Assessing the consistency of modeling in complex ontologies: A study of the musculoskeletal system of the Foundational Model of Anatomy

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Abstract
Biomedical ontologies with many types of relations allow a domain of interest to be modeled with a high level of semantic specificity and expressivity. However, the complexity of modeling with many relations can introduce inconsistencies and errors into the representation. Using the Foundational Model of Anatomy as a case study, we identified and analyzed the musculoskeletal content to show both consistencies and inconsistencies in the use of relations for modeling. We also share our early work in addressing the problem of consistency in ontology modeling through use of ontology-specific design patterns.

Keywords
Ontology, Anatomy, Quality assurance, Ontology auditing, Knowledge representation

1. Introduction

Biomedical ontologies are a crucial component of the data and knowledge infrastructure of modern health research, basic science research, and clinical practice. By representing domain-specific knowledge about entities in the world as classes and relations between the classes, they serve as both a source of standardized terms for annotating data and as a computable knowledgebase. In response to these needs, some ontologies have evolved into very large representations with many types of relations. The use of many types of relations within an ontology allows for a high level of semantic specificity and expressivity, but this complexity creates challenges for ontology authors and curators in maintaining consistent modeling and for ontology users in understanding the relations.

1.1. The Foundational Model of Anatomy

The Foundational Model of Anatomy (FMA) is a theory of anatomy expressed in the form of an ontology. As a theory, the FMA asserts that anatomy can be represented using a series of organizing units that represent different levels of granularity. These units include “Cell”, “Portion of tissue”, “Organ”, and “Organ system”. The theory accounts for all structures and spaces produced by coordinated expression of an organism’s genes, as well as immaterial boundary of entities [1], [2]. As a computational artifact embodying this theory of anatomy, the FMA is a reference ontology of canonical human anatomy represented in OWL. It consists of over 100,000 classes and 130 types of relations between classes—making it one of the largest biomedical ontologies in existence. It is recognized as the most comprehensive ontology for adult human gross anatomy.

The FMA is intended to serve as a knowledgebase for software applications requiring knowledge of human anatomy and as a reference ontology for construction of application-specific anatomy ontologies. However, inconsistencies have crept into the modeling of the FMA, resulting in similar

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structures within the body represented in different ways. Causes of these inconsistencies include changes in modeling schemes used by the Structural Informatics Group at the University of Washington during the 20-year development of the FMA and inter-author variation. In addition, the last decade of development was funded through projects focused on specific regions of anatomy—which provided little opportunity to address consistency and completeness of the whole-body model. These issues of inconsistency and incompleteness compromise the ability of the FMA to serve as a knowledgebase for the next generation of intelligent biomedical informatics applications.

1.2. Previous quality assurance work on the FMA

The size and complexity of the FMA have made it a subject of study for groups working on quality assurance methods for ontologies. General auditing techniques, including examining class and part relationships, have been performed by several teams [3]–[5]. In a linguistic approach, unexpected sibling classes were detected by examining directional modifiers within class names (for example, "superior" and "inferior, "anterior" and "posterior", "right" and "left")[6]. Other auditing approaches have been more specific to the structure and anatomical content of the FMA. Modeling of the lymphatic system has been examined using the *efferent_to* relation (a connectivity relation indicating a "downstream" structure) and anatomical knowledge about constraints on the connectivity of lymphatic chains and vessels [7]. Our work was inspired by this example of applying anatomical knowledge to audit organ-system-specific content of the FMA.

1.3. The musculoskeletal system as modeled in the FMA

The FMA class "Organ system" (FMA ID 7149) is defined as "Anatomical structure, each instance of which has as its direct parts instances of one or more organ types which are interconnected with one another by zones of continuity." This definition emphasizes the structural (rather than functional) modeling of the FMA. "Musculoskeletal system" (FMA ID 7482) is defined through its constitutional parts, which are "Entire musculature" and "Skeletal system". (For purposes of this work we are not including the neural network and vasculature of the musculoskeletal system, which has very little modeling.). "Skeletal system" has constitutional parts "Skeleton" and "Set of all skeletal ligaments".

Because the musculoskeletal system consists of a large number anatomical structures of a limited number of types that display a great deal of repetition in how they relate to one another, it serves as an excellent test case for examining consistency in a complex biomedical ontology. The purpose of this work is to demonstrate how we identified the musculoskeletal content of the FMA, to present our analysis highlighting consistencies and inconsistencies in the modeling, and to share our early work in addressing the problem of consistency in ontology modeling.

2. Method of analysis

This study uses the latest version of the FMA (version 5.0.0, created April 2019, retrieved from http://sig.biostr.washington.edu/share/downloads/fma/release/latest/fma.zip). Manual inspection of the FMA was performed using Protégé Desktop [8] version 5.5.0. In addition, a Resource Description Framework (RDF) triple store database was built using the Apache Jena 3.12.0 framework on a MacOS 10.15.7 (Catalina) laptop using OpenJDK 13.0.2. This allowed us to query the triple store using the SPARQL query language via the Jena command line tool tdb2.tdbquery.

Our analysis proceeded in five steps:

Step 1: The class hierarchy of the entire FMA ontology was manually inspected to identify classes relevant to the musculoskeletal system. A list of "superclasses of interest" was created that consisted of classes for which all subclasses represent parts of the musculoskeletal system. We anticipate these classes (such as "Zone of bone organ", and "Articular capsule") will be useful for describing modeling schemes for the musculoskeletal system. Classes that do not have children (such as "Joint of sternum") or do not appear to be fully classified in the FMA (such as "Subdivision of compartment of palm of hand") were not included in this list. Classes for anatomical points, lines, and conduits were not included. An additional three classes (“Skeleton”, “Musculoskeletal system”, and “Skeletal system”) do not have children but were included in the list of superclasses for modeling purposes.

Step 2: Two types of SPARQL queries were performed to identify the relations (known as object properties in OWL) used to construct triples that make assertions about instances belonging to classes relevant to the musculoskeletal system. The first query identified triples for which the subject is a subclass of a “superclass of interest”. The second query identified triples for which the object is a subclass of a “superclass of interest”. Using the sets of triples returned from the queries, counts of the use of each type of relation were tabulated.

Step 3: Lists of relations were examined for their relevance to modeling the musculoskeletal system. The subset of relations describing how parts of the musculoskeletal system relate to one another were designated as “relations of interest”.

Step 4: SPARQL queries were performed to identify triples that contain a subject (or object) that is a subclass of a “superclass of interest” and relation that is a “relation of interest”. The object (or subject) of these triples was then classified using the “superclasses of interest” list. Queries are provided in a Gitlab repository at https://gitlab.com/roggsky/ontologyauditor.git.

Step 5: The types and frequencies of the classified triples were examined to identify consistent and inconsistent use of relations, their subject classes, and their object classes.

3. Results of analysis

Manual inspection of the FMA identified 55 superclasses of interest for representing the musculoskeletal system. These classes and their placement in the class hierarchy is shown in Table 1. Our SPARQL queries identified a total of 69 relations used to form triples with these classes. Table 2 shows the 29 relations of interest for this work, as well as those relating musculoskeletal structures to those of other organ systems (n=14), describing spatial relationships between anatomical structures (n=18), and describing developmental anatomy (n=7).

Table 1

FMA superclasses of interest (in bold)

FMA ID	Class
62955	Anatomical entity
61775	Physical anatomical entity
67112	Immaterial anatomical entity
5897	Anatomical space
67552	Anatomical cavity
2799577	Anatomical cluster space
11356	**Synovial cavity of joint**
12237	Organ cavity
24021	**Cavity of bone organ**
11349	Cavity of serous sac
9678	**Cavity of bursa**
40900	**Cavity of synovial tendon sheath**
67165	Material anatomical entity
55652	Anatomical set
329058	Set of anatomical clusters
73023	**Set of joints**
78590	Set of heterogeneous anatomical structures
317741	**Heterogeneous set of bones**
32558	**Musculature**
70779	Set of organs
71324	**Set of bone organs**
71454	**Set of bursae**
70773	**Set of ligaments**
303662	**Set of skeletal cartilage organs**
303658	**Set of skeletal ligaments**
303660	**Set of skeletal membrane organs**
84357	**Set of tendon sheaths**
303630	**Skeleton***

continued next page

05751	Anatomical structure
67135	Postnatal anatomical structure
49443	Anatomical cluster
9647	Anatomical compartment
321219	**Intervertebral compartment**
5898	Anatomical junction
7490	Joint
7491	**Nonsynovial joint**
7501	**Synovial joint**
64988	**Sutural junction**
64989	Heterogeneous anatomical cluster
9608	**Bone marrow**
82472	Cardinal organ part
14065	Organ component
225625	**Articular part of bone organ**
83129	**Bony part of bone organ**
75445	Membrane organ component
27984	**Fibrous membrane of articular capsule**
36928	**Fibrous membrane of synovial bursa**
40877	**Fibrous membrane of synovial tendon sheath**
82485	Organ component layer
82496	Membranous layer of organ wall
32692	**Endosteum**
297498	Muscle body
297500	**Skeletal muscle body**
297481	Muscle fiber group
9725	Striated muscle fasciculus
68013	**Skeletal muscle fasciculus**
9721	**Tendon**
67619	Organ region
55268	Organ zone
10483	**Zone of bone organ**
304784	**Zone of cartilage organ**
10474	**Zone of muscle organ**
86103	Region of organ component
302036	**Region of bony part of bone**
329204	**Region of skeletal membrane organ component**
298716	Region of skeletal muscle body
298816	**Distal region of muscle body**
298728	**Head region of muscle body**
9719	**Muscle belly**
299586	**Region of part of muscle belly**
281759	Region of surface layer of organ
281765	**Region of surface layer of bone organ**
298404	**Region of tendon**
67498	Organ
55671	Cavitated organ
55673	Organ with cavitated organ parts
5018	**Bone organ**
55672	Organ with organ cavity
9689	Serous sac
66760	Synovial sac
9692	**Synovial bursa**
256694	**Synovial capsule of joint**
45087	**Synovial tendon sheath**
55670	Solid organ
55665	Nonparenchymatous organ
55107	Cartilage organ
302988	**Skeletal cartilage organ**
21496	Ligament organ
25624	**Skeletal ligament**
7145	Membrane organ
302986	Skeletal membrane organ
34836	**Articular capsule** *continued next page*

64125	**Capsule of nonsynovial joint**
54839	**Interosseous membrane**
5022	**Muscle organ**
7149	Organ system
7482	**Musculoskeletal system***
67509	Organ system subdivision
23881	**Skeletal system***
85544	**Subdivision of skeletal system**
9637	Portion of tissue
9641	Portion of muscle tissue
67905	Striated muscle tissue
14069	**Skeletal muscle tissue**
9669	Portion of body substance
280556	Portion of body fluid
280564	Portion of body fluid suspension
20932	Portion of serous fluid
12277	**Portion of synovial fluid**

* These classes do not have subclasses

Table 2
Relations used with classes relevant to the musculoskeletal system

Relations of interest for this work	*articulates with* *attaches to* *attributed part* *bounded by* *bounds* *branch* *branch of* *connected to* *constitutional part* *constitutional part of*	*contained in* *contains* *continuous distally with* *continuous proximally with* *continuous with* *has insertion* *has origin* *insertion of* *member* *member of*	*muscle attachment* *origin of* *part* *part of* *receives attachment from* *regional part* *regional part of* *surrounded by* *surrounds*
Relations to other organ systems	*arterial supply* *arterial supply of* *lymphatic drainage* *lymphatic drainage of* *nerve supply*	*nerve supply of* *primary segmental supply* *primary segmental supply of* *secondary segmental supply* *secondary segmental supply of*	*segmental supply* *segmental supply of* *venous drainage* *venous drainage of*
Spatial relations	*adjacent to* *anterior to* *anteromedial to* *direct left of* *direct right of* *distal to*	*inferior to* *lateral to* *left lateral to* *left medial to* *medial to* *posterior to*	*posteromedial to* *posterosuperior to* *proximal to* *right lateral to* *right medial to* *superior to*
Developmental relations	*derives* *derives from* *fuses with*	*matures from* *matures into*	*transforms from* *transforms into*

Table 3 displays counts of subject-relation pairs. It shows that some relations are used with many different types of subject-relation pairs, while others are used with only a few types of subject-object pairs. Some relations are used thousands of times, while others much less frequently.

Examples of counts of classified triples are shown in Tables 4, 5, and 6. Table 4 demonstrates that some triples can be identified as errors simply based on their subject-relation-object scheme. For example, “Portion of synovial fluid” cannot be a regional part of “Synovial bursa” (but it is allowed to be a constitutional part in the modeling of the FMA). Table 5 examines the subject and object superclasses used with the *attaches_to* and *articulates_with* relations. (Articulation refers to a connection between bone organs or a bone and cartilage organ). We found that the vast majority of *articulates_with* are used with a subject and object that are both a “Bone organ”, and that *attaches_to* most commonly describes the relation between a “Tendon” and “Zone of bone organ”. Table 6 demonstrates some of the variety of relations describing connections between organs and parts of organs within the musculoskeletal system.

Table 3
Counts of subject-relation pairs for 12 frequently used relations

Subject	*connected to*	*constitutional part*	*constitutional part of*	*contained in*	*contains*	*continuous distally with*	*continuous proximally with*	*continuous with*	*member*	*member of*	*regional part*	*regional part of*
Synovial cavity of joint			172		119							1
Cavity of bone organ			309								213	214
Cavity of bursa			7		27							7
Cavity of synovial tendon sheath			104		18						3	3
Set of joints			46						1098	131		
Heterogeneous set of bones			5						25	3		
Musculature			148	8					1535	127	44	4
Set of bone organs			64						464	110	13	4
Set of bursae			3						21			
Set of ligaments			9						53	7		
Set of skeletal cartilage organs			5						53	5	5	
Set of skeletal ligaments			1						89	22		
Set of skeletal membrane organs												
Set of tendon sheaths												
Skeleton			1						2			
Intervertebral compartment		23										
Nonsynovial joint	70	126	20							290	92	1
Synovial joint		1241	82						676		9	4
Sutural junction			7									
Bone marrow		2								1		
Articular part of bone organ			1									
Bony part of bone organ		1097	310								33	
Fibrous membrane of articular capsule			7									55
Fibrous membrane of synovial bursa												12
Fibrous membrane of synovial tendon sheath			36								3	3
Endosteum			74									
Skeletal muscle body		306	342					9			209	12
Skeletal muscle fasciculus		3	2									51
Tendon		5	722			16	16	79			53	98
Zone of bone organ	52	790	174							17	2307	2648
Zone of cartilage organ												10
Zone of muscle organ		361	84	6				3		24	312	689
Region of bony part of bone			9									17
Region of skeletal membrane organ component												
Distal region of muscle body			57			12	9	84			9	78
Head region of muscle body		2	82			9	16	81			31	116
Muscle belly			5			13	9	97			11	347
Region of part of muscle belly								18				27
Region of surface layer of bone organ												
Region of tendon			9	3				6				36
Bone organ	14	1430	335	1						356	1215	21
Synovial bursa		21	21							21	22	
Synovial capsule of joint		2	3								10	
Synovial tendon sheath		204	36									
Skeletal cartilage organ			83							35	252	3
Skeletal ligament		7	498							113	62	126
Articular capsule		28	210								115	1
Capsule of nonsynovial joint			2								2	
Interosseous membrane			1									
Muscle organ		875	277	163						1360	918	55
Musculoskeletal system		4	3								6	
Skeletal system		3	1								5	
Subdivision of skeletal system		360	122							2	125	76
Skeletal muscle tissue			255								3	
Portion of synovial fluid			9	164								6

Table 4

Examples of classifications of triples — Examining use of objects with subject-relation pairs

Subject	Relation	Object	Count	Comment
Synovial joint	*constitutional part*	Zone of bone organ	9	
		Synovial cavity of joint	171	
		Portion of synovial fluid	2	
		Skeletal ligament	351	
		Synovial capsule of joint	3	Different than articular capsule?
		Skeletal cartilage organ	24	
		Articular capsule	210	
		Synovial bursa	2	Describes median atlanto-axial joint
	constitutional part of	Subdivision of skeletal system	22	
	member of	Set of joints	676	
	regional part	Synovial cavity of joint	1	Error: should be *constitutional part*
		Portion of synovial fluid	1	Error: should be *constitutional part*
		Skeletal ligament	2	Error: should be *constitutional part*
		Articular capsule	1	Error: should be *constitutional part*
		Synovial joint	2	Describes humeroulnar joint of elbow
	regional part of	Set of skeletal cartilage organs	2	Error: sets do not have regional parts
		Synovial joint	2	
Portion of synovial fluid	*constitutional part of*	Synovial joint	2	
		Synovial bursa	7	
	contained in	Cavity of synovial tendon sheath	18	
		Cavity of bursa	27	
		Synovial cavity of joint	119	
	regional part of	Synovial joint	1	Error: should be *constitutional part*
		Synovial bursa	5	Error: should be *constitutional part*
Skeletal cartilage organ	*articulates with*	Bone organ	38	
	constitutional part of	Nonsynovial joint	25	
		Synovial joint	24	
		Subdivision of skeletal system	24	
	member of	Set of skeletal cartilage organs	35	
	regional part	Zone of bone organ	36	Error: these are different organ types
		Zone of cartilage organ	10	
	regional part of	Set of cartilage organs	3	Error: should be *member of*

Table 5

Examples of classifications of triples — Examining use of subjects and relations for a given relation

Relation	Subject	Object	Count	Comment
articulates with	Skeletal cartilage organ	Bone organ	38	
	Subdivision of skeletal system	Bone organ	4	
	Bone organ	Bone organ	604	
		Skeletal cartilage organ	38	
		Subdivision of skeletal system	4	
attaches to	Skeletal ligament	Zone of bone organ	18	
	Zone of cartilage organ	Zone of bone organ	12	
	Region of tendon	Zone of bone organ	9	Difference in granularity of attachment of muscle to Zone of bone organ
	Muscle organ	Zone of bone organ	11	
	Zone of muscle organ	Zone of bone organ	2	
	Tendon	Zone of bone organ	207	
		Subdivision of skeletal system	3	

Table 6
Examples of classifications of triples — Examining use of relations for subject-object pairs

Subject	Object	Relation	Count
Zone of bone organ	Zone of muscle organ	*insertion of*	60
		origin of	98
		receives attachment from	2
	Muscle organ	*insertion of*	46
		receives attachment from	11
	Tendon	*origin of*	1
		receives attachment from	207
Skeletal ligament	Zone of bone organ	*attaches to*	18
		has insertion	24
		has origin	36
Muscle organ	Bone organ	*has insertion*	6
		has origin	8
	Zone of bone organ	*attaches to*	11
		has insertion	46
		has origin	61

4. Discussion of findings

Our approach to identifying and analyzing the musculoskeletal content of the FMA highlights the usefulness of this type of audit for assessing consistency and detecting errors.

Infrequent subject-relation-object as tool for error detection: As shown in Table 4, we detected a number of invalid subject-relation-object combinations. Most of these combinations occurred with low frequency, suggesting that low-frequency combinations could serve as a flag for verification by a curator. We note that not all triples with unusual subject-relation-object combinations are incorrect—they may simply represent anatomical configurations that occur less frequently. For example, of 262 triples using *attaches_to*, 259 of those have a "Zone of bone organ" class as the object, while the remaining three use a "Subdivision of skeletal system" as the object. These triples describe the attachment of the proximal tendon of the temporalis to a region of the cranium spanning more than one bone organ, so this explains the unusual classification. As another example, the combination "Skeletal ligament" *origin_of* "Muscle organ" was detected only once in our audit, but the triple with this classification ("Ligamentum nuchae" *origin_of* "Serratus posterior superior") is anatomically valid. Several additional triples, including "Ligamentum nuchae" *origin_of* "Trapezius" could be modeled following this scheme.

Inconsistent use of relations: We found two different methods used for modeling the relation of muscles to the structure they attach to. One method employs the relation *attaches_to* (inverse: *receives_attachment_from)*. The other uses *has_origin* (inverse: *origin_of)* and *has_insertion* (inverse: *insertion_of)*. The latter method is intended to denote which bone does not move during muscle contraction, but this is complicated by the fact that many muscles can change their functional origin and insertion based on the joint that is being mobilized during a given contraction. Although not explored in this audit, an additional relation *(muscle_attachment)* is used in a 23 cases to model a ternary relationship among a muscle organ, its site of origin or insertion, and the region of the muscle involved in the attachment. This lack of standardized modeling for the attachment of muscles highlights that inconsistent use of relations in the FMA makes it difficult to use as a computable knowledgebase.

Our audit also points to several additional issues:

Lack of definitions for relations: The *fuses_with* relation was introduced into the FMA while modeling craniofacial anatomy to describe time-based relationships between anatomical structures during development [9]. However, three triples use this relation to represent how fibers of the distal tendon of biceps femoris intermingle with those of the fibular collateral ligament. This is not necessarily an error (because the relation does not have a definition), but the term "fuses with" is not generally used outside of embryological development (*attaches_to* is a more appropriate relation for this example).

Constitutional parts of the Musculoskeletal system are incomplete: FMA modeling aims to represent exhaustive partitions of structures when they are described using either the *constitutional_part* or *regional_part* relations. Tracing the constitutional parts of "Musculoskeletal system" through the part hierarchies accounts for the muscle organs, bone organs, cartilage organs, and skeletal ligaments organs. But the synovial sac organs and skeletal membrane organs are missing from this partonomy.

Updates needed to legacy naming and modeling: We encountered a few labels of classes that reflect early modeling. For example, "Region of bony part of bone" should be interpreted as "Region of bony part of bone organ" (the term "bone" has been deprecated and replaced with wording that clarifies whether the bone organ or a portion of bone tissue is referred to). The relations *part* and *part_of* are no longer to be used in constructing triples (current modeling uses either *regional_part* or *constitutional_part*), but we found these relations used in 15 triples.

5. Developing and expressing ontology-specific patterns for complex ontologies

To address issues of consistency in large biomedical ontologies such as the FMA, we are in the early stages of developing a method to represent knowledge of how domain-specific entities relate to one another in a machine readable format. Our approach is similar to the use of design patterns for ontologies, which are schema that serve as reusable solutions to common modeling tasks in ontology development [10]–[12]. However, the patterns we are developing are specific to the FMA.

These ontology-specific patterns are specifications of subgraphs that are machine readable and have parameterized properties which layer "closed world" constraints onto the "open world" assumptions of OWL. In the context of the FMA, they place restrictions and requirements on relations between types of anatomical structures. Our process for developing these patterns begins with analyzing the FMA to understand variations in modeling, as shown in this paper. We then construct the patterns in the form of diagrams based on existing modeling in the FMA, the intent of the FMA, and expert anatomical knowledge. Figure 1 shows a diagram of a preliminary pattern for the class "Synovial joint".

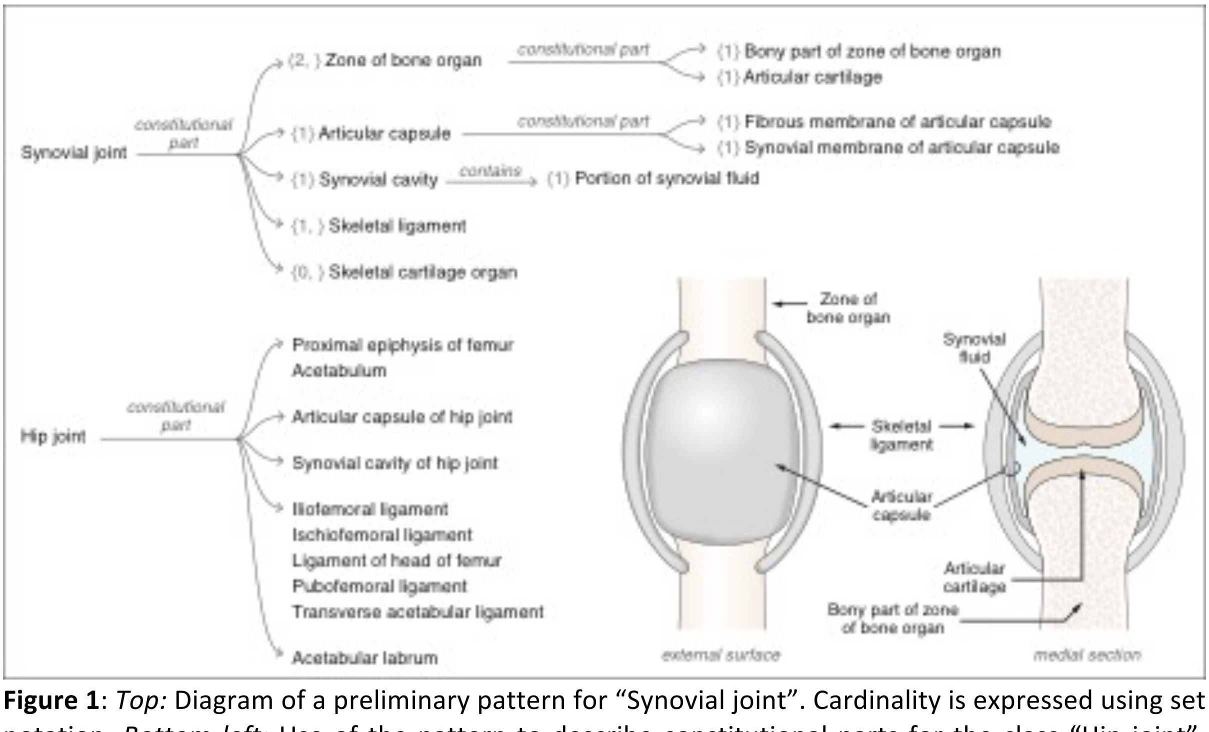

Figure 1: *Top:* Diagram of a preliminary pattern for "Synovial joint". Cardinality is expressed using set notation. *Bottom left:* Use of the pattern to describe constitutional parts for the class "Hip joint". *Bottom right:* Schematic illustration of a synovial joint.

5.1. Opportunities to use ontology-specific patterns with complex ontologies

We envision four ways in which this type of pattern can be applied to the development and use of ontologies:

- **Guided content creation.** When the authors have provided a pattern for classes of a given type (such as muscle organs), editors creating new classes of that type (for example, Biceps brachii) can use the pattern as a template for how that class is to be represented in the ontology. This would help enforce consistent modeling.
- **Guided content retrieval.** If content has been modelled uniformly, patterns can be used to facilitate content retrieval because they specify the relations that may be of interest to users (such as retrieving tendons related to a muscle organ via the *constitutional_part* property).
- **Guided error checking.** If patterns were not used consistently to guide content creation, then patterns can be used to find areas of content that violates patterns. Depending on how the patterns are specified, they could find not only incomplete modeling, but also the use of relations or types of classes that are prohibited.
- **Documentation.** Users of complex ontologies need to make sense of the modeling schemes employed, and simply browsing an ontology may not reveal these schemes. Providing human-readable diagrams of patterns will allow viewers to better understand the ontology's structure, particularly when they cannot directly ask the author(s).

6. Conclusion

The FMA provides an excellent case study for the development of ontology-specific patterns. As demonstrated in this work, the musculoskeletal system consists of a number of organ types that relate to one another in predictable ways. Additional organ systems, such as the nervous system, circulatory system, are also good candidates for describing with patterns. Patterns could be applied to the FMA to describe modeling of other repetitive structures, such as anatomical cavities, their walls, and their contents.

Our approach to developing ontology-specific patterns is intended to be generalizable to any ontology, and could be useful for ensuring consistency in other biomedical ontologies that use a large number of relations, such as SNOMED CT and the Cell Ontology.

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