

## Lessons Learned from Aligning two Representations of Anatomy

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*The objective of this study is to analyze the comparison, through their results, of two distinct methods applied to aligning two representations of anatomy. The same versions of FMA and GALEN were aligned by each method. 2199 concept matches were obtained by both methods. For matches identified by one method only (337 and 336 respectively), we analyzed the reasons that caused the other method to fail. Alignment 1 could be improved by addressing partial lexical matches and identifying matches based solely on structural similarity. Alignment 2 may be improved by taking into account synonyms in FMA and identifying semantic mismatches. However, both methods identify only a fraction of all possible matches and new approaches need to be explored in order to handle more complex matches.*

### INTRODUCTION

Anatomy is central to the biomedical domain. While macroscopic anatomy is required for the representation of diseases and procedures, subcellular anatomy has become increasingly important for molecular biology. Not only is a sound representation of anatomy fundamental to biomedicine, but the various representations of anatomy currently available also need to be aligned in order to ensure interoperability. This need inspired two groups of researchers to take up the challenge of aligning two sizeable representations of anatomy: the Foundational Model of Anatomy (FMA) and the GALEN common reference model.

The first effort in aligning these two systems occurred at the US National Library of Medicine (NLM). In parallel, but unrelated to it, another alignment was performed at Microsoft Research. Both approaches use a combination of lexical and structural techniques. In addition, the first approach takes advantage of domain knowledge, while the second approach is domain-independent and thus can be applied to other domains.

The contribution of this study is a comparison and analysis of the results of the two alignments in an

effort to determine the strengths and weaknesses of each. This analysis illustrates how each approach can be improved based on the results of the other.

### MATERIALS

#### FMA and GALEN

The Foundational Model of Anatomy<sup>1</sup> (FMA) [July 2, 2002 version] is an evolving ontology that has been under development at the University of Washington since 1994 [1, 2]. Its objective is to conceptualize the physical objects and spaces that constitute the human body. The underlying data model for FMA is a frame-based structure implemented with Protégé-2000 [3]. 58,957 concepts cover the entire range of macroscopic, microscopic and subcellular canonical anatomy. Concept names in FMA are pre-coordinated, and, in addition to preferred terms (one per concept), 28,499 synonyms are provided (up to 6 per concept).

The Generalized Architecture for Languages, Encyclopedias and Nomenclatures in medicine<sup>2</sup> (GALEN) [v. 4] has been developed as a European Union AIM project led by the University of Manchester since 1991 [4, 5]. The GALEN common reference model is a clinical terminology represented using GRAIL [6], a formal language based on description logics. GALEN contains 23,428 concepts and intends to represent the biomedical domain, of which canonical anatomy is only one part. Concept names in GALEN are post-coordinated, and only one name is provided for each non-anonymous concept. There are 2,960 anonymous concepts.

Both FMA and GALEN are modeled by *is-a* relationship. Additionally, FMA uses two kinds of partitive relationships and GALEN 26. The hierarchy of associative relationships is also more extensive in GALEN (514) than in FMA (54). In addition to inter-concept relationships, there are 85 slots in FMA describing atomic properties of concepts, whose types are Boolean, Integer, Symbol, and Instance.

<sup>1</sup> <http://fma.biostr.washington.edu/>

<sup>2</sup> <http://www.opengalen.org/>

## The UMLS

An additional resource used in the alignment is the Unified Medical Language System<sup>®</sup> (UMLS<sup>®</sup>)<sup>3</sup> developed by NLM. The UMLS Metathesaurus<sup>®</sup> is organized by concept or meaning. A concept is defined as a cluster of terms representing the same meaning (synonyms). The 14th edition (2003AA) of the Metathesaurus contains over 1.75 million unique English terms drawn from more than sixty families of medical vocabularies, and organized in some 875,000 concepts. In the Metathesaurus, each concept is categorized by at least one semantic type from the UMLS Semantic Network. A subset of these semantic types is used to define the domain of anatomy. Also part of the UMLS distribution is the SPECIALIST Lexicon, a large syntactic lexicon of both general and medical English.

## METHODS

### Alignment 1

Alignment 1 first compares the concepts between FMA and GALEN in two steps: lexical alignment and structural alignment [7]. Then, based on the matching concepts identified, Alignment 1 compares the associative relationships across systems [8].

The **lexical alignment** identifies shared concepts across systems lexically through exact match and after normalization. Concepts exhibiting similarity at the lexical level across systems are called anchors, as they are going to be used as reference concepts in the structural alignment and associative relationship comparison. Additional anchors are identified through UMLS synonymy. Two concepts across systems are considered anchors if their names are synonymous in the UMLS Metathesaurus (i.e., if they name the same concept) and if the corresponding concept is in the anatomy domain (i.e., has a semantic type related to *Anatomy*). For FMA, both preferred concept names and synonyms were used in the lexical alignment process. For GALEN, only non-anonymous concept names were used.

The **structural alignment** first consists of acquiring the semantic relations explicitly represented within systems. Inter-concept relationships are generally represented by semantic relations  $\langle concept_1, relationship, concept_2 \rangle$ , where *relationship* links *concept<sub>1</sub>* to *concept<sub>2</sub>*. For the purpose of aligning the two ontologies, we considered as only one *part-of* relationship the various subtypes of partitive relationships present in FMA (e.g., *part of*, *general part of*) and in GALEN (e.g., *isStructuralComponentOf*, *IsDivi-*

*sionOf*). Only hierarchical relationships were considered at this step, i.e., *is-a*, *inverse-is-a*, *part-of*, and *has-part*. Implicit semantic relations are then extracted from concept names and various combinations of hierarchical relations. Augmentation and inference are the two main techniques used to acquire implicit knowledge from FMA and GALEN.

**Augmentation** attempts to represent with relations knowledge that is otherwise embedded in the concept names. Augmentation based on reified *part-of* relationships consists of creating a relation  $\langle P, part-of, W \rangle$  between concepts *P* (the part) and *W* (the whole) from a relation  $\langle P, is-a, Part\ of\ W \rangle$ , where the concept *Part of W* reifies, i.e., embeds in its name, the *part-of* relationships to *W*. For example,  $\langle Neck\ of\ Femur, part-of, Joint \rangle$  was added from the relation  $\langle Neck\ of\ Femur, is-a, Component\ of\ Joint \rangle$ , where the concept *Component of Joint* reifies a specialized *part-of* relationship. Examples of augmentation based on other linguistic phenomena include  $\langle Prostate\ gland, is-a, Gland \rangle$  (from the concept name *Prostate gland*) and  $\langle Extensor\ Muscle\ of\ Leg, part-of, Leg \rangle$  (from the concept name *Extensor Muscle of Leg*).

**Inference** generates additional semantic relations by applying inference rules to the existing relations. These inference rules, specific to this alignment, represent limited reasoning along the *part-of* hierarchy, generating a partitive relation between a specialized part and the whole or between a part and a more generic whole. For example,  $\langle First\ tarsometatarsal\ joint, part-of, Foot \rangle$  was inferred based on the relations  $\langle First\ tarsometatarsal\ joint, is-a, Joint\ of\ foot \rangle$  and  $\langle Joint\ of\ foot, part-of, Foot \rangle$ .

With these explicit and implicit semantic relations, the structural alignment identifies structural similarity and conflicts among anchors across systems. Structural similarity, used as **positive structural evidence**, is defined by the presence of common hierarchical relations among anchors across systems, e.g.,  $\langle c_1, part-of, c_2 \rangle$  in one system and  $\langle c_1', part-of, c_2' \rangle$  in another where  $\{c_1, c_1'\}$  and  $\{c_2, c_2'\}$  are anchors across systems. Conflicts, on the other hand, are used as **negative structural evidence**. The first type of conflict is defined by the existence of opposite hierarchical relationships between the same anchors across systems, e.g.,  $\langle c_1, part-of, c_2 \rangle$  in one system and  $\langle c_1', has-part, c_2' \rangle$  in another. The second type of conflict is based on the disjointedness of top-level categories across systems. For example, *Nail* in FMA is a kind of *Skin appendage* which is an *Anatomical structure*, while *Nail* in GALEN is a *Surgical Fixation Device* which is an *Inert Solid Structure*. *Anatomical structure* and *Inert Solid Structure* being disjoint top-level categories, the two concepts of *Nail*

<sup>3</sup> <http://umlsinfo.nlm.nih.gov/>

across systems are semantically distinct, although they share the exact same name.

Based on the anchors (except those receiving negative structural evidence), **associative relationships** are compared across systems. The most frequent matches indicate a correspondence between an associative relationship in one system and one relationship (hierarchical or associative) or combination thereof in the other. For example, from *Heart - contained in* → *Middle mediastinum -part-of* → *Mediastinum* in FMA and *Heart -boundsSpace* → *Mediastinum* in GALEN, the relationship match {FMA: *contained in - part-of*, GALEN: *boundsSpace*} can be extracted.

### Alignment 2

The second alignment also includes a lexical phase and a structural phase, followed by a hierarchical match phase [9]. For each phase, generic schema matching algorithms were adapted to 1) cope with the number of concepts present and 2) handle the more expressive modeling environments (Protégé-2000 and GRAIL). Summarizing from [9], the second alignment proceeds as follows.

The **lexical phase** identifies concepts whose names are similar. Each concept name from FMA and GALEN is first mapped to the UMLS Metathesaurus after normalization and reduced to a set of UMLS concept identifiers. Each concept identifier is further annotated with part-of-speech information identified using the SPECIALIST Lexicon. The similarity between two concepts from FMA and GALEN depends on the ratio of shared UMLS concepts to the total number of UMLS concept mapped to. Part-of-speech information is further used to distinguish between roots (nouns and verbs) and modifiers (adjectives and adverbs) [10].

For example, *Valve In Heart* from GALEN is first normalized to *heart valve* and mapped to two UMLS concepts. *Cardiac Valve* from FMA is normalized to *cardiac valve* and mapped to three UMLS concepts, two of which being shared with the mappings of *Valve In Heart*. Based on this, the similarity between *Valve In Heart* and *Cardiac Valve* was assigned a score of .8 (where 0 indicates no similarity and 1.0 indicates a perfect match).

The **structural phase** attempts to identify concepts (and relationships) that are used similarly in both systems. The first step is to reify every relation present in FMA or GALEN, thereby creating new, artificial concepts. For example, one such concept is created from the relation <*Cardiac Valve*, *part-of*, *Heart*>. Similarity scores can then be assigned to matches among these artificial concepts, corresponding to relation matches. The similarity of two relations in a

match is estimated to be the average similarity of the concepts and relationships involved in the relations. This process makes it possible to identify the similarity of relations, not only concepts. For example, this is how we identified that both FMA and GALEN assert that cardiac valves are part of the heart.

Moreover, the similarity between relations can be *back-propagated* to improve the similarity of the corresponding concepts and relationships. Whenever two concepts (or relationships) are mentioned in similar relations, the similarity between those concepts is increased. This back-propagation detects similarity of use, especially between relationships. For example, the similarity between *isBranchOf* and *branch of* increases from .28 to .98 using back-propagation.

The final **hierarchical phase** attempts to identify concepts with similar descendants. Similarity scores across leaf concepts were established during the previous phases, but few higher-level correspondences were identified. In this final phase, the similarity between two concepts is increased if there are many descendants that match. In theory, similarity is pushed up the inheritance hierarchy from the leaves, but [11] notes that few matches were found in this manner.

### Comparing Alignment 1 and 2

Alignment 1 identified a set of concept matches across systems with an indication of the presence of structural evidence and relationship matches with their frequency. A concept match is supported by Alignment 1 if it receives positive structural evidence; not supported otherwise.

Alignment 2 identified a set of matches for both concepts and relationships, each match being qualified by similarity score. A match is supported by Alignment 2 if its similarity score is higher than or equal to a pre-specified threshold; not supported otherwise. The threshold selected in this study is .83, determined heuristically by examining the validity of a subset of matches.

We compared the concept matches obtained by Alignment 1 and 2 by classifying them into four categories: 1) matches supported by both alignments, 2) matches supported by Alignment 1 but not supported or identified by Alignment 2, 3) matches supported by Alignment 2 but not supported or identified by Alignment 1, and 4) matches ignored by both alignments. We then used a similar approach to compare the relationship matches obtained by the two alignments.

## RESULTS

The matches obtained in Alignment 1 and 2 are first presented separately. Then, we analyze the results of their comparison. These results are summarized in Table 1 (concept matches).

			Alignment 2		
			Identified		Not identified
			Similarity $\geq .83$	Similarity $< .83$	
Alignment 1	Identified	Positive evidence	2,199	42	295
		No evidence	168	3	29
		Negative evidence	36	0	4
	Not identified	132	1,074		

Table 1 – Concept matches in Alignment 1 and 2

### Matches in Alignment 1

2,410 pairs of matching concepts across systems were identified by lexical alignment between FMA and GALEN. Through UMLS synonyms, 366 additional pairs of matching concepts were found across systems, resulting in totally **2,776 concept matches** in Alignment 1.

By structural alignment, 2,536 (91.4%) of the 2,776 matches received positive evidence, 40 (1.4%) negative evidence and 200 (7.2%) no evidence. *Cardiac valve* (synonym: *Valve of heart*) in FMA and *Valve In Heart* in GALEN exemplify a match with positive evidence as they share hierarchical links to some of the other anchors across systems, e.g., *Heart (part-of)*, *Tricuspid valve (inverse-is-a)* and *Mitral valve (inverse-is-a)*. *Pectoral girdle* (synonym: *Shoulder girdle*) in FMA and *Shoulder Girdle* in GALEN, although matching lexically, were identified to be a mismatch from the conflicting relationships these concepts have across systems, i.e.,  $\langle$ *Pectoral girdle, has-part, Shoulder* $\rangle$  in FMA and  $\langle$ *Shoulder Girdle, part-of, Shoulder* $\rangle$  in GALEN. Finally, although linked to anchors including *Cardiovascular System (part-of)* and *Body Part (is-a)* in GALEN, *Carotid Body* does not have any hierarchical links to other anchors in FMA, and therefore receives no structural evidence.

The alignment of associative relationships resulted in **182 relationship matches**. Matches with high frequency include  $\{FMA: \textit{branch of}, GALEN: \textit{isBranchOf}\}$  and  $\{FMA: \textit{tributary of}, GALEN: \textit{isBranchOf}\}$ .

In summary, a total of 2,958 matches (2,776 for concepts and 182 for relationships) were identified between FMA and GALEN by Alignment 1.

### Matches in Alignment 2

A total of 3,780 matches were identified by Alignment 2, 3,503 of them in the lexical phase, 64 in the structural phase, and 213 in the hierarchical phase. 2,583 (68.3%) of the 3,780 matches were assigned similarity scores above the threshold of .83. As a matter of fact, 2,539 of these matches have the similarity score of 1.0 (e.g.,  $\{FMA: \textit{Pancreas}, GALEN: \textit{Pancreas}\}$ ). 1,197 (31.7%) of the 3,780 matches have a similarity score lower than .83 and were ignored (e.g.,  $\{FMA: \textit{Upper lobe of lung}, GALEN: \textit{Lobe of Left Lung}\}$  has a similarity of .5).

Among the 3,780 matches, there are **3,654 concept matches** and **22 relationship matches** (e.g.,  $\{FMA: \textit{part-of}, GALEN: \textit{IsDivisionOf}\}$  has a similarity of 1.0). The remaining 104 matches associate things other than two concepts or two relationships. In 102 cases, a concept in one system matches a relationship in the other (e.g.,  $\{FMA: \textit{insertion}, GALEN: \textit{Insertion Point}\}$ ). Finally, two FMA Boolean-typed slots match GALEN relationships (e.g., *has dimension* in FMA and *hasDimension* in GALEN).

### Concept matches supported by both alignments

2,776 concept matches were identified by Alignment 1 and 3,654 by Alignment 2. Among them, 2,199 both received positive structural evidence and had a similarity score above the threshold of .83, as shown in the upper left part of Table 1. These matches are supported by both alignments. For example, the match  $\{FMA: \textit{Cardiac valve}, GALEN: \textit{Valve In Heart}\}$ , presented earlier, received positive evidence in Alignment 1, and its similarity score is .88 in Alignment 2.

### Concept matches supported by Alignment 1 only

As shown in the upper right part of Table 1, 42 concept matches received similarity scores lower than the threshold by Alignment 2, and 295 were not identified by Alignment 2. However, these 337 matches were supported by positive structural evidence of Alignment 1.

- 167 are FMA synonyms matching GALEN concept names in Alignment 1. Alignment 2 failed to identify or to select these matches in the lexical phase because it did not use synonyms in FMA. For example, *Prostate* in FMA was matched to *Prostate Gland* in GALEN by Alignment 1 because the former has a synonym *Prostate gland* in FMA. The positive structural evidence for this match includes their sharing *is-a* link to *Gland*

and *has-part* link to *Lobe of prostate* across systems.

- 158 were obtained through UMLS synonyms in Alignment 1. One such match is {FMA: First Tarsometatarsal joint, GALEN: First Tarso Metatarsal Joint}. This match received positive structural evidence from the shared hierarchical links to other anchors such as *Foot (part-of)* and *Joint of foot<sup>4</sup> (is-a)* across systems. It was not obtained by Alignment 2 because the two alignments used slightly different matching criteria for mapping to UMLS concepts.
- 12 are FMA preferred concept names matching GALEN concept names in Alignment 1, e.g., {FMA: Immunoglobulin M, GALEN: Immunoglobulin M}, which shared hierarchical links to anchors such as *Immunoglobulin (is-a)* and *Protein (is-a)* across systems. The reasons why these matches were not obtained by Alignment 2 were investigated and found to be essentially unimportant.

#### Concept matches supported by Alignment 2 only

The lower left part of Table 1 shows the concept matches with similarity scores above the threshold by Alignment 2 but not supported or identified by Alignment 1.

- 168 received no structural evidence by Alignment 1, e.g., {FMA: Carotid body, GALEN: Carotid Body}, presented earlier. Although its similarity score is 1.0 by Alignment 2, this match was not supported by Alignment 1 because no structural evidence could be found (in this case, because of a lack of relations being represented in FMA for this concept).
- 36 received negative structural evidence by Alignment 1. Both {FMA: Nail, GALEN: Nail} and {FMA: Pectoral girdle, GALEN: Shoulder Girdle}, with negative evidence in Alignment 1 as presented earlier, received the similarity score of 1.0 by Alignment 2. These 36 matches were inappropriately supported by Alignment 2 because, unlike Alignment 1, this method does not attempt to identify semantic mismatches.
- 132 were only identified by Alignment 2.
  - 78 could have been obtained by Alignment 1 through UMLS synonymy. They were filtered out by Alignment 1 because they caused two different concepts in one system to be synonymous. In the UMLS Metathesaurus, the terms *Prostate*, *Prostate gland* and *Prostatic gland*

are synonymous. In FMA, *Prostate* refers to the organ while *Prostatic gland* is subdivision of the organ. Being different concepts in FMA, their matching to the same UMLS synonym was rejected. Therefore, Alignment 1 did not get the match {FMA: Prostatic gland, GALEN: Prostate Gland} while Alignment 2 did.

- 18 were rejected by Alignment 1 through the Semantic Network filter for Anatomy, e.g., {FMA: Flatulence, GALEN: Flatus} (similarity = 1.0). Neither *Flatulence* nor *Flatus* is related to Anatomy in UMLS and this match was rejected by Alignment 1 for this reason.
- 36 were not identified by Alignment 1 because at least one of the concept names did not match any UMLS synonyms. For example, Alignment 1 missed {FMA: Colic flexure, GALEN: Colonic Flexure} (similarity = 1.0) through UMLS because *Colonic Flexure* in GALEN does not match any UMLS synonyms. Some of these matches of Alignment 2 were determined to be valid by a domain expert.

#### Concept matches ignored by both alignments

The lower right part of Table 1 shows the concept matches ignored by both alignments. These matches are either not identified by one alignment and not supported by the other or identified but not supported by either alignment.

- 1,074 were only identified by Alignment 2 but their similarity scores are lower than the threshold. 72 are FMA concepts matching GALEN anonymous concepts, purposely ignored by Alignment 1. 1,002 are FMA concepts matching GALEN non-anonymous concepts. Most of these matches correspond to partial matches, not addressed by Alignment 1 (e.g., {FMA: Ligament of knee joint, GALEN: Ligament of Knee}, with a similarity score of .35).
- 32 received no structural evidence by Alignment 1, while 3 of them had similarity scores lower than the threshold and 29 were not identified by Alignment 2.
- 4 received negative structural evidence by Alignment 1 and were not identified by Alignment 2.

#### Relationship matches

182 relationship matches were identified in Alignment 1. Alignment 2 identified 22 matches, of which 17 were supported by a similarity score above .83. Seven relationship matches were identified by both alignments (e.g., {FMA: nerve supply, GALEN: is-ServedBy}). Seven were supported by Alignment 2 only (e.g., {FMA: lymphatic drainage, GALEN: is-

<sup>4</sup> The anchor is named *Foot Joint* in GALEN.

*ServedBy*). Alignment 1, relying on the concepts already aligned, failed to identify these matches, because these relationships occurred among concepts that have not been aligned. Finally, in three cases, the match identified by Alignment 2 corresponded to a match created manually in Alignment 1 between the subtypes of *part-of* relationships (e.g., {*FMA: part-of, GALEN: IsDivisionOf*}).

## DISCUSSION

### Improving the alignments

In fact, the philosophy behind each method is different. Alignment 1 takes advantage of domain knowledge. It requires lexical matches to be supported by structural matches, at the cost of inaccurately rejecting some valid matches. Therefore, it favors precision over recall. On the other hand, Alignment 2 relies on generic algorithms and, by imposing no penalty for lack of structural matches, favors recall over precision. Theoretically, the two approaches could be combined. In practice, however, despite their differences, their results are surprisingly close and any improvement would only be marginal at best.

Nevertheless, each approach can be improved based on the results of the other. Alignment 1 would benefit from addressing partial lexical alignment and identifying matches based solely on structural similarity. Alignment 2 could be improved by taking into account synonyms in FMA and identifying semantic mismatches.

Of particular interest are the 875 relation matches obtained by Alignment 2 in the structural phase for the purpose of increasing the similarity scores of the corresponding concepts and relationships. In addition to increasing the chances of identifying concept matches, these relation matches could be used for themselves. For example, the match by {*FMA: <Lung, contained in, Thoracic cavity>, GALEN: <Lung, isSpecificallyNonPartitivelyContainedIn, Pleural Membrane>*} whose similarity score is .33, captured the difference the two ontologies have in representing the knowledge about equivalent concepts.

### Validating the alignments

The validation of the results of the alignment has been an issue for both groups. Anatomy is a vast domain and, in addition to domain knowledge, the experts are also required to have some knowledge of the two systems under investigation. No group has achieved a comprehensive evaluation of its results. One interest of disposing of two alignments is that there is the possibility of a cross-validation. In fact, while the matches of Alignment 1 can certainly validate those of Alignment 2, the contrary is not neces-

sarily true. In Alignment 1, a lexical match is required to be supported by some structural evidence. Conversely, in Alignment 2, lexical matches get the highest score possible and structural evidence, if any, is only used to increase the score of partial lexical matches. However, matches from Alignment 2 supported by structural evidence could be used to validate the results of Alignment 1. Unfortunately, the similarity score used in Alignment 2 to indicate the quality of the match does not strictly reflect the presence of structural evidence.

### Challenges

Neither alignment identified enough matches. A total of 3,982 concept matches were identified by the two alignments together, only accounting for about 7% of FMA concepts and 17% of GALEN concepts. All concept matches identified by the two alignments are one-to-one matches. However, there are more complex cases where a single concept in one ontology may match a group of concepts in the other [11]. Groups of concepts may also match across ontologies. For example, along the *is-a* hierarchy of FMA, *Lobe of lung* is first modeled by upper/lower positions (i.e., *Upper lobe of lung* and *Lower lobe of lung*). These concepts are further subdivided by laterality (including *Upper lobe of left lung* and *Upper lobe of right lung*). On the other hand in GALEN, *Lobe of Lung* is first modeled by laterality (i.e., *Lobe of Left Lung* and *Lobe of Right Lung*) and further subdivided by upper/lower positions (i.e., *Upper Lobe of Left Lung* and *Lower Lobe of Left Lung*). These modeling differences revealed that *Lobe of Left Lung* in GALEN, rather than to one single concept in FMA, should be matched to two concepts: *Upper Lobe of left lung* and *Lower lobe of left lung*. New alignment techniques need to be explored to handle such complex cases.

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