisons. The University of Utah’s Center for High Performance Computing was required to complete this large number of comparisons. A special parallel matching [151] Java program was designed to work with the Message Passing Interface (MPI) [152] to compute a virtual matrix of all comparisons. Essentially the MPI was configured to pass instructions to a job (Java programs), indicating to each a specific portion of the matrix to compute. While each job computed its specific portion of the matrix, it would write the similarity scores and matrix coordinates to a file. At the end of the process all files were aggregated using Linux utilities for analysis. One of the benefits of this strategy is that more jobs and CPUs can be added to reduce computing time. It is also highly scalable due to the fact that similarity computations can be dynamically subdivided and executed in parallel tasks based on the available computing resources.

4.2.7.3 Reference Alignment: REDCap Data Elements

Preliminary exploration of the computed comparison data indicated that match candidates were infrequent, 3 per 1000 pairs, indicating an unreasonably large random sample would have been required for human review while maintaining both an accurate sample distribution and conclusive confidence interval; therefore, a stratified random sample was assembled with 12 buckets based on the computed Concept Bag Similarity scores, 10 buckets distributed between 0 and 1 (0 < score <= 0.10, 0.10 < score <= 0.20, … , 0.90 < score < 1.0), plus one bucket where the scores equaled 0, and another bucket where scores equaled 1. A set of 1200 DE pairs were then randomly sorted and manually reviewed for semantic matches by a professional clinical data architect. The alignments identified by the architect were used as the reference alignment.

4.2.8 Comparison of Alignment Performance

In this work we compare alignment performance and calculate the potential savings. The “%Savings” (Equation 4.2 below) represents the percentage of errors that were corrected by the CB over the next-best algorithm. It is also the percentage of additional manual mappings that would have been required to create a perfect alignment. Error percentages and savings were calculated as follows:

$$Alignment\ Errors = \frac{(False\ Positive + False\ Negative)}{|Alignment\ Tasks|} \qquad [4.1]$$

$$\%Savings = \frac{Alignment\ Error_{second} - Alignment\ Error_{best}}{100} \qquad [4.2]$$

This strategy is the equivalent of evaluating and comparing matching accuracy [153] between the top two evaluated systems and the percentage of work saved between the two systems.

4.2.9 Summary of Data Element Analysis

Both of the two DE data sets, the UMLS DEs and the REDCap DEs, were analyzed by first computing the descriptive statistics described in Descriptive Data Element Statistics. Then, each set was tested against its designated reference alignment to measure alignment compliance. Both the descriptive and alignment compliance statistics were reported in the results, and then interpreted in the discussion section.

4.3 Application: Semantic Similarity Between Medical Terms

Aligning DEs challenged the CB algorithms' ability to identify exact semantic matches but did not measure its ability to identify partial semantic matches. Computing partial concept similarity is potentially useful for terminology development, decision support, information retrieval, document retrieval, or patient cohort identification [86, 87, 125].

To test how well CB and HCB perform on partial semantic matches, a published concept similarity benchmark was utilized [87]. The benchmark contained a set of 30 medical term pairs that have been curated and judged by physicians, terminologists, and informaticists. The pairs were systematically selected to test a full range of similarity comparisons. Correlation scores between the annotators and several concept similarity algorithms have been published and stand as a recognized benchmark [87, 120].

Four implementations of the CB and HCB were tested using the benchmark. The first two are the same as shown in Figure 4.1, and the third and forth are shown in Figure 4.2. In the third and forth implementations, MetaMap was restricted to SNOMED CT and the highest-ranking match. The author resolved ties, leaving a single SNOMED CUI hierarchy for comparisons.

Each of the 4 similarity algorithm configurations produced similarity values for each of the 30 pairs from the benchmark data. Correlations were measured and compared to the expert benchmark between the four CB algorithm configurations above and the 7 highest-correlating algorithms published in [120]. The compared concept similarity algorithms and the supporting knowledge bases they used were as follows:

1. Leacock and Chadorow (LC) [122] with UMLS

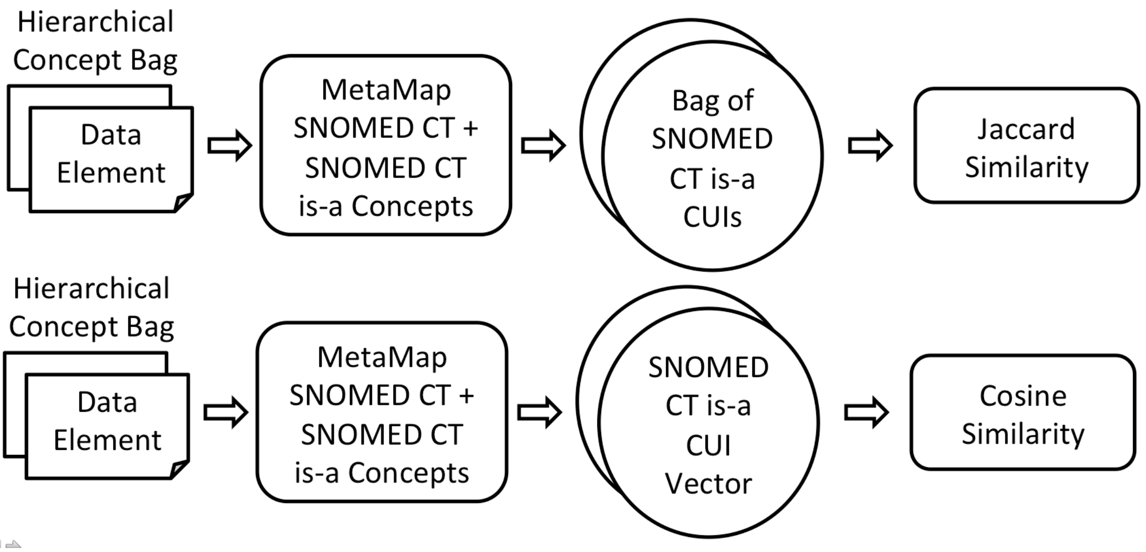

Hierarchical Concept Bag
Data Element
MetaMap SNOMED CT + SNOMED CT is-a Concepts
Bag of SNOMED CT is-a CUIs
Jaccard Similarity
Hierarchical Concept Bag
Data Element
MetaMap SNOMED CT + SNOMED CT is-a Concepts
SNOMED CT is-a CUI Vector
Cosine Similarity

Figure 4.2 Third and fourth implementations of the Concept Bag and Hierarchical Concept Bag algorithms tested in the medical term similarity study (Figure 4.1 shows the first and second).

2. LC with SNOMED CT
3. Wu and Palmer (WP) [123] with UMLS
4. WP with SNOMED CT
5. Personalized PageRank (PPR) [121] with UMLS
6. PPR with SNOMED CT
7. Context Vector [87].

The Dice coefficient [95, 110] was also included to compare one of the top-performing lexical methods with the concept similarity methods.

4.4 Application: Matching Discharge Summaries

The next application was to test the CB on larger bodies of clinical text, namely clinical documents. The operational use case is matching discharge summaries for similarity such that clinicians could "find patients like mine" using clinical text similarity as a proxy for patient similarity. For this purpose we used an online resource, the MIMIC-II online database [154] tools and services, and it offered deidentified intensive care unit (ICU) discharge summaries from 2001 to 2007. Access was requested via an online request process. The requirements were straightforward; standard research training and affiliations were required but IRB approval from the University of Utah was not necessary. The MIMIC-II IRB was as follows [155]:

> This study was approved by the Institutional Review Boards of Beth Israel Deaconess Medical Center (Boston, MA) and the Massachusetts Institute of Technology (Cambridge, MA). Requirement for individual patient consent was waived as the study did not impact clinical care and all data were deidentified.

Our request for access to the data was granted within 2 days. A light amount of reading was necessary to learn how to use the provided online query tools, but this process was straightforward and the resource proved to be valuable for research.

One thousand randomly selected electronic text-based ICU Discharge Summaries (DS) were downloaded from the MIMIC-II database. DSs were deidentified within the MIMIC-II database but were otherwise fully intact. Patient and provider data had been removed and dates were randomly offset by the same random offset keeping time intervals between events accurate; patient ages and other time range lengths were computable when they were not explicitly stated.

4.4.1 Discharge Summary Benchmark

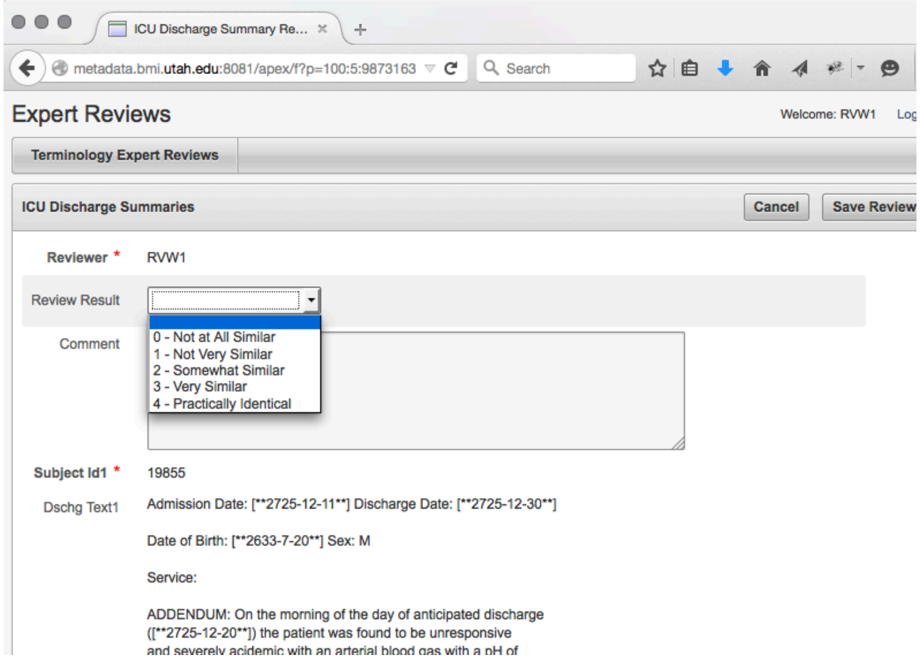
One hundred random pairs were assembled from the 1000 DSs that were downloaded. Two biomedical terminologists manually reviewed each pair. They were given specific instructions on how to login to the secure web site and how to judge each pair of DSs for similarity. For the review, they were instructed to "...[rank the document similarity] to indicate to other clinicians there are common features between these ICU visits that are worth/not worth observing for the sake of case comparisons." Reviewers were given choices from a 5-point Likert scale to mark how similar the DSs were (see Figure 4.1). Reviewers were also given the chance to add comments when they could not decide. Comments and answers were stored in the relational database for reference.

4.4.2 Discharge Summary Similarity Comparator Algorithms

The CB and HCB algorithms were compared with terminologists, Dice [110], and TF-IDF [156]. Dice is a specific form the n-gram method (see section 2.2.1), is a form of Shingling (see section 2.4.1), and performs well comparing DEs [111]. TF-IDF performs well matching "documents." Evaluating and comparing the performance of each algorithm on the much larger DSs provides additional evidence about where the textual boundaries are for each algorithm. The CB and HCB implementations used were the same two that were used in both of the previous studies, 1) MetaMap with Jaccard Similarity, and 2) MetaMap with hierarchical SNOMED CT CUIs and Jaccard Similarity. They are diagramed in Figure 4.3.

4.4.3 Algorithm Correlation Analysis

Similarity measures were computed between the 100 randomly selected DS pairs using the CB, HCB, and comparator algorithms. Two terminologists reviewed the same 100 DS pairs to provide human-expert comparisons. Correlations between all similarity measurements were then calculated between each algorithm and expert. The R statistics software was used to measure correlation via the Spearman method.



Reviewer * RVW1

Subject Id1 * 19855

Dschg Text1 Admission Date: [**2725-12-11**] Discharge Date: [**2725-12-30**]

Date of Birth: [**2633-7-20**] Sex: M

Service:

ADDENDUM: On the morning of the day of anticipated discharge ([**2725-12-20**]) the patient was found to be unresponsive and severely acidemic with an arterial blood gas with a pH of

Figure 4.3 The application used to perform ICU Discharge comparisons for similarity. A small portion of the first discharge summary is shown and the second follows below it (not shown).

CHAPTER 5

RESULTS

The results of the use cases discussed in Chapter 4 are presented in this chapter. The previous chapter, Chapter 4, served as the methods chapter and, in general, is where the reasoning for the chosen methodologies was documented. Also, within this chapter specific sections are referenced to help the reader find the supportive text. In other cases, we restate assumptions and specific values. We also included elements of the results-specific discussion into this chapter for the same reason. The general discussion, future directions, and conclusions are contained in Chapter 6.

5.1 Descriptive Statistics for Studied Data Sets

This section contains the descriptive statistics for the four studied data sets, 1) the UMLS data elements (DE) used for the DE alignment study, 2) the REDCap DEs used for the alignment study, 3) the medical term similarity benchmark used to test degrees of semantic similarity, and 4) the intensive care unit (ICU) discharge summaries used to measure patient case similarity.

The descriptive statistics show that each of these data sets had different textual features such as characters per element, words per element, and controlled vocabulary coverage. These measurements are useful for comparing corpora and for identifying the contexts where algorithms perform well and where they do not. Comparing the textual features of the studied data sets (Table 5.1), one can see that each of the data sets had rather different textual characteristics. The text size averages varied from 13.4 to 2347.5 characters per element, while the mean number of concepts per word varied from 1.0 to 3.2. These statistics confirm that our goal to test the new Concept Bag (CB) and Hierarchical Concept Bag (HCB) methods on dissimilar data sets could be accomplished using the selected data sets. The results for each method can then be used to make some generalizable conclusions on the advantages and disadvantages of using CB and HCB for different types of data sets.

Table 5.1 Descriptive statistics for the studied data sets, UMLS-selected DEs, REDCap DEs, the medical terms reference, and the ICU discharge summaries.

	Data sets			
	UMLS DEs	REDCap DEs	Medical Terms	ICU Discharge Summaries
Element Counts	315	899649	60	200
Mean Characters/Element	24 +/- 13.1	43.1 +/- 74.9	13.4 +/- 6.0	2347.5 +/- 1111.2
Mean Words/Element	3.1 +/- 1.5	7.1 +/- 11.8	1.6 +/- 0.7	308.8 +/- 164.6
Concepts/Data set	380	4187	133	7177
Hierarchical Concepts/Data set	753	6929	740	19685
Mean Concepts/Element	9.8 +/- 6.7	10.4 +/- 10.0	2.6 +/- 1.9	316.0 +/- 150.7
Mean Concepts/Word	3.2 +/- 1.8	2 +/- 1.4	1.5 +/- 0.6	1.0 +/- 0.2
Mean Hierarchical Concepts/Word	15.6 +/- 11.0	12.8 +/- 14.5	20.0 +/- 14.3	2.8 +/- 0.6

5.2 Data Element (DE) Alignment Compliance

Heterogeneous DEs from two DE corpora were aligned using multiple algorithms. Alignment compliance measures are based on decision analysis where algorithm alignments are compared to expert alignments. The expert's alignments are in the form of binary decisions (align = true or false). Algorithm-based similarity measures are not inherently binary, they are real values between 0 and 1; therefore, to compare the two, the algorithm measures must be converted into binary decisions by selecting an appropriate cutoff such that they can be compared with the expert's decisions. Once converted, the alignment compliance analysis was performed.

Alignment compliance of the controlled (UMLS) and uncontrolled (REDCap) DE vocabularies is depicted in the following tables and graphs. Tables for each data set contain the confusion matrix results and statistics for each algorithm. Receiver operator characteristic (ROC) curves are plotted and graphed for each data set and each algorithm to show the performance results graphically.

5.2.1 UMLS and REDCap Data Elements

Section 4.2.5 describes the methods that were used to obtain the UMLS DEs as well as how the alignment statistics were obtained. Similarly, Section 4.2.7 contains information about REDCap DEs and the methods that were used to obtain the REDCap DE alignment results. Both data sets were compared with three comparable methods from the literature; they are contained in Table 5.2 and Table 5.3 for UMLS and REDCap, respectively. The ROC curves follow in Figure 5.1 and Figure 5.2, respectively.

The 315 UMLS DEs are synonyms and abbreviations of 17 DEs (see Table 2.1)

Table 5.2 UMLS DE alignment statistics for each algorithm including standard confusion matrix statics, the Optimum Cutoff points used as the similarity score decision points, the area under the curve (AUC), and the F-measure.

Measure	Dice	Lev	Jaro	CB	HCB
Opt Cutoff	0.25	0.24	0.61	0.04	0.02
Sensitivity	0.80	0.68	0.71	0.86	0.82
Specificity	0.91	0.82	0.79	0.96	0.93
PPV	0.50	0.29	0.27	0.73	0.57
NPV	0.98	0.96	0.96	0.98	0.98
FP	4031	8083	9352	1573	3031
FN	981	1596	1456	701	911
AUC	0.88	0.80	0.82	0.92	0.89
F-meas	0.61	0.41	0.39	0.79	0.67

Table 5.3 REDCap DE alignment statistics for each algorithm including standard confusion matrix statics, the Optimum Cutoff points used as the similarity score decision points, the area under the curve (AUC), and the F-measure.

Measure	Dice	Lev	Jaro	CB	HCB
Opt Cutoff	0.49	0.45	0.73	0.91	0.92
Sensitivity	0.88	0.78	0.75	0.85	0.91
Specificity	0.79	0.81	0.82	0.89	0.86
PPV	0.27	0.26	0.27	0.41	0.37
NPV	0.99	0.98	0.97	0.99	0.99
FP	235	214	200	118	151
FN	12	21	24	15	9
AUC	0.89	0.85	0.81	0.92	0.91
F-measure	0.41	0.39	0.39	0.55	0.53

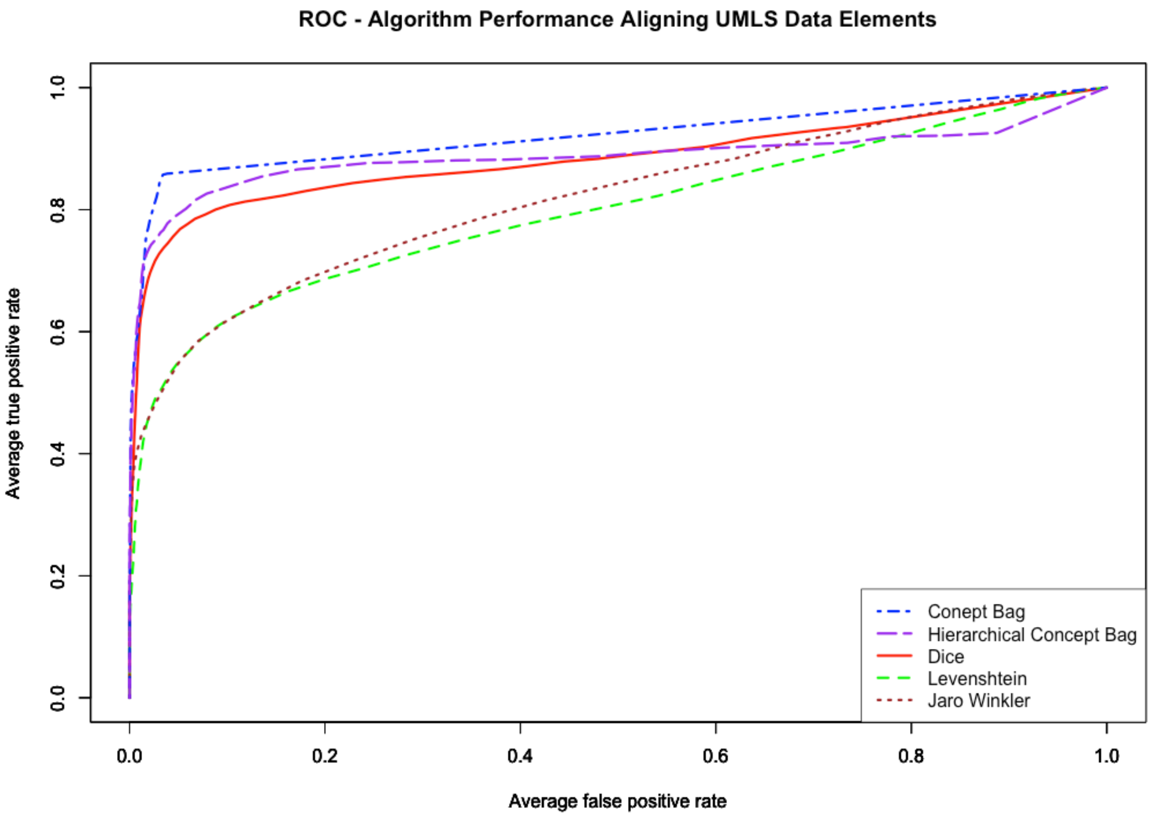


Figure 5.1 ROC curve of the UMLS DE alignment algorithm performance. Curves closest to the top left corner are the best performers.

and the intention of this data set was to test and tune the CB and HCB algorithms. The reference alignment was simple to create using the UMLS relationships to determine semantic alignments. The chances of success were higher than they would likely be for data sets collected in the wild, but it was a great way to test and observe the algorithms.

The optimal cutoff score range is 0 <= cutoff score <= 1 (same as the similarity measurement range), and indicates what the semantic similarity score needs to be to decide to align or not align the tested DE pair. The CB and HCB have very low cutoffs for the UMLS set (Table 5.2) and this indicates that even a slight similarity score is sufficient to confidently decide to make the alignment decision.

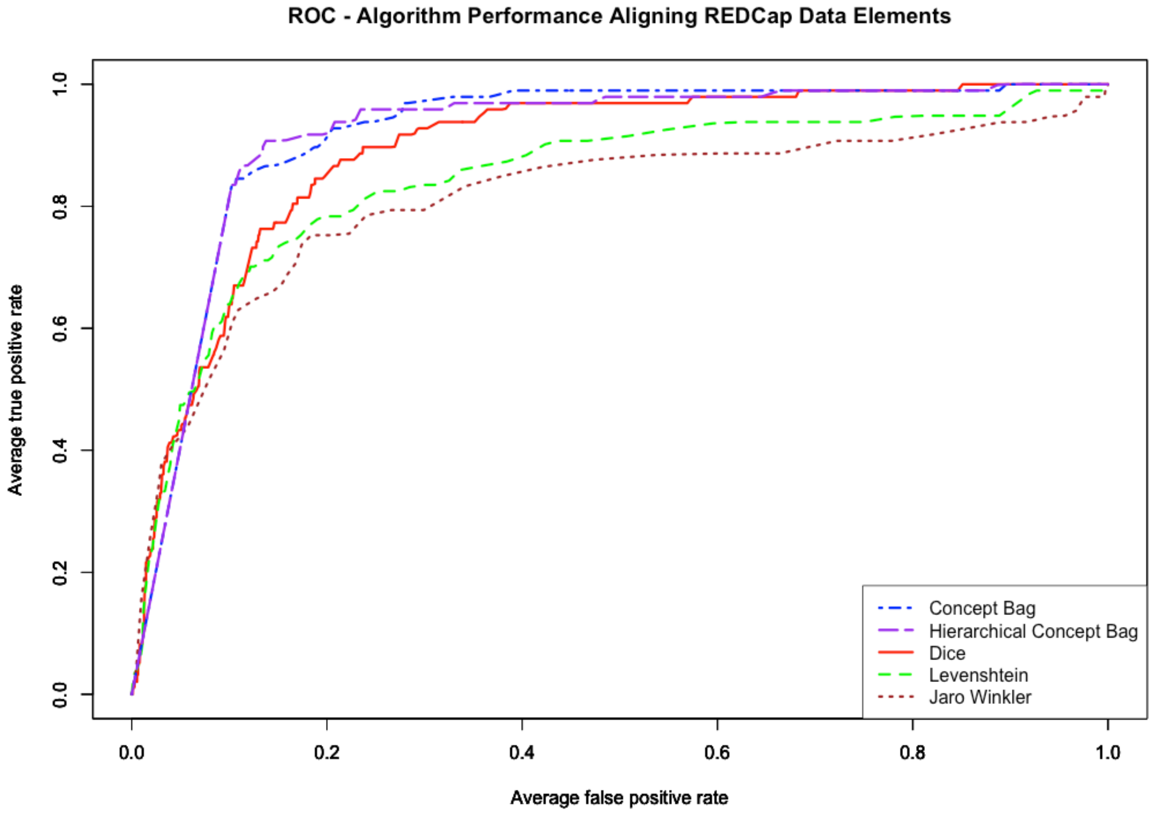


Figure 5.2 ROC curve of the REDCap DE alignment algorithm performance. Curves closest to the top left corner are the best performers.

In terms of performance, the CB performs the best in this group according the area under the curve (AUC), F-measure, and receiver operating characteristics (ROC) curve. The false positive and false negative rates (error rates) are significantly lower than they were for the others. Given that there were only 17 logical DEs to choose from in the UMLS data, to make the correct alignment decision, the alignment only needed a minor signal to have a very high chance of success, i.e., the chances of having one concept match an erroneous DE was very low. Additionally, named entity recognition (NER) software essentially acts as a preprocessor and filters out unrecognized text, but in this case there should not be any unrecognized text. All of the DEs were taken from the same controlled vocabulary.

The HCB alignment performance was also respectable at aligning UMLS DEs but produced twice the false positives of the CB. Adding hierarchical concepts essentially added partial matches to the CBs (versus only equivalent matches), making the bags more sensitive but less specific. Despite this, the HCB still outperformed all the other methods considered here.

As we compare the REDCap alignment performance statistics (Table 5.3), notice the difference in the cutoff scores. The CB cutoff increased from 0.04 for the UMLS DEs to 0.91 for REDCap for the same reason that there was a lower alignment error rate; in the UMLS data, the chance of having one concept match an erroneous DE was much lower. In the REDCap data set the opposite was true: there were 1,199 other DEs to choose from in the REDCap reference alignment, versus 17 in the UMLS set, indicating that a much stronger similarity measurement signal was required to predict a semantically equivalent alignment.

In terms of performance, the CB performed very well at the task of aligning REDCap DEs, as indicated by the AUC of 0.92, F-measure of 0.55, and ROC curve in Figure 5.2. These performance numbers are slightly lower than the UMLS DE alignment performance numbers, but this is certainly expected due to the more complex nature of the REDCap DEs. REDCap DEs were created without a controlled vocabulary or a formal curating process, allowing arbitrary abbreviations and local jargon. Even with the added complexities of REDCap DEs, the CB still had much lower combined false positive and false negative rates than the other algorithms did.

The HCB alignment performance was also good with an AUC = 0.91 and F-measure = 0.53 for REDCap DEs, and AUC = 0.89 and F-measure = 0.67 for UMLS DEs. The increased error rate (more false positives and negatives) is consistent with what happened with the UMLS data, adding hierarchical concepts to CBs added partially matching concepts to the CB and made the algorithm more specific but less sensitive. Had the goal been to identify degrees of semantic similarity where correctly identifying partial matches was considered a success, the HCB would have likely performed better. The stated goal and criterion for performing auto-alignments was to identify exact semantic matches, and therefore, adding partially similar concepts added error.

The DE alignment results show that CB reduces errors and improves DE alignment accuracy on the two data sets studied, and the highly dissimilar characteristics of these data sets infer that this finding is generalizable. The results also indicate that CB is adequate for automatic discovery systems where the goal is to search large volumes of heterogeneous data to discover semantically equivalent DEs. For example, the use case "find echocardiogram data mine" would require an analyst to input echocardiogram DEs; from there the algorithm performs the similarity measures and identifies the semantically equivalent DEs that were discovered. On the other hand, if the application were used to automatically discover and align patient records for patient care without further manual review, none of the studied algorithms were adequate and the improvements reported for CB would not accomplish the levels of performance that may be required in such use cases.

The CB is definitely appropriate for semiautomatic alignment. The improved performance reduces the amount of matching corrections an expert must fix. For instance, the total number of UMLS DE mapping tasks is 49,455, and using the top-performing algorithm, CB, only 2,274 corrections (4.60% error) would have been required. Using the next-best algorithm, Dice, 5,012 corrections (10.13% error) would have been required. And similar results are derived when using the CB algorithm to align DEs from REDCap. The DE alignment results show that the CB and HCB are competitive options to other methods in the same class. The CB was better at identifying exact semantic matches and decreased the error rate by 5.54% on the UMLS set and by 5.18% on the REDCap set.

5.2.2 Error Analysis

Additional analysis was performed to compare the nature of the CB, HCB, and Dice errors. Table 5.4 contains a list of examples. The examples that show the false positives from the CB (1,2,3 in Table 5.4) are caused by underinterpretation, when the NER software did not recognize some or several of the textual expressions and therefore did not output concept codes for those expressions; unrecognized expressions and codes that may modify the meaning are not included in the bags.

False negatives were often due to overinterpretation, when the NER could not disambiguate text and would output multiple codes for a single concept, negatively impacting the similarity ratio. In the CB (4,5,6 in Table 5.4) the false negatives are largely boundary cases where the strict cutoff score (0.91) filtered out otherwise high scores. The method of choosing the cutoff score was to optimize performance, but was intolerant of near misses. Consequently, concept bags had to contain either a perfect match or a ratio equivalent to 11 out of 12 equal concept codes for the alignment to be made automatically.

Table 5.4 Three example errors for each of the CB, HCB, and Dice in terms of false positive (FP) false negatives (FN) errors and comparisons between algorithms. Examples are from the REDCap DE alignment results.

Case	**#**	**DE 1**	**DE 2**	**Reason**
CB FP	1	CHARLSON CATEGORY 1	QNST SUBTEST 7 CATEGORY	"Category" was the only NER-extracted concept.
	2	WEIGHT	OVERHEAD PRESS WEIGHT	"Weight" was the only NER-extracted concept.
	3	DATE OF ADMISSION4	DATE (CATH)	"Date" was the only concept; others unrecognized.
CB FN	4	2. HOW MUCH DID THE CHILD WEIGH AT BIRTH?	2. BIRTH WEIGHT	22 concepts in DE 1. 24 concepts in DE 2; 19 in common and 8 non-overlapping.
	5	OTHER MEDICAL HISTORY?	PLEASE SPECIFY OTHER MEDICAL HISTORY	10/11 codes matched; missed cutoff off by 0.01
	6	INFANT BLOOD DRAW (DATE)	BABY BLOOD DRAW 1 (DATE)	The "1" is the only non-matching concept; 14/16 = 0.88
HCB FP	7	NON-WEBCAMP TOTAL 6100	TOTAL SOFA 1	Concept is “Total”
	8	DATE OF BLOOD GAS#44	BLOOD SHIPMNT DATE	"Date" and "Blood" were the only to concepts
	9	MAP	MAP ACH2	"Map" was the only concept
HCB FN	10	5. DURING THE PAST 30 DAYS, FOR ABOUT HOW MANY DAYS HAVE YOU FELT VERY HEALTHY AND FULL OF ENERGY?	45. DURING THE PAST 30 DAYS, FOR ABOUT HOW MANY DAYS HAVE YOU FELT VERY HEALTHY AND FULL OF ENERGY?	"5" has two conceptual meanings; phrase has 12 other concepts; 12/14 of leaf-level matches.
	11	5) UNITS	49. UNITS	"5" has two conceptual meanings.
	12	2. HOW MUCH DID THE CHILD WEIGH AT BIRTH?	2. BIRTH WEIGHT	"Child" is unique; "Birth weight" is not mined from the first.
Dice FP	13	HISTORY OF SYPHILIS?	HISTORY OF STRICTURES	Similar spellings different concepts
	14	LOW HEDONIC IMAGE 30, APPEALING RATING AFTER MEAL	LOW HEDONIC IMAGE 04, DESIRE RATING BEFORE MEAL	Similar spellings different concepts
	15	DATE AND TIME ADMITTED TO CNMC	AST (DATE AND TIME)	Similar spellings different concepts

Table 5.4 continued

Case	#	DE 1	DE 2	Reason
Dice FN	16	H3B. HOW WOULD YOU DESCRIBE YOUR SYMPTOMS?	1498. OTHER SYMPTOMS	Different lexical phrases with same meaning.
	17	PLEASE DESCRIBE YOUR ROLE	WHAT IS YOUR ROLE	Different lexical phrases with same meaning.
	18	29C. DOSE	8) DOSE	Leading numbers do not match.
CB agrees with experts, Dice does not	19	H3B. HOW WOULD YOU DESCRIBE YOUR SYMPTOMS?	1498. OTHER SYMPTOMS	Conceptually the same, lexically different.
	20	PLEASE DESCRIBE YOUR ROLE	WHAT IS YOUR ROLE	Conceptually the same, lexically different.
	21	DATE __________	BB42. DATE	Difference in noise.
Dice agrees with experts, CB does not	22	HOW MUCH TIME DURING THE PAST FOUR WEEKS HAVE YOU FELT DOWNHEARTED OR BLUE?	HOW MUCH OF THE TIME DURING THE PAST 4 WEEKS HAVE YOU FELT DOWNHEARTED AND BLUE?	Very small lexical difference. Boundary case for CB - "Four" and "4" are different concepts.
	23	V1A F5 HISPANIC OR LATINO ORIGIN OR DESCENT?	ARE YOU HISPANIC, LATINO/A, OR SPANISH ORIGIN?	Lexical differences less significant. "Latino/a" not recognized by NER.
	24	INFANT BLOOD DRAW (DATE)	BABY BLOOD DRAW 1 (DATE)	"Baby" and "infant" are not the same concept; more significant to the match ratio than lexical differences.
HCB agree with experts, CB does not	25	V1A F5 HISPANIC OR LATINO ORIGIN OR DESCENT?	ARE YOU HISPANIC, LATINO/A, OR SPANISH ORIGIN?	Boundary case - adding hierarchy increased the match ratio slightly.
	26	LESION 9 - BRAINSTEM MAX PT DOSE (GY)	LESION 1 - BRAINSTEM MAX PT DOSE (GY)	Boundary case - adding hierarchy increased the match ratio slightly.
	27	OTHER MEDICAL HISTORY?	PLEASE SPECIFY OTHER MEDICAL HISTORY	Boundary case - adding hierarchy increased the match ratio slightly.
CB agrees with experts, HCB does not	28	(none)		HCB only increases the probability of a match - adds hierarchies. Nothing is ever removed.

Similar to the CB, the false positive examples from the HCB (7,8,9 in Table 5.4) were also caused by underinterpretation, when the NER software did not recognize textual expressions. The false negatives of the HCB (10,11,12 in Table 5.4) were also boundary cases where the strict cutoff score (0.92) again filtered out close matches. Adding hierarchical codes to the bags increased the weight of a match since many codes in the hierarchy would match as a result of a single leaf concept code match. This was the reason that HCB would sometimes succeed when the CB would not (see examples 25,26,27 in Table 5.4); in boundary cases the larger number of matched concept codes would push the ratio value over the cutoff boundary.

The lexical methods, such as Dice, produce false positives on phrases that are spelled similarly but are not exactly the same semantically (see examples 13,14,15 in Table 5.4). Lexical methods produce false negatives when lexical representations are different but are semantically similar, or when there is excessive noise or misspellings. Dice outperformed CB and HCB in several cases where small lexical differences (see 22, 23, 24 in Table 5.4) were subject to multiple semantic interpretations. Numbers, for example, may be added for display ordering or they may have a significant meaning. The number “4” may indicate that it is the fourth question or may be part of a question related to, “4 times a day.” The NER software may not recognize the difference and erroneously overinterprets and outputs concept codes that do not represent the true meaning in the context of use.

In summary, CB and HCB errors were cased by overinterpretation, underinterpretation, or by the chosen boundary restrictions. Overinterpretation occurred when NER could not disambiguate text and would output multiple meaning codes for a single concept, negatively impacting the similarity ratio. Underinterpretation occurred when the NER dictionary did not cover the domain adequately, creating false positives when two texts were really just misunderstood. And boundary restrictions resulted in false negatives that were very close similarity measurements but were just slightly below specification due to underinterpretation or overinterpretation errors.

5.3 Medical Term Similarity

5.3.1 Correlation with Physicians and Terminologists

The goal of testing the CB and HCB algorithms for medical term similarity was to test their ability to assess the degrees of similarity between two terms versus their ability to identify exact semantic matches. For example, “first name” and “given name” are exactly the same and perfectly similar, whereas “name” is only partially similar to “first name,” “last name,” and “middle name.” In the automatic alignment study, only the exact alignment was acceptable. In this study we were interested in how similar 2 medical terms were.

To assess the CB and HCB with a full range of similarity measurements, we utilized a published benchmark of carefully curated medical term pair similarity measurements. In this benchmark terminology experts and physicians evaluated pairs of medical concepts and ranked their similarity using a Likert scale. CB and HCB similarity calculations were compared with the benchmark and other published results on the same benchmark. Each of the compared methods was described in Section 2.3 and is referenced individually in Table 5.5. For reference, the breakdown for correlation measures is as follows [157]:

Table 5.5 Correlation of the similarity scores obtained with Hierarchical Concept Bag (HCB), Concept Bag (CB), Dice [110], Leacock and Chadorow (LC) [122], Wu and Palmer (WP) [123], Personalized PageRank (PPR) [121], and Context Vector [87]. The results obtained with the algorithms highlighted in gray were previously published in reference [120].

	Configurations	Physicians	Terminologists
1	SNOMED HCB	0.72	0.76
2	SNOMED HCB-Vector	0.65	0.67
3	UMLS CB	0.46	0.59
4	UMLS HCB	0.46	0.57
5	Dice	0.27	0.37
6	SNOMED LC	0.50	0.66
7	UMLS LC	0.60	0.65
8	SNOMED WP	0.54	0.66
9	UMLS WP	0.66	0.74
10	SNOMED PPR	0.49	0.61
11	UMLS PPR	0.67	0.76
12	Context Vector	0.84	0.75

- correlation = 0.0 indicates no relationship,
- 0 < correlation <= 0.30 indicates a very weak relationship,
- 0.30 < correlation <= 0.50 indicates a weak relationship,
- 0 .50 < correlation <= 0.70 indicates a moderate relationship,
- 0.70 < correlation < 1.0 indicates a strong relationship,
- correlation = 1.0 indicates a perfect relationship.

Of the four CB algorithms tested (the first four methods in Table 5.5), the HCB using SNOMED CT concepts, “is-a” hierarchy, and Jaccard similarity measure performed the same as the highest published result on these data, with a correlation of 0.76 with the terminologists and 0.72 with the physicians [87]. Overall, the HCB correlation scores matched or exceeded 31 other published algorithms [120]. The seven highest correlating algorithms were added to Table 5.5 for comparison. Of the nine similarity algorithms and 31 published combinations of similarity algorithms and concept sources, the HCB performed as well as the Leacock and Chadorow's (LC in chapter 2) path-based measure [122, also configured with SNOMED CT's "is-a" hierarchy, correlating with terminologists at 0.76. All of the other published results had lower correlations except for one, Pedersen's Context Vector [87], which had the highest reported correlation with physicians, 0.84, not surprising because the data set had been augmented with physician-based information content (IC) from a large physician-created corpus.

The SNOMED HCB-Vector implementation (Table 5.5) was also based on SNOMED CT concepts and SNOMED CT's "is-a" hierarchy. SNOMED concept vectors were constructed using concepts obtained using the HCB method and then compared via the cosine similarity function. Using this approach, correlation with terminologists was 0.67 and 0.65 with physicians. The only difference between the SNOMED HCB and the SNOMED HCB-Vector was the similarity calculation method. This result implies the HCB with Jaccard similarity method correlates better with human experts than it does when using the cosine similarity method. The HCB results are comparable with other respectable methods reported in the literature [87, 120].

The other two CB-based approaches tested here also performed moderately well, with correlation scores close to or above the other reported methods. The CB and HCB methods using UMLS (USABase library) and Jaccard similarity measure had a correlation value of 0.46 with physicians, while the correlation with terminologists was higher for both, 0.59 and 0.57 for the CB and HCB, respectively. The lower correlations are likely due to the broader concept coverage contained in UMLS (contains SNOMED CT) with over 1.3 million concepts [138], i.e., UMLS produces larger concept bags than it does when there is a reduced set of source vocabularies. In general terms this implies the results of the CB comparisons will be more sensitive (more hits) and less specific (more error), and even more so with HCB. Adding additional hierarchical concepts magnify this effect.

The Dice algorithm did not correlate well with physicians and terminologists comparing medical terms from the benchmark. While the medical terms in the benchmark are semantically similar, they do not appear to be lexically similar, illustrating specific examples where lexical methods are not as effective as concept similarity methods.

Overall this portion of the study demonstrated that the HCB performed particularly well comparing medical terms for partial similarity. We learned that the SNOMED HCB approach (see Table 5.5) correlated highest with terminology experts, tying the highest published approach and exceeding 31 others. We learned that both the Jaccard similarity method and Cosine similarity method are valid methods for computing concept bag similarity, and that the Jaccard similarity function using HCBs was correlated higher with human experts than the Cosine similarity method was. We also learned that HCB using the SNOMED CT vocabulary set alone produced higher correlation with experts than it did with the MetaMap's UMLS vocabulary set. This finding about SNOMED versus UMLS is consistent with other published findings on this benchmark [120].

5.4 ICU Discharge Summary Similarity

Computing similarity between larger medical texts is more complex than comparing specific medical terms or DEs, in terms of both semantic complexity and computation. The methods we have explored so far have been focused on relatively short expressions from 1.6 to 7.1 mean words (see Table 5.1). The studied ICU discharge summaries (DS) have a mean size of 308.8 words, two orders of magnitude larger. Due to this size difference we chose a slightly different comparator lineup, TF-IDF (Section 2.4.2), Dice (Section 2.2.2), CB (Section 3.1), and HCB (Section 3.2). The reasoning behind why these algorithms were selected is given in Section 4.4.2.

One hundred randomly selected ICU discharge summary (DS) pairs were evaluated by 2 terminologists and 4 algorithms, the CB (see Section 3.1), the HCB (see Section 3.2), Dice (see Section 2.2.2), and TF-IDF (see Section 2.4.2). The instructions terminologists were asked to follow are included in Section 4.4.1.

The results are correlations between the similarity scores given by the different approaches. A correlation of 0.0 indicates there was absolutely no linear relationship between the two sets compared, whereas a correlation of 1.0 indicates the relationship is perfectly linear. See the correlation results in Table 5.6. A reference for correlation value interpretations was provided in Section 5.2.1.

Determining similarity between DSs is much more complicated and challenging than any of the other two applications discussed above. The text size difference implies there is significantly more semantic complexity. Moreover, DSs include a large number of nonspecific common words, increasing the computational challenge of identifying the key words that truly characterize the document.

Table 5.6 ICU discharge summary similarity measurement correlations across algorithms CB, HCB, Dice, TF-IDF and two terminologists

	CB	HCB	Dice	TF-IDF	Terminologist 1	Terminologist 2
CB	1					
HCB	0.91	1				
Dice	0.40	0.51	1			
TF-IDF	0.38	0.42	0.58	1		
Terminologist 1	0.15	0.20	0.24	0.06	1	
Terminologist 2	0.17	0.25	0.23	0.08	0.42	1

The relatively low correlation between the two terminologists is clear evidence of the semantic challenge. Despite this complexity, CB, HCB, and Dice were approximately 2 to 3 times more likely to be correlated with terminology experts than TF-IDF, the algorithm behind industry-leading document-indexing products [131].

The CB and HCB similarity scores were most highly correlated with each other at 0.91, as was expected since they were based on highly similar methodologies and concepts. In this study, the Dice method had the highest overall correlation with the other methods and the experts.

CHAPTER 6

GENERAL DISCUSSION, FUTURE DIRECTIONS, AND CONCLUSIONS

6.1 General Discussion

6.1.1 Advancing Methods for Computing Similarity

A new method for computing semantic similarity has been introduced and described, the Concept Bag method (CB). The original purpose of its creation was to align heterogeneous datasets by auto-aligning data elements (DE), and it performed particularly well at this task. Comparing the CB with Dice, the next closest non-CB algorithm, the performance gain of the CB reduced the amount of alignment work by over 5% in both tested data sets (5.54% for the controlled set and 5.18% for the uncontrolled set). The results were surprisingly replicable between two very different data sets, a small set of DEs derived from a controlled vocabulary and a very large set from an uncontrolled vocabulary. We consider this a significant finding that advances the field of biomedical data integration research.

6.1.2 Expanding Concept Bags with Hierarchical Concepts

The Hierarchical Concept Bag (HCB) was the second configuration of the CB and it was essentially the same except that hierarchical semantics were added. The original CB contained only concept matches produced by the named-entity recognition (NER) software. The HCB had the highest overall standing of the three applications. In the case of aligning DEs, the HCB was only second to the CB but still outperformed the other algorithms. On the medical term set the HCB was ranked 2nd when compared 7 to other well-established algorithms [120]. And comparing intensive care unit (ICU) discharge instructions, the HCB appeared to be second to the Dice algorithm. Due to its versatility, the HCB would be the best "catch-all" algorithm if requirements were unclear.

One of the surprises of the HCB results was that vector-based HCB correlations were lower than the bag-based approach for the medical term study. Vector-based solutions are behind many of the highly successful algorithms in the document similarity space [158]. One of the consequences of having a small data set with short strings was that there were not many concepts to establish frequency weights. HCB Vectors were not weighted like they are in many vector-based implementations. Weights only make sense when there are significant frequency metrics, however.

6.1.3 Comparison with Compositional Semantics

"Compositional semantics" is based on the definition of compositionality, where the meaning of an expression is determined by the structure and the meaning of its components [159]. CBs and HCBs are composed of conceptual codes and are lexicon-free, but do not support structure beyond set membership and potentially set order when sets are extended to vectors. They do not contain adequate structure to reverse engineer meaningful language-based lexical expressions, but they are compositions of semantic expressions (as expressed by concept codes) that are used to mathematically compare semantics. The CBs and HCBs are similar to compositional semantics but are not considered compositional semantics as described in the literature.

6.1.4 ICU Discharge Similarity

The first two studies had conclusive results, but the results of the ICU discharge summary study were inconclusive. The correlation between human experts and/or algorithms was too low. The terminologists who judged ICU discharge summaries were admittedly challenged, despite multiple verbal conversations and explicit written instructions. This is consistent with the literature. Human-based annotation of biomedical text is recognized as challenging, often requiring a multistep process to achieve modest consistency [160]. In this experiment terminologists were asked to make a single judgment between two texts averaging over 300 words each, whereas the task of annotating texts typically requires sentence-level interpretation. Perhaps a more granular approach could be followed, annotating the ICU discharge instructions at the sentence level first, and then using these annotations a final similarity judgment could be made. Whichever strategy is chosen, more effort needs to be applied to establish a suitable reference for correlation.

The only highly correlated algorithms were the CB and HCB, and this is a consequence of one being a derivative of the other. The high correlation between the two is validation that the methods are not exactly the same but perform similarly, as we saw in the results of the other studies. One of the weak signals that had a potentially interesting implication was the fact that all three non-TF-IDF methods had slightly higher correlations between the other methods and with terminologists. What makes this interesting is that it starts to form evidence that indicates that the text sizes of the ICU discharge summaries may not have reached the threshold where TF-IDF starts to outperform the other set comparison approaches (Jaccard and Dice). The TF-IDF algorithm is “the one to beat” in document matching [158], although we did not find studies that validated a boundary or rule-of-thumb that identifies when algorithms for “short” strings are better than algorithms for documents. This was not a conclusive finding but is an interesting topic that could benefit from more research.

6.1.5 Concept Bag Is Highly Configurable and Generalizable

The CB method is highly configurable and versatile. It was designed such that it could be tuned for a variety of use cases. The three primary opportunities for tuning the algorithm are, 1) the named-entity recognition (NER) software and underlying vocabularies can be changed, 2) the implementation of the concept bag can be a set or a weighted vector, 3) and the concept bag analysis method could be any number of analytical methods. Moreover, secondary configuration options include settings that can be manipulated on the NER software. MetaMap has nearly 100 settings and multiple underlying vocabularies that contain additional semantic knowledge similar to the SNOMED CT hierarchy. Additional tuning options for the concept bag implementation include the way that concept bags are populated, how concepts are selected from the NER tool output, and how concepts are weighted. CB analysis methods could be simple sets or vector-based, with a sophisticated weighting strategy. With all of these options there are many opportunities for further exploration.

All of the options available to configure the CB make it a broadly generalizable similarity algorithm that can be tailored to perform similarity measurements for nearly any topic.

6.1.6 Scalability and Performance

Given the datasets that were used for the studies, only the REDCap DEs were big enough to be a computer time/speed performance concern. The term “big” is not used in terms of bytes, but in terms of the number of comparisons that had to be performed. Comparing 899,649 DEs from 20,724 data sets requires nearly half a trillion comparisons. This places the REDCap DE alignment project in the “large schema matching” category. This study was based on matching DEs and did not scale up to individual data sets, although this work is feasible, based on what has been done already. The idea of aggregating aligned data elements is mentioned below in the future work. We did not find any comparison studies that were in the same category.

Our solution, the parallel matching [151] process (see section 4.2.7.2), was configured to run 256 parallel jobs using the Center for High Performance Computing and took 4.1 +/- 1.3 hours for all 256 jobs to complete. One of the benefits of this strategy is that more jobs and CPUs can be added to reduce the elapsed computing time required; it is highly scalable due to the fact that similarity computations can be dynamically subdivided and executed in parallel tasks based on the available computing resources.

6.1.7 Suggested Use

The CB and HCB are recommended for projects where the 5% savings in errors outweighs the added sophistication required to implement the algorithms. The lexical methods are very simple and do not require terminologies, database software, or the described process to implement the CB and HCB. The CB and HCB software could be simplified by bundling the software into a product that would behave almost as simply as the lexical methods, but still requires more sophisticated computational support, especially for large numbers of data set comparisons. The cost of implementation would definitely payoff in a big data project but may not be as compelling for small-ish alignment projects.

6.2 Future Directions

6.2.1 MetaMap Settings

Several discoveries and realizations occurred during and after the initial experiments were completed. More experience with MetaMap, for example, helped us recognize more opportunities for tuning MetaMap. As mentioned, MetaMap has nearly 100 settings for configuring and tuning input and output. The first tuning target will be to filter out low confidence matches using MetaMap's confidence score. The second will be to identify and select relevant semantic types that are associated with UMLS concepts. The third will focus on selecting the most relevant source vocabularies. We intend to use the current dataset and linear regression to identify which of these settings impact the output most positively.

6.2.2 Aligning Data Sets and Projects

One of the interesting results of this method is that concept bags can be aggregated based on any kind grouping that is desired. The concept bag approach applies to a project in a similar way that large bags of words are created for large documents.

Converting individual DE concept bags into larger sets by performing a union of all the bags in a given data set creates the "data set" concept bag, and similarly for a project. Or, by aggregating DE alignments by data set we can identify data set alignments. This becomes an "n-way" matching problem [78]. Dataset matching techniques normally focus on 2-way matching, aligning one dataset to another. Preforming data set matching with these data is performing a 20,724-way matching solution. This is logically conceivable to imagine but is not trivial to implement, making it a great future research topic. Or how about comparing institutions, states, or countries? We do not understand where the limits are yet, but this is the idea, to learn about the concept bag approach on larger sets.

6.2.3 Comparing Diagnosis and Procedure Codes

Concept bags could be created from diagnosis, procedure codes, laboratory codes, or using any kinds of codes. Choosing which codes and how to apply weights basically serves the same function as feature vector engineering that is performed for machine learning, except that these methods are unsupervised. The use of diagnosis codes and procedure codes, for example, is a particularly interesting combination. It seems intuitive that people who share diagnosis and procedure codes would share other things in common as well.

6.2.4 Reducing Comparisons

A significant amount of the effort for performing big data set analysis is identifying methods that reduce the data and/or computational complexity as much as possible before the analysis takes place [151, 161]. We recognized significant space-reduction opportunity that could be highly beneficial to bag set comparison algorithms. For the purposes of comparing and aligning DEs, the concept counts could be used to reduce the number of comparisons required before the actual comparisons are computed. Two DEs that have a significantly different number of concepts may not even be worth comparing. Assuming the DE alignment similarity cutoff point is known, the comparison cutoff is as follows:

$$compare\ if\ \frac{\min(|DE1_{concept}|,|DE2_{concept}|)}{\max\,(|DE1_{concept}|,|DE2_{concept}|)} \geq DE\ alignment\ cutoff \qquad [6.1]$$

This formula computes the maximum possible similarity score based on concept code counts without actually performing the set comparisons, and compares it with the DE alignment cutoff. If the maximum comparison score does not meet the cutoff requirement, no comparison is required. Time and computation savings may not be significant enough for small-set comparisons but would likely save time and CPU cycles as sets get large. Using the REDCap DE comparison set as an example, the number of comparisons would have been reduced to 1/30 its original size, from nearly half a trillion to just over 16 billion comparisons. If count comparisons are less expensive than computing set similarities, this has the potential to make a significant impact on the number comparisons that are required.

6.2.5 Adding Philological Relationships

The HCB uses SNOMED CT's is-a hierarchy to measure similarity. Adding concept codes that share additional philological relationships is a natural extension of the work that has been performed. Semantic relationships are used to formulate concept definitions with 80% to 90% accuracy [162], implying that concepts with similar relationships would have similar definitions as well. It stands to reason that adding additional philological relationships to Concept Bags would have the same effect; similar definitions imply similar concepts. A specific strategy to accomplish this was introduced in Section 3.2. The idea is to pair philological relationships with concepts to create a composite key that becomes an additional Concept Bag set element. The added elements essentially add the full meaning of the concept code and philological relationship to the Concept Bag. We believe this is an interesting new idea that deserves additional research.

6.3 Conclusions

Automatic alignment of heterogeneous biomedical data is very challenging due to the sophisticated semantics of clinical data. In this dissertation we introduced a new method that compares ”concept bags” to compute similarity and apply it to the automatic alignment problem. The algorithm was tested against two diverse data element sets, one from a controlled vocabulary and one from an uncontrolled vocabulary, and the new similarity algorithm consistently decreased the alignment error rate by more than 5% as compared to other well-established alignment methods.

To demonstrate the concept bag's generalizability, the new method was configured in different ways, in two ways for the DE alignment study, in four ways for the medical term similarity study, and two ways for the ICU discharge summary study. Evaluating medical terms for similarity, the CB ranked second among 7 well-established semantic similarity algorithms after it was configured to utilize SNOMED CT concept semantics. Measuring patient case similarity between ICU discharge instructions was much more complex, and human expert judgments had a very low correlation. More exploration needs to be performed in this area to establish a source of truth such that algorithms can be iteratively tuned and tested. As with most customizable algorithms, high performance, both in terms of algorithm accuracy performance and computational performance, requires iterative tuning and experimentation. Computational performance was measured on the largest set of comparisons, but performance was not an issue for the other applications. The similarity methods that were used (Jaccard and TF-IDF) have been proven to be highly scalable in real-world Big Data applications; it stands to reason that the new concept bag algorithm will scale similarly. We believe this work applies to large-scale data-set-alignment projects where the number of data sets is large and auto-discovery of alignments would help to identify data sets with similar data.

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