A Formal Theory for Spatial Representation and Reasoning in Biomedical Ontologies

Maureen Donnelly[1], Thomas Bittner[1], Cornelius Rosse[2]

Institute for Formal Ontology and Medical Information Science, Saarland University, Saarbrücken, Germany[1]*;*
Structural Informatics Group, Department of Biological Structure,
University of Washington, Seattle, WA, USA[2]*.*

Correspondence: Maureen Donnelly, IFOMIS Saarland University Postbox 151150, D-66041 Saarbrücken, Germany.
maureen.donnelly@ifomis.uni-saarland.de

Abstract

This paper presents a formal theory of parthood and location relations among individuals, called Basic Inclusion Theory (BIT). Since biomedical ontologies are comprised of assertions about classes of individuals (rather than assertions about individuals), we define parthood and location relations among classes in the extended theory BIT+Cl (Basic Inclusion Theory for Classes). We then demonstrate the usefulness of this formal theory for making the logical structure of spatial information more precise in two ontologies concerned with human anatomy: the Foundational Model of Anatomy (FMA) and GALEN. In particular, we show how formal characterizations of the parthood and location relations assumed by biomedical ontologies can help disambiguate assertions within the ontologies and clear the way for stronger automatic reasoning capabilities. In addition, a precise characterization of relations is necessary for the alignment of different ontologies. Although we focus here on the simplest and most pervasive of the spatial relations used in biomedical ontologies (parthood and location), the strategy employed in this paper can be used in analogous treatments of other kinds of spatial relations among classes.

Keywords:
Ontology, Knowledge Representation, Anatomy, Mereology, Spatial Reasoning

1. Introduction

Spatial reasoning is a central component of medical research and practice and must be incorporated into any successful medical informatics program. The spatial concepts most often used in biology and medicine are not the quantitative, point-based concepts of classical geometry, but rather qualitative relations among extended objects such as body parts. The purpose of this paper is to propose a formal basis for the kind of qualitative spatial reasoning that is found in biology and medicine. We focus in this paper only on the most basic qualitative spatial relations—parthood and location relations. But the general approach taken here can be extended to also include other, more complex, qualitative spatial relations which are important in biomedical reasoning such as adjacency, connectedness, and continuity.

Spatial reasoning in biology and medicine concerns either individuals or classes of individuals. By an *individual*, we mean a concrete entity which, at each moment of its existence, occupies a unique spatial location. Individuals can be either material (my liver, your brain) or immaterial (the cavity of my stomach). Individuals are distinguished from *classes* (also called universals, kinds, or types) which may have, at each moment, multiple individual instances. Examples of classes are *Liver* (the class whose instances are individual livers) and *White Blood Cell* (the class whose instances are individual white blood cells). (Throughout this paper, we use italics and initial capitals for class names.) Although with time classes may gain and lose instances (when, e.g., white blood cells are created or die), the class itself does not change its identity. In the design of biomedical ontologies, a particular challenge is presented by the need for associating spatial relations with classes, since in reality such relations hold only among individuals (see below).

In recent years, much work has been done on constructing formal theories that model reasoning about qualitative spatial relations among individuals [1, 6, 9, 21]. A *mereology* is a formal theory of parthood and of relations--such as overlap (having a common part) and discreteness (having no common part)--defined in terms of parthood. Since its relations apply directly to concrete individuals and require neither quantitative data nor mathematical abstractions (points, lines, etc), a mereology is a natural basis for qualitative spatial reasoning in medicine.

In Section 2 of this paper, we present an extended mereology, Basic Inclusion Theory (BIT), which includes location relations in addition to the usual mereological relations. By *location relations*, we mean relations that depend only on the locations of relevant individuals and not on whether they share parts. Though not incorporated into most mereologies, the distinction between mereological relations and location relations is crucial for medicine since human bodies include immaterial spaces (cavities and lumina) which have no material parts but which may contain material structures or substances. For example, a parasite (a material entity) may be located in an intestinal lumen (an immaterial space) but the parasite is not itself part of the lumen or of the intestines and does not share parts with them. Similarly, a portion of blood (a material substance) currently located in the cavity of my right ventricle (an immaterial space) is not part of the right ventricle or its cavity.

All mereologies, including BIT, apply directly only to individuals such as my stomach or the lumen of a particular patient's small intestine. A more complicated form of qualitative spatial reasoning -- reasoning about relations among classes of individuals -- is also common in medical contexts. In canonical anatomy, we find assertions such as "the stomach is continuous with the esophagus", "the right ventricle is part of the heart" or "the brain is contained in the cranial cavity". As is emphasized in [22], it is important to distinguish these sorts of assertions from claims about relations among individuals (e.g. "patient X's right ventricle is part of patient X's heart" or "my stomach is continuous with my esophagus").

Since they apply to multiple individuals, the class-level relations are defined formally in terms of relations among individuals using universal quantification. For example, [22] uses universal quantification and a mereologically-formalized parthood relation to define relations among classes corresponding to the use of "part of" in assertions of canonical anatomy such as "the right ventricle is part of the heart". In Section 3 of this paper, we show how the same strategy can be used to define class-level versions of any relations among individuals, including all relations of BIT. Here we develop an extension of BIT, called Basic Inclusion Theory for Classes (BIT+Cl), which formally characterizes mereological and location relations among classes. In Section 4, we examine the logical properties of the defined class relations. We find that different versions of the class relations have significantly different logical properties. We also see that several important logical properties of the individual relations do not transfer automatically to the corresponding class relations. Thus, though a strong formal theory of relations among individuals is a necessary foundation for a formal theory of relations among classes, it is important to also investigate the distinct logical properties of the class relations and to determine how they behave with respect to particular kinds of classes.

A formal analysis of relations among classes, such as that presented in BIT+Cl, is critical for the development and alignment of biomedical ontologies including the Foundational Model of Anatomy (FMA) [17], GALEN [14, 15], and the Gene Ontology (GO) [10], as well as terminologies such as SNOMED-RT [23] and the UMLS. These ontologies and terminologies consist mainly of claims about relations among biological classes. For example, in the FMA, we have assertions such as: *Right Ventricle* part_of *Heart*; *Liver* contained_in *Abdominal Cavity*. In GALEN, we have: *Left Heart Ventricle* isDivisionOf *Heart*; *Liver* isContainedIn *Abdominal Cavity*. (Throughout this paper, we use Arial font for the relations of specific ontologies.) By establishing links between their relation terms and the relations of a formal theory, the developers of a biomedical ontology can ensure that all curators use their relation terms consistently within the biomedical ontology and make the meanings of their relation terms clear to outside ontologists. In particular, formal analyses of the relation terms in the FMA and GALEN are needed to determine whether these ontologies attribute the same meanings to similar terms (e.g. the FMA's contained_in vs. GALEN's isContainedIn). In addition, formal analyses of relation terms are required for strong, consistent automated reasoning within the ontologies. In Section 5 of this paper, we use BIT+Cl to analyze and compare the most general of the parthood and containment relations in the FMA and GALEN. We show how precise and consistent characterizations of these relations would improve the clarity of the information embodied in these ontologies and lead to stronger automated reasoning capabilities.

Because we focus in the end of this paper on the FMA and GALEN, our discussion throughout the paper focuses on examples from human anatomy. However, the formal theory developed here is very general and can be used to for reasoning about other kinds of classes of spatially or spatio-temporally located individuals (e.g. classes of chemical substances or classes of diseases).

2 Mereological and Location Relations among Individuals

Several different mereologies have been proposed in recent literature, for example [1, 6, 21]. Mereologies have been extended to include also location relations in [5, 9]. In this section, we present a version of the formal theory of [5] and discuss how it can be used to model medical reasoning about individual human bodies and the parts and occupants of those bodies. We present the basic axioms, definitions, and theorems in sections 2.1 and 2.2. We call the formal theory consisting of these axioms and definitions Basic Inclusion Theory (BIT).

Notice that mereological and location relations may hold between individuals at some times but not at other times. For example, the sinus venosus was part of my heart at an earlier developmental stage but no longer exists. Fully formed organisms also gain and lose parts: blood cells that are part of my body today will not be part of my body in twenty days. However, for reasons of simplicity, mereologies typically do not deal with time and change. We will follow that procedure and treat mereological and location relations throughout this paper as time-independent relations. The theory thus developed here describes, within a given time-frame, a static spatial arrangement of individuals. An important project for further work is to incorporate time and change into our theory. Some progress is being made in this direction [3, 4].

2.1 Mereological Relations

In this section, we introduce the basic mereological relations, axioms, and theorems. The theory is formulated in first-order predicate logic with identity.

Parthood (symbolized as "P") is the relation that holds between two individuals, x and y, whenever x is part of y. In the mereologies presented in [9, 21], parthood is treated as a primitive relation. This means that, instead of being defined, axioms fixing the logical properties of the parthood relation are built into the theory. The parthood relation must then be interpreted in applications in a way that conforms to these axioms. Axioms that are included in nearly every mereology are:

(P1)[1] Pxx (every object is part of itself)[2]

(P2) Pxy & Pyx $\rightarrow$ x = y (if x is part of y and y is part of x, then x and y are identical)

(P3) Pxy & Pyz $\rightarrow$ Pxz (if x is part of y and y is part of z, then x is part of z)

(P1) tells us that P is *reflexive*, (P2) tells us that P is *antisymmetric*, and (P3) tells us that P is *transitive*. Thus, P is a *partial ordering* (a reflexive, antisymmetric, and transitive binary relation). Axioms (P1)-(P3) are not very strong. They cannot distinguish the parthood relation from other partial orderings such as the less-than-or-equal-to relation on the real numbers or the is-a-factor-of relation on the positive integers. For this reason, most

[1] Axioms specific to the parthood relation are labeled with a "P".
[2] Throughout this paper, initial universal quantifiers are dropped unless they are needed for clarity.

mereologies include additional axioms which further restrict the parthood relation [20]. We suggest a few additional axioms that seem appropriate for anatomical reasoning in Section 2.3.

Proper parthood and overlap are binary relations among individuals that are defined in terms of parthood.

Proper Parthood: x is a *proper part* of y, if x is any part of y other than y itself. Symbolically:

$$PPxy =: Pxy \ \& \ x \neq y.$$

For example, my hand is a proper part of my body. My body is a part of itself, but it is not a proper part of itself.

Overlap: x and y *overlap*, if there is some object, z, that is part of both x and y. Symbolically:

$$Oxy =: \exists z \ (Pzx \ \& \ Pzy).$$

My bony pelvis and my vertebral column overlap: my sacrum and my coccyx are part of both.

Inverse Relations: Inverses of the relations above may be introduced. The inverse of a binary relation *S* is the binary relation S^{-1} defined: $S^{-1}xy$ if and only if *S*yx. (Here, *S* can be *any* binary relation, including a relation among classes such as those introduced in Section 3. However, we focus now only on binary relations among individuals.) Thus, $PP^{-1}xy$ if and only if PPyx. For example, PP^{-1}(my heart, my right ventricle) tells us that my heart has my right ventricle as one of its proper parts.

Notice however that when *S* is a *symmetric* relation (i.e. for all x and y, *S*xy if and only if *S*yx), S^{-1} is the same relation as *R*. For example, the overlap relation is symmetric and, therefore, is its own inverse ($O^{-1} = O$).

Additional relations (and their inverses) can be easily introduced into a mereology, but will not be considered in this paper. For example, we could say that two individuals are *discrete* when they do not overlap (e.g. brain and my cranial cavity are discrete) and that two individuals *properly overlap* when they overlap but neither is part of the other (e.g. my bony pelvis and my vertebral column properly overlap).

Basic Mereological Theorems: Because BIT is formulated in first-order predicate logic, we can derive an infinite number of additional formulae from the axioms and definitions of BIT. These additional formulae are the *theorems* of BIT. Most of the theorems of any theory are uninteresting reformulations of the axioms and definitions. But some are important logical consequences of the axioms and definitions that may not be obvious.

Even BIT's relatively weak mereological axioms yield interesting theorems. These include the following.

(PT1)[3] $PPxy \ \& \ PPyz \rightarrow PPxz$ (proper parthood is transitive)

(PT2) $PPxy \rightarrow \sim PPyx$ (proper parthood is asymmetric: if x is a proper part of y, then y is not a proper part of x)

(PT3) $\sim PPxx$ (proper parthood is irreflexive: nothing is a proper part of itself)

(PT4) $Oxy \rightarrow Oyx$ (overlap is symmetric: if x overlaps y then y overlaps x)

(PT5) Oxx (overlap is reflexive: everything overlaps itself)

(PT6) $PPxy \rightarrow Oxy$ (if x is a proper part of y, then x overlaps y)

(PT7) $Oxy \ \& \ Pyz \rightarrow Oxz$ (if x overlaps y and y is part of z, then x overlaps z)

For example, from:

patient x's left ventricle is a proper part of patient x's heart

and

patient x's aortic vestibule is a proper part of patient x's left ventricle

it follows that

patient x's aortic vestibule is a proper part of patient x's heart.

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[3] Theorems which can be derived from just the mereological axioms of BIT are labeled with "PT".

2.2 Location Relations

Basic Inclusion Theory needs to be further extended to include also location relations among individuals. We can already say something about the relative location of two objects using mereological relations: if x is part of y, then x is *located in* y in the sense that x's location is included in y's location. Also, if x and y overlap, then x and y *partially coincide* in the sense that x's location and y's location overlap. The location relations enable us to, in addition, describe the relative location of objects that may coincide wholly or partially without being part of one another or overlapping. A parasite in the interior of a person's intestine is located in the lumen of his intestines, but it is not part of the lumen of his intestines. As another example, my esophagus partially coincides with my mediastinal space, but does not overlap (i.e. share parts with) my mediastinal space.

Human bodies have not only material parts (livers, hearts, etc) but also immaterial parts such as passageways and spaces (the lumen of an esophagus, the cavities of the ventricles of a heart, an abdominal cavity) through which substances pass and in which anatomical structures are located. Since the material entities which are temporarily or permanently located in these spaces and passageways never share parts with them, mereological relations are not useful for describing the positions of material individuals relative to spaces and passageways. For these reasons, anatomical reasoning requires location relations distinct from mereological relations [8, 11, 16, 18].

In both [5] and [9], all location relations are introduced in terms of a region function, r, that maps each individual to the unique spatial region at which it is exactly located at the given moment. Spatial regions are here assumed to be the parts of an independent background space in which all individuals are located. Because we are abstracting here from temporal change and, in particular, from movement, we treat r as a time-independent primitive function. BIT's axioms for the region function are as follows.

(L1)[4] $Pxy \rightarrow Pr(x)r(y)$ (if x is part of y, then x's region is part of y's region)

(L2) $r(r(x)) = r(x)$ (x's spatial region is its own spatial region)

The location relations are defined using the region function and mereological relations.

Located In: x is *located in* y if x's region is part of y's region. Symbolically:

$$\text{Loc-In}(x, y) =: Pr(x)r(y).$$

For example, my brain is located in (but not part of) my cranial cavity. A parasite may be located in (but not part of) a patient's intestinal lumen.

Partial Coincidence: x and y *partially coincide* if x's spatial region and y's spatial region overlap. Symbolically:

$$\text{PCoin}(x, y) =: Or(x)r(y) .$$

For example, my esophagus partially coincides with my mediastinal space. Notice that here the stronger relation Loc-In does not hold. My esophagus' region is not part of the region of my mediastinal space since part of my esophagus lies outside of my mediastinal space. As another example, a bolus of food that is just beginning to enter my stomach cavity partially coincides with (but is not located in) my stomach cavity.

Inverse Relations: Inverses of the relations above may be introduced. For example, x stands in the Loc-In^{-1} to y if and only if Loc-In(y,x). Thus, Loc-In^{-1}(my cranial cavity, my brain) tells us that my brain is located in my cranial cavity.

Figure 1 is a composite of different configurations of the individuals x and y which can be distinguished in BIT. Below each component of the figure, we list: first, the strongest relation (or conjunction of relations and their

[4] Axioms specific to the region function are labeled with "L".

negations) which holds from x to y; second, the strongest relation (or conjunction of relations and their negations) which holds from y to x; and third, an example of two anatomical individuals that stand in these relations.[5] A solid line separating x and y indicates that x and y do not share any parts. A dotted line separating x and y indicates that x and y overlap.

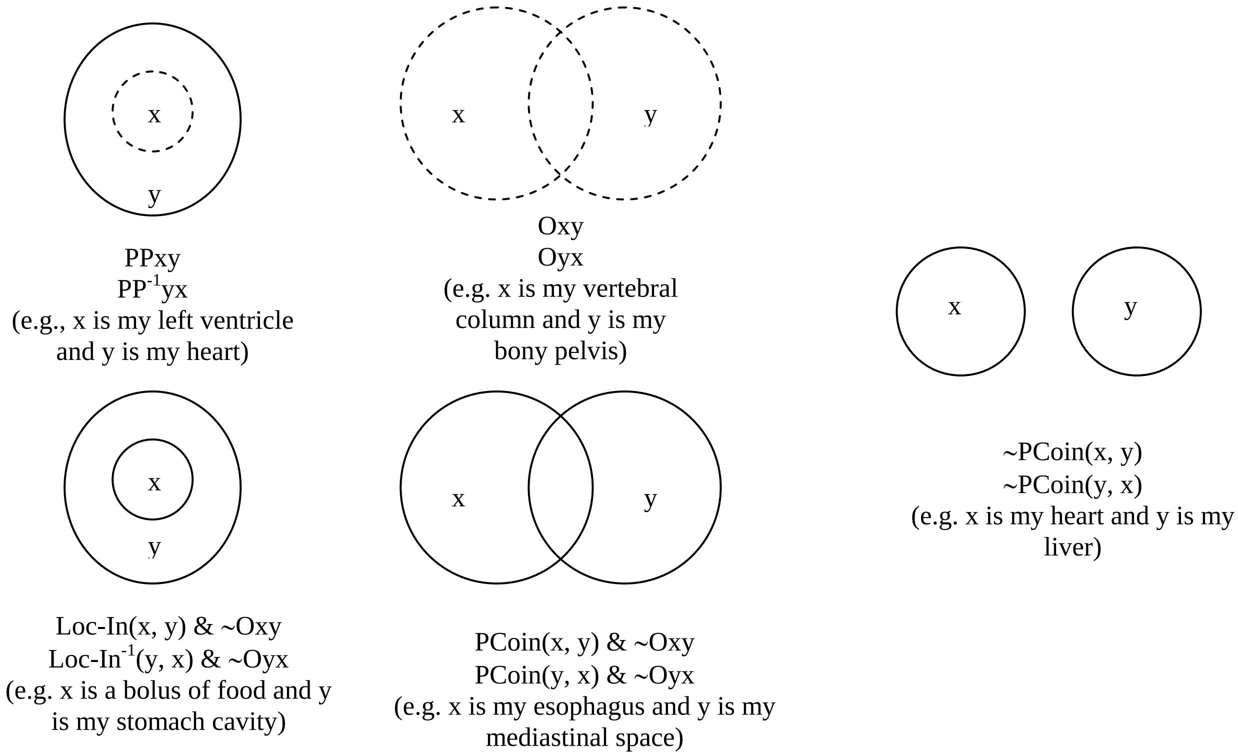

Figure 1: Basic Spatial Inclusion Theory (BIT) relations

As with the mereological relations, additional location relations could be easily added to BIT, but will not be considered in this paper. For example, we could say that two individuals are *non-coincident* if they do not partially coincide (e.g. my heart and my liver are non-coincident).

Theorems Involving Location Relations: From the axioms and definitions of BIT, we can derive the following theorems concerning the location relations.

(LT1)[6] Loc-In(x, x) (the located in relation is reflexive: every individual is located in itself)
(LT2) Loc-In(x, y) & Loc-In(y, z) $\rightarrow$ Loc-In(x, z) (the located in relation is transitive: if x is located in y and y is located in z, then x is located in z)
(LT3) Pxy $\rightarrow$ Loc-In(x, y) (if x is part of y, then x is located in y)
(LT4) PPxy $\rightarrow$ Loc-In(x, y) (if x is a proper part of y, then x is located in y)
(LT5) Loc-In(x, y) & PPyz $\rightarrow$ Loc-In(x, z) (if x is located in y and y is a proper part of z, then x is located in z)
(LT6) PPxy & Loc-In(y, z) $\rightarrow$ Loc-In(x, z) (if x is a proper part of y and y is located in z, then x is located in z)
(LT7) PCoin(x, x) (partial coincidence is reflexive)
(LT8) PCoin(x, y) $\rightarrow$ PCoin(y, x) (partial coincidence is symmetric)
(LT9) Oxy $\rightarrow$ PCoin(x, y) (if x and y overlap, then x and y partially coincide)

[5] Note that the shapes of the drawings are not intended to correspond to the shapes of the individuals used as examples.
[6] Theorems that are derived using the region function axioms are labeled with "LT".

(LT10) Loc-In(x, y) $\rightarrow$ PCoin(x, y) (if x is located in y, then x partially coincides with y)

Using, for example, (LT5) we can derive:

patient x's heart is located in patient x's thoracic cavity

from

patient x's heart is located in patient x's middle mediastinal space

and

patient x's middle mediastinal space is a proper part of patient x's thoracic cavity.

2.3 Additional Axioms

BIT's restrictions on the mereological and location relations are rather weak. In particular, they are significantly weaker than those of the theories presented in [1, 5, 6, 9, 21]. As pointed out in Section 2.1, axioms (P1) - (P3) cannot distinguish the parthood relation from very different partial orderings, such as the less-than-or-equal-to relation on the real numbers. The logical properties of BIT's other relations are also only loosely constrained.

The purpose of this subsection is to briefly give a few examples of kinds of axioms that might be added to BIT to further restrict the interpretations of its relations. It is important for the developers of a biomedical ontology to attempt to link their relational terms to the relations of a strong formal theory. Even if additional axioms, such as those listed here, are too complex to be implemented in an automated reasoning system, they can serve as guides to the curators of the ontology and more precisely convey the intended understanding of the relational terms to outside ontologists.

We mention here only on restrictions that can be placed directly on the mereological relations. These restrictions would in turn affect the other relations since these relations are all delimited in terms of the parthood relation. For other examples of possible additional axioms (including axioms that apply directly to location relations) see [5, 9, 20].

The following principle cannot be derived from the axioms and definitions of BIT, but embodies an important intuitive assumption about the mereological structure of concrete individuals such as body parts.

(*P4)[7] PPxy $\rightarrow \exists$z(PPzy & ~Ozx) (if x is a proper part of y, then there is some proper part z of y that does not overlap x)

(*P4) tells us that if an individual y has a proper part x then, since x does not comprise all of y, there must be at least one proper part z that makes up some of what there is to y besides x. For example, since my right ventricle is a proper part of my heart, there must be at least one proper part of my heart that does not overlap my right ventricle. In fact there are several proper parts of my heart that do not overlap my right ventricle: my left ventricle, my right and left atriums, my mitral valve, my aortic valve, and so on.

If added to BIT, (*P4) would allow us to derive the following theorem which prohibits individuals from having only one proper part.

(*T1) PPxy $\rightarrow \exists$z(PPzy & z $\neq$ x) (if x is a proper part of y, then y has some proper part besides x)

The following stronger axiom can be added to BIT instead of (*P4):

[7] The labels for all additional axioms and theorems begin with an asterisk (*). The reader should keep in mind that these axioms are not included in BIT and these theorems cannot be derived from the axioms of BIT.

(*P5) If x is a proper part of y, then y has proper parts $x_1, ..., x_n$ such that none of x, $x_1, ..., x_n$ overlap and y is the sum of x, $x_1, ..., x_n$.[8]

(*P5) tells us, for example, that since the body of my stomach is a proper part of my stomach, my stomach must have other proper parts, namely, the fundus of my stomach and the pylorus of my stomach, such that none of these parts overlap and, taken together, the three parts add up to my whole stomach. (In this case, we can say that the collection consisting of the body of my stomach, the fundus of my stomach, and the pylorus of my stomach form a *partition* of my stomach. See [4] for a formal treatment of partitions.)

As a final example, BIT could be further strengthened by the addition of the following axiom.

(*P6) $\forall y \exists x$ PPxy (for every individual y there is some individual x such that x is a proper part of y)

(*P6) tells us that every individual has some proper part. For example, my heart has millions of cells as proper parts. The cells have membranes, cytoplasm, and nuclei as proper parts. And so on.

3. Relations among Classes

The assertions of canonical anatomy such as

the right ventricle is part of the heart

or

the brain is contained in the cranial cavity

are not limited to specific individuals but rather apply to all instances (or all *normal* instances) of the related anatomical classes. The first assertion tells us roughly that any right ventricle is part of a heart and any heart has a right ventricle as a part. The second assertion tells us roughly that any brain is contained in a cranial cavity and any cranial cavity contains a brain. Thus, these general statements imply that certain spatial relations hold among very many specific individuals.

The purpose of this section is to present a general procedure for extending of a formal theory of spatial relations among individuals, such as BIT, to also include relations among classes corresponding to those made use of in the two assertions above.

3.1. The Instantiation Relation

Since spatial relations hold directly only among concrete individuals, the "spatial" relations among classes, such as those assumed in the assertions of canonical anatomy, must be defined in terms of spatial relations among the individual instances of the classes. Thus to define parthood and location relations among classes, we require, in addition to the relations of BIT, a relation that links a class to its individual instances. We use here the time-independent instantiation relation, Inst, of [22]. For a time-dependent version of this relation, see [4].

Following [22], we adopt the convention of restricting the variables x, y, z to individuals and using the variables A, B, C, D specifically for classes. The Greek letters α, β, χ will be used as variables that range over all members of the domain (including all individuals and all classes).

For simplicity, we assume throughout the remainder of this paper that all anatomical classes are restricted to human anatomy, although we do not usually explicitly mention this restriction. Thus, *Heart* is the class of all human hearts, *White Blood Cell* is the class of all human white blood cells.

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[8] (*P5) can be approximated formally, but the necessary formula is long and tedious and requires more formal machinery than we have introduced in this paper.

The binary relation Inst holds between an individual x and a class A if x is an instance of A. In this case, we write

$$\text{Inst}(x, A).$$

For example, Inst(my heart, *Heart*) and Inst(my cranial cavity, *Cranial Cavity*).

Axioms for the instantiation relation include the following.

(I1)[9] $\text{Inst}(\alpha, \beta) \rightarrow \sim\text{Inst}(\beta, \chi) \ \&\ \sim\text{Inst}(\chi, \alpha)$ (if α is an instance of β, then β cannot be an instance of any member of the domain and α cannot have any member of the domain as an instance)

(I2) $\exists A\ \text{Inst}(\alpha, A) \vee \exists x\ \text{Inst}(x, \alpha)$ (for any member of the domain, α, α is either an individual instance of some class or α is a class)

(I3) $\exists A \forall x\ \text{Inst}(x, A)$ (there is some class of which every individual is an instance)

Axiom (I1) tells us that individuals (understood as instances) and classes (understood as entities that are instantiated) are disjoint sorts of entities. For example, my heart (an individual) cannot have instances and *Heart* (a class) cannot be an instance of another class.[10] It is because of axiom (I1) that we can i) equate individuals with instances and classes with entities that are instantiated and ii) adopt the convention of using separate variables for individuals (x, y,..) and classes (A, B, ...).

Axiom (I2) tells us that the domain of our theory is restricted to instances and classes.

Axiom (I3) tells us that there is some root class, where a root class is understood as a class of which every individual (in the domain of the theory) is an instance. Since we assume that the domain includes not only anatomical individuals but also independent spatial regions which human bodies (and other kinds of objects) can occupy, the root class must be broader than *Anatomical Entity*. Depending on the application, the root class might be as broad as *Spatial Individual* (including all individuals that are located in space) or, broader still, *Spatio-Temporal Individual* (including also individuals such as processes or events that are extended through time).

The Is_a subsumption relation between classes plays a key structuring role in most biomedical ontologies and can be defined in terms of Inst as follows.

$$\text{Is\_a}(A, B) =: \forall x(\ \text{Inst}(x, A) \rightarrow \text{Inst}(x, B))$$

This definition tells us that Is_a(A, B) (A is subsumed by B) means: every instance of A is also an instance of B. For example Is_a(*White Blood Cell*, *Cell*) and Is_a(*Heart*, *Organ*).

We can also use the Inst relation and the overlap relation (O) of BIT to define a property of classes which will turn out to be useful in our discussion of the logical properties of class relations below (Section 4). We will say that class A is *discrete* if and only if no two instances of A overlap one another. Symbolically:

$$\text{Discrete}(A) =: \forall x\ \forall y(\text{Inst}(x, A)\ \&\ \text{Inst}(y, A)\ \&\ x \neq y \rightarrow \sim Oxy)$$

Most familiar examples of anatomical classes are discrete classes. For example, *Heart*, *Liver*, *Cranial Cavity*, and *Cell* are all discrete classes-- two distinct hearts do not overlap, two distinct livers do not overlap, and so on. Examples of non-discrete classes include many general classes such as *Anatomical Structure*, *Organ System*, or *Subdivision of Skeletal System* (my alimentary system and my respiratory system are overlapping organ systems; my bony pelvis and my vertebral column are overlapping subdivisions of my skeletal system) and substance classes such as *Blood* or *Urine* (the portion of blood that is currently in the right side of my heart overlaps the portion of blood that is currently in my right ventricle).

Notice that if a class A is discrete, then so are all of its subclasses.

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[9] Axioms for the instantiation relation are labeled with "I". Theorems are labeled with "IT".

[10] But of course, *Heart* can be a subclass of another; e.g., *Heart* is a subclass of *Organ*.

(IT1) Discrete(B) & Is_a(A, B) $\rightarrow$ Discrete(A)

Thus, for example, since *Cell* is a discrete class, the subclasses of *Cell* (*Epithelial Cell*, *Muscle Cell*, *Neural Cell*, and so on) are all discrete classes.

3.2 Spatial Relations between Classes

Let ***T*** be any formal theory whose domain is restricted to individuals. ***T*** can be, for example, BIT or any other formal theory of spatial relations among individuals. (In particular, ***T*** can be an extension of BIT which includes more relations or more axioms than BIT.) ***T***+Cl is the formal theory whose domain includes all individuals in the domain of ***T*** plus classes of those individuals. The axioms of ***T***+Cl are the axioms of ***T*** plus axioms (I1)-(I3). For example, the axioms of BIT+Cl are (P1)-(P3), (L1)-(L2), and (I1)-(I3).

Let *R* be any binary relation from ***T***. *R* is then a relation on individuals -- for example, the parthood relation (P), the overlap relation (O), the located in relation (Loc-In), or any of the other relations of BIT. In ***T***+Cl, we can use *R* and the instantiation relation to define the following three relations among classes. (See also [4, 19, 22] where these distinctions are made for different versions of class parthood relations. [2] uses description logic for distinguishing versions of class parthood relations.)

R_1(A, B) =: $\forall$x (Inst(x, A) $\rightarrow$ $\exists$y(Inst(y, B) & *R*xy))

R_2(A, B) =: $\forall$y (Inst(y, B) $\rightarrow$ $\exists$x(Inst(x, A) & *R*xy))

R_{12}(A, B) =: R_1(A, B) & R_2(A, B)

R_1 class relations place restrictions on all instances of the *first* argument. R_1(A, B) tells us that something is true of all A's -- each A stands in the *R* relation to some B.

R_2 class relations place restrictions on all instances of the *second* argument. R_2(A, B) tells us that something is true of all B's -- for each B there is some A that stands in the *R* relation to it.

R_{12} class relations place restrictions on all instances of *both* arguments. R_{12}(A, B) tells us that something is true of all A's and something else is true of all B's-- each A stands in the *R* relation to some B *and* for each B there is some A that stands in the *R* relation to it.

As an example, we consider how three such class-level relations are defined when *R* is the proper part relation (PP).

PP_1 is the relation that holds between class A and class B if and only if every instance of A is a proper part of some instance of B. For example, every instance of *Human Female Reproductive System* is a proper part of some instance of *Human Being*. Thus, PP_1(*Human Female Reproductive System*, *Human Being*).

PP_2 is the relation that holds between class A and class B if and only if every instance of B has some instance of A as a proper part. For example, every instance of *Heart* has an instance of *Cell* as a proper part. Thus, PP_2(*Cell*, *Heart*). But notice that PP_2(*Human Female Reproductive System*, *Human Being*) does NOT hold, since not all human beings have female reproductive systems. Also notice that PP_1(*Cell*, *Heart*) does NOT hold, since not all cells are part of a heart.

PP_{12} is the relation that holds between class A and class B if and only if: i) every instance of A is a proper part of some instance of B and ii) every instance of B has some instance of A as a proper part. For example, every instance of *Human Nervous System* is a proper part of some instance of *Human Being* and every instance of *Human Being* has some instance of *Human Nervous System* as a proper part. Thus, PP_{12}(*Human Nervous System*, *Human Being*). By contrast, neither PP_{12}(*Human Female Reproductive System*, *Human Being*) nor PP_{12}(*Cell*, *Heart*) hold.

A few examples of assertions using other relations defined on classes are the following:

O_{12}(*Bony Pelvis*, *Vertebral Column*) (every bony pelvis overlaps some vertebral column and every vertebral column overlaps some bony pelvis)

O_1(*Male Genital System*, *Urinary System*) (every male genital system overlaps some urinary system)

O_2(*Genital System*, *Male Urinary System*) (every male urinary system overlaps some genital system)

Loc-In_{12}(*Brain*, *Cranial Cavity*) (every brain is located in some cranial cavity and some cranial cavity has a brain located in it)

Loc-In_2(*Blood*, *Cavity of the Right Ventricle*) (blood is located in every cavity of a right ventricle)

$PCoin_{12}$(*Esophagus*, *Mediastinal Space*) (every esophagus partially coincides with some mediastinal space and every mediastinal space partially coincides with some esophagus)

For the purposes of this paper, we assume that assertions such as the following hold:

PP_1(*Cell Nucleus*, *Cell*) (every cell nucleus is a proper part of some cell)

PP_{12} (*Thumb*, *Hand*) (every thumb is a proper part of some hand and every hand has some thumb as a proper part).

To be precise, not every cell nucleus is part of a cell -- a cell nucleus can be removed from a cell. But *normally* nuclei are parts of cells.[11] Similarly, not every thumb is part of a hand and not every hand has a thumb as a part, but *normally* thumbs are proper parts of hands and hands have thumbs as proper parts. Canonical anatomy is concerned with anatomically normal individuals and not with aberrant cases. In a full theory of anatomical classes, we will need a variant of the Inst relation (the *normal-instance-of* relation) that can distinguish the normal from abnormal instances of a class. But such a relation involves complications which go beyond the scope of this paper. We do not deal here with abnormal instances of anatomical classes. In other words, we assume that the domain of our theory is restricted to anatomically normal individuals. This policy is consistent with the treatment of anatomical classes in the FMA. It also fits the treatment of classes in the part of GALEN which is concerned exclusively with normal anatomy.

Finally, we note briefly that other strengths of class relations can be defined in terms of binary spatial relations on individuals using either universal or existential quantification. For example, a much stronger type of class relation than R_1, R_2, or R_{12} would hold between classes A and B only when *all* A's stand in relation R to *all* B's. A weaker type of class relation than R_1, R_2, or R_{12} would hold between classes A and B when *some* A's stand in relation R to *some* B's. (See [19] for other possibilities.) We do not explore such varieties of class relations in this paper because they are not useful for analyzing (in Section 5) the current state of parthood and location assertions for canonical anatomy in the FMA and GALEN. But such class relations could be useful either in some other context or for expanding the type of anatomical information currently in the FMA and GALEN.

4 Reasoning about Relations among Classes

The axioms and definitions of BIT fix the logical properties of the spatial relations among individuals introduced in that theory. However, most biomedical ontologies deal with relations between anatomical classes and not with relations between individuals. We are thus particularly interested in determining the logical properties of class relations such as those introduced by the definition schemas of Subsections 3.2.

[11] Notice, however, that there are some cells (red blood cells) that do not normally have nuclei. Thus, even if we limit our domain to normal individuals, PP_2(*Nuclei*, *Cell*) does not hold.

In this section, we discuss the logical properties of the R_1, R_2, and R_{12} types of class relations. Section 4 is divided into two parts. Subsection 4.1 considers how the logical properties of the class relations correspond to the logical properties of the underlying relations among individuals. Subsection 4.2 focuses both on the interaction between R_1, R_2, and R_{12} relations and on the interaction between these each of these relations and the Is_a (class subsumption) relation. Throughout the section, we keep the discussion as general as possible, giving results that apply to ***T***+Cl where ***T*** is any underlying formal theory of relations among individuals. But we frequently focus on BIT+Cl for specific examples and list theorems of BIT+Cl that are useful for our discussion of the FMA and GALEN in Section 5.

4.1 Transferring Properties of Individual Relations to Class Relations

Let ***T*** be, as above, any formal theory of relations among individuals. We consider here which of the logical properties of the relations in ***T*** are inherited by the defined class relations in ***T***+Cl. For example, if the relation *R* in ***T*** is a *strict partial ordering* -- irreflexive, asymmetric, and transitive (as is the relation PP in BIT) -- does it follow that in ***T***+Cl that R_1, R_2, and R_{12} are also strict partial orderings? The answer is: not necessarily. When *R* is a strict partial ordering, then each of R_1, R_2, and R_{12} must be transitive, but the class relations need not be irreflexive or asymmetric. For example, in BIT+Cl we can prove that each of PP_1, PP_2, and PP_{12} is transitive, but we cannot prove that any of these relations are irreflexive or asymmetric.

We will see that in BIT+Cl, the R_1, R_2, and R_{12} class relations lack several logical properties of their BIT counterparts. But first we discuss important properties of the relations among individuals that are transferred to at least some of the class relations.

4.1.1 Transitivity. Let *R* be any transitive relation on individuals in theory ***T***. Then in ***T*** + Cl, each of R_1, R_2, and R_{12} is also transitive. Thus, since P, PP, and Loc-In are transitive relations of BIT, the class relations P_1, P_2, P_{12}, PP_1, PP_2, PP_{12}, Loc-In_1, Loc-In_2, and Loc-In_{12} are all transitive.

(ClT1-3)[12] $P_i(A, B)\ \&\ P_i(B, C) \rightarrow P_i(A, C)$ $\quad$ i = 1, 2, 12[13]

(ClT4-6) $PP_i(A, B)\ \&\ PP_i(B, C) \rightarrow PP_i(A, C)$ $\quad$ i = 1, 2, 12

(ClT7-9) $\text{Loc-In}_i(A, B)\ \&\ \text{Loc-In}_i(B, C) \rightarrow \text{Loc-In}_i(A, C)$ $\quad$ i = 1, 2, 12

For example, it follows logically from

PP_2(*Cell*, *Heart*)
(every heart has some cell as a proper part)

and

PP_2(*Heart*, *Cardiovascular System*)
(every cardiovascular system has some heart as a proper part)

that

PP_2(*Cell*, *Cardiovascular System*)
(every cardiovascular system has some cell as a proper part).

Also, it follows logically from Loc-In_{12}(*Heart*, *Middle Mediastinal Space*) and Loc-In_{12}(*Middle Mediastinal Space*, *Thoracic Cavity*) that Loc-In_{12}(*Heart*, *Thoracic Cavity*).

But care must be taken not to mix R_1 and R_2 class relations together in transitivity reasoning. For example, from

[12] Theorems specific to BIT+Cl are labeled with "ClT". We in general list explicitly only those theorems of BIT+Cl which are useful for our discussion of the FMA and GALEN in Section 5.

[13] To save pointless repetitions, we frequently condense into one line three distinct theorems which differ only in indexing of the class relations. Thus, for example, this line is a condensed representation of the following three BIT+Cl theorems:

(ClT1) $P_1(A, B)\ \&\ P_1(B, C) \rightarrow P_1(A, C)$

(ClT2) $P_2(A, B)\ \&\ P_2(B, C) \rightarrow P_2(A, C)$

(ClT3) $P_{12}(A, B)\ \&\ P_{12}(B, C) \rightarrow P_{12}(A, C)$.

$$PP_1(\textit{Uterus}, \textit{Pelvis})$$
(every uterus is a proper part of a pelvis)

and

$$PP_2(\textit{Pelvis}, \textit{Male Human Being})$$
(every male human being has a pelvis as a proper part)

we cannot infer either

$$PP_1(\textit{Uterus}, \textit{Male Human Being})$$
(every uterus is a proper part of a male human being)

or

$$PP_2(\textit{Uterus}, \textit{Male Human Being})$$
(every male human being has a uterus as a proper part).

In general, for transitive R, $R_i(A, B) \,\&\, R_j(B, C) \rightarrow R_k(A, C)$ holds only when i = j = k.[14] For this reason, it is important for biomedical ontologies that use more than one of the relations R_1, R_2, R_{12} for a given R (for example, both PP_1 and PP_2) to explicitly distinguish these relations.

4.1.2 Reflexivity. Let R be any reflexive relation on individuals in theory $\boldsymbol{T}$. Then the class relations R_1, R_2, and R_{12} of $\boldsymbol{T}$ + Cl must be reflexive on the sub-domain of classes. Thus, P_1, P_2, P_{12}, O_1, O_2, O_{12}, Loc-In$_1$, Loc-In$_2$, Loc-In$_{12}$, PCoin$_1$, PCoin$_2$, and PCoin$_{12}$ are reflexive relations on classes in BIT+Cl. For example, for any class A, $P_{12}(A, A)$ -- each instance of A is part of some instance of A (itself) and each instance of A has some instance of A (itself) as a part.

4.1.3 Symmetry. Let R be any symmetric relation on individuals in $\boldsymbol{T}$. Then the R_{12} class relations of $\boldsymbol{T}$ + Cl must also be symmetric. Thus, the relations O_{12} and PCoin$_{12}$ of BIT + Cl are symmetric. For example, from

$$O_{12}(\textit{Bony Pelvis}, \textit{Vertebral Column})$$
(every bony pelvis overlaps some vertebral column and every vertebral column overlaps some bony pelvis)

we can in BIT+Cl derive:

$$O_{12}(\textit{Vertebral Column}, \textit{Bony Pelvis})$$
(every vertebral column overlaps some bony pelvis and every bony pelvis overlaps some vertebral column).

But R_1 and R_2 need not be symmetric class relations even if R is a symmetric relation among individuals. In BIT+Cl, we may have $O_1(A, B)$ but not $O_1(B, A)$; $O_2(A, B)$ but not $O_2(B, A)$; PCoin$_1$(A, B) but not PCoin$_1$(B, A); and PCoin$_2$(A, B) but not PCoin$_2$(B, A). For example, O_1(*Hand*, *Nerve*) (every hand overlaps some nerve) does NOT imply O_1(*Nerve*, *Hand*) (every nerve overlaps some hand). Also PCoin$_2$(*Anatomical Cavity*, *Esophagus*) (every esophagus partially coincides with some anatomical cavity) does NOT imply PCoin$_2$(*Esophagus*, *Anatomical Cavity*) (every anatomical cavity partially coincides with some esophagus).

However, we can prove that if R is symmetric, then the following equivalence holds:

$$R_1(A, B) \leftrightarrow R_2(B, A)$$

Thus, O_1(*Hand*, *Nerve*) implies, not O_1(*Nerve*, *Hand*), but O_2(*Nerve*, *Hand*). PCoin$_2$(*Anatomical Space*, *Esophagus*) implies, not PCoin$_2$(*Esophagus*, *Anatomical Space*), but PCoin$_1$(*Esophagus*, *Anatomical Space*).

Once again, we see that it is important for biomedical ontologies to explicitly distinguish class relations of type R_1, R_2, and R_{12}.

4.1.4 Simple Implications. Certain simple implications involving relations among individuals hold also for their class relation counterparts. For example, let R and S be binary relations of $\boldsymbol{T}$. Suppose that $\boldsymbol{T}$ includes a theorem stating that for any individuals x and y

$$Rxy \rightarrow Sxy$$

Then in $\boldsymbol{T}$+Cl we can prove that, for any classes A and B, all of the following hold:

$$R_1(A, B) \rightarrow S_1(A, B)$$

[14] But note, as will be discussed in Subsection 4.2, that the stronger R_{12} relation may replace a R_1 or R_2 relation in the antecedent of a conditional in the form of $R_i \,\&\, R_j \rightarrow R_k$. Thus, for example, for any transitive relation R, $R_1(A, B) \,\&\, R_{12}(B, C) \rightarrow R_1(A, C)$.

$$R_2(\mathrm{A, B}) \rightarrow S_2(\mathrm{A, B})$$
$$R_{12}(\mathrm{A, B}) \rightarrow S_{12}(\mathrm{A, B}).$$

For example, since PPxy $\rightarrow$ Loc-In(x, y) in BIT (theorem (LT3), subsection 2.2), we have the following theorems in BIT+Cl:

(ClT10-12) $\mathrm{PP_i(A, B)} \rightarrow \mathrm{Loc\text{-}In_i(A, B)}$ i = 1, 2, 12

Similarly, when either Rxy & Syz $\rightarrow$ Rxz or Sxy & Ryz $\rightarrow$ Rxz are theorems of ***T***, then the three class relation counterparts of each of these formulae are theorems of ***T***+Cl. For example, from theorems (LT5) and (LT6) of BIT (Subsection 2.2), we can derive the following theorems in BIT+Cl:

(ClT13-15) $\mathrm{Loc\text{-}In_i(A, B)}$ & $\mathrm{PP_i(B, C)} \rightarrow \mathrm{Loc\text{-}In_i(A, C)}$ i = 1, 2, 12
(ClT16-18) $\mathrm{PP_i(A, B)}$ & $\mathrm{Loc\text{-}In_i(B, C)} \rightarrow \mathrm{Loc\text{-}In_i(A, C)}$ i = 1, 2, 12

Thus, it follows from $\mathrm{Loc\text{-}In_{12}}$(*Heart*, *Middle Mediastinal Space*) and $\mathrm{PP_{12}}$(*Middle Mediastinal Space*, *Thoracic Cavity*), that $\mathrm{Loc\text{-}In_{12}}$(*Heart*, *Thoracic Cavity*).

As with transitivity inferences, implications that involve mixes of different types of class relations will not in general be derivable. For example, neither $\mathrm{Loc\text{-}In_1(A, B)}$ & $\mathrm{PP_2(B, C)} \rightarrow \mathrm{Loc\text{-}In_1(A, C)}$ nor $\mathrm{Loc\text{-}In_1(A, B)}$ & $\mathrm{PP_2(B, C)} \rightarrow \mathrm{Loc\text{-}In_2(A, C)}$ are theorems of BIT+Cl. This matches our intuitions about anatomical reasoning. From

$\mathrm{Loc\text{-}In_1}$(*Prostate*, *Pelvic Cavity*)
(every prostate is located in some pelvic cavity)

and

$\mathrm{P_2}$(*Pelvic Cavity*, *Female Pelvis*)
(every female pelvis has a pelvic cavity as a part)

we can infer neither

$\mathrm{Loc\text{-}In_1}$(*Prostate*, *Female Pelvis*)
(every prostate is located in some female pelvis)

nor

$\mathrm{Loc\text{-}In_2}$(*Prostate*, *Female Pelvis*)
(every female pelvis has some prostate located in it).

Also, implications involving negation, existential quantification, or a switch in the variables'argument places need not transfer from the relations among individuals to their class relation counterparts. For example, we have already seen that $\mathrm{O_1(A, B)} \rightarrow \mathrm{O_1(B, A)}$ and $\mathrm{O_2(A, B)} \rightarrow \mathrm{O_2(B, A)}$ are not theorems of BIT +Cl, although Oxy $\rightarrow$ Oyx is a theorem of BIT. We will see below more examples of implications involving relations among individuals that do not carry over to the class relations.

4.1.5 Inverses. Recall that for any binary relation R in theory ***T***, the inverse of R is the relation R^{-1} such that for any individuals x and y

$$R^{-1}\mathrm{xy} \leftrightarrow R\mathrm{yx}.$$

In ***T***+Cl, $(R^{-1})_{12}$ must be the inverse of R_{12}. In other words, we can prove in ***T*** +Cl that for any classes A and B

$$(R^{-1})_{12}(\mathrm{A, B}) \leftrightarrow R_{12}(\mathrm{B, A}).$$

In BIT+Cl, we have the following theorems:

(ClT19) $(\mathrm{PP}^{-1})_{12}(\mathrm{A, B}) \leftrightarrow \mathrm{PP}_{12}(\mathrm{B, A})$
(ClT20) $(\mathrm{Loc\text{-}In}^{-1})_{12}(\mathrm{A, B}) \leftrightarrow \mathrm{Loc\text{-}In}_{12}(\mathrm{B, A})$.

Thus, it follows from $\mathrm{PP_{12}}$(*Right Ventricle*, *Heart*) that $(\mathrm{PP}^{-1})_{12}$(*Heart*, *Right Ventricle*) and vice versa.

However, inverse equivalences are not preserved for the weaker R_1 and R_2 class relations. In ***T***+Cl, the following equivalences do NOT in general hold:

$$(R^{-1})_1(\mathrm{A, B}) \leftrightarrow R_1(\mathrm{B, A})$$

$$(R^{-1})_2(\mathrm{A, B}) \leftrightarrow R_2(\mathrm{B, A}).$$

Instead, the following equivalences are derivable in ***T***+Cl:

$$(R^{-1})_2(\mathrm{A, B}) \leftrightarrow R_1(\mathrm{B, A})$$

$$(R^{-1})_1(\mathrm{A, B}) \leftrightarrow R_2(\mathrm{B, A}).$$

Thus, in BIT+Cl, $(\mathrm{PP}^{-1})_2$ is the inverse of PP_1, $(\text{Loc-In}^{-1})_2$ is the inverse of Loc-In_1, $(\mathrm{PP}^{-1})_1$ is the inverse of PP_2, and $(\text{Loc-In}^{-1})_1$ is the inverse of Loc-In_2.

(ClT21) $(\mathrm{PP}^{-1})_2(\mathrm{A, B}) \leftrightarrow \mathrm{PP}_1(\mathrm{B, A})$
(ClT22) $(\mathrm{PP}^{-1})_1(\mathrm{A, B}) \leftrightarrow \mathrm{PP}_2(\mathrm{B, A})$
(ClT23) $(\text{Loc-In}^{-1})_2(\mathrm{A, B}) \leftrightarrow \text{Loc-In}_1(\mathrm{B, A})$
(ClT24) $(\text{Loc-In}^{-1})_1(\mathrm{A, B}) \leftrightarrow \text{Loc-In}_2(\mathrm{B, A})$.

For example, PP_1(*Cell Nucleus*, *Cell*) (every cell nucleus is a proper part of some cell) is equivalent to $(\mathrm{PP}^{-1})_2$(*Cell*, *Cell Nucleus)* (for every cell nucleus there is some cell which has it as a proper part). PP_1(*Cell Nucleus*, *Cell*) is NOT equivalent to $(\mathrm{PP}^{-1})_1$(*Cell*, *Cell nucleus)* (every cell has some cell nucleus as a proper part). Once again, we see the importance of distinguishing between the R_1, R_2, and R_{12} types of class relations.

4.1.6 Logical Properties of Relations which do not necessarily Transfer to Class Relations

Many of the theorems of the theory ***T*** need not hold in ***T***+Cl for the class relation counterparts of the relations among individuals. We have already seen above several examples of this discrepancy between the logical properties of relations among individuals and the logical properties of the R_1 and R_2 types of class relations. Table 1 gives additional information about which properties transfer automatically to the class relations and which do not.

Among Individuals	**Among Classes**		
R is...	R_1 must also be...?	R_2 must also be...?	R_{12} must also be...?
Reflexive	Yes	Yes	Yes
Irreflexive	No	No	No
Symmetric	No	No	Yes
Asymmetric	No	No	No
Antisymmetric	No	No	No
Transitive	Yes	Yes	Yes

Table 1: Correlation between the logical properties of a relation *R* for individuals and the logical properties of the class relations R_1, R_2, and R_{12}

For example, in BIT+Cl, we cannot prove that the relations PP_{12}, PP_1, and PP_2 are irreflexive or asymmetric. In particular, the following two formulae are NOT theorems of BIT+Cl:

$$\sim\mathrm{PP}_{12}(\mathrm{A, A})$$

$$\mathrm{PP}_{12}(\mathrm{A, B}) \rightarrow \sim\mathrm{PP}_{12}(\mathrm{B, A})$$

We also cannot prove in BIT+Cl that the relations P_{12}, P_1, and P_2 are antisymmetric. In particular, the following formula is NOT a theorem of BIT+Cl:

$$\mathrm{P}_{12}(\mathrm{A, B})\ \&\ \mathrm{P}_{12}(\mathrm{B, A}) \rightarrow \mathrm{A} = \mathrm{B}.$$

4.1.7 Discrete Classes. Recall that a discrete class is a class A such that any two instances of A are discrete. Recall also that many typical anatomical classes (e.g. *Heart*, *Liver*, *Cell*) are discrete. When reasoning is restricted to a sub-domain of discrete classes, more of the logical properties of the relations of BIT are preserved in the class relations. We can prove in BIT+Cl that, if all classes in a sub-domain *D* are discrete, then

i) PP_1, PP_2, PP_{12}, $(\mathrm{PP}^{-1})_1$, $(\mathrm{PP}^{-1})_2$, and $(\mathrm{PP}^{-1})_{12}$ are irreflexive and asymmetric on *D*;

ii) P_1, P_2, P_{12}, $(P^{-1})_1$, $(P^{-1})_2$, and $(P^{-1})_{12}$ are antisymmetric.

Thus, for example, given that *Heart* and *Right Ventricle* are discrete classes, PP_{12}(*Right Ventricle*, *Heart*) and PP_{12} (*Heart*, *Right Ventricle*) cannot both hold. Also, for any discrete class A, none of the following can hold: $PP_1(A, A)$, $PP_2(A, A)$, and $PP_{12}(A, A)$.

Of course, when A is a non-discrete class (e.g. *Anatomical Entity* or *Blood*), it may still be the case that none of $PP_1(A, A)$, $PP_2(A, A)$, $PP_{12}(A, A)$ hold or that $PP_{12}(A, B)$ and $PP_{12}(B, A)$ do not both hold for any class B. But these assertions cannot be derived in BIT+Cl.

4.1.8 Definitional Equivalences. In addition to logical properties, such as irreflexivity and asymmetry, listed in the chart above, many of the equivalences introduced in the definitions of BIT also do not carry over to the class relation setting and this is so even when reasoning is restricted to a sub-domain of discrete classes. For example, according to the definition of the overlap relation in BIT, for any x and y

$$Oxy \leftrightarrow \exists z(Pzx \ \& \ Pzy)$$

(x and y overlap if and only if there is some individual z that is part of both x and y)

But none of the following equivalences is derivable in BIT + Cl:

$$O_1(A, B) \leftrightarrow \exists C\ (P_1(C, A)\ \ \&\ P_1(C, B))$$
$$O_2(A, B) \leftrightarrow \exists C\ (P_2(C, A)\ \ \&\ P_2(C, B))$$
$$O_{12}(A, B) \leftrightarrow \exists C\ (P_{12}(C, A)\ \ \&\ \ P_{12}(C, B))$$

The R_1 and R_2 versions of the equivalence clearly not appropriate for anatomical reasoning. For example, P_1(*Uterus*, *Pelvis*) (every uterus is part of some pelvis) and P_1(*Uterus*, *Female Reproductive System*) both hold, but O_1(*Pelvis*, *Female Reproductive System*) (every pelvis overlaps some female reproductive system) does NOT hold. Also, P_2(*Cell*, *Heart*) (all hearts have cells as parts) and P_2(*Cell*, *Liver*) (all livers have cells as parts), but NOT O_2(*Heart*, *Liver*) (all livers overlap some heart).

However, the R_{12} version of the equivalence does seem plausible in an anatomical context. In fact, half of this equivalence is derivable in BIT+Cl. It is a theorem of BIT+Cl that:

(ClT25) $\exists C\ (P_{12}(C, A)\ \ \&\ \ P_{12}(C, B)) \rightarrow O_{12}(A, B)$ (if there is a class C that stands in the P_{12} relation to both A and B, then every instance of A overlaps an instance of B and vice versa).

The full equivalence would tell us that, in addition, whenever instance of A overlaps an instance of B and vice versa, there is a class C that stands in the P_{12} relation to both A and B.

4.1.9 Conclusions. We draw at least two important conclusions from the points made in this subsection. First, as emphasized throughout, it is crucial for biomedical ontologists to explicitly distinguish between R_1, R_2, and R_{12} relations.

Second, logical properties imposed on relations among individuals in a formal theory may not automatically transfer to the class relations that are defined in terms of them. This is one reason why it is important to always clearly distinguish the class-level relations from the individual-level relations. In some cases, it is appropriate that the logical properties of the individual-level relations do not transfer to the class-level relations. For example, O_1 does not behave as a symmetric relation on anatomical classes (e.g. O_1(*Hand*, *Nerve*) but not O_1(*Nerve*, *Hand*)), so it is an advantage of BIT+Cl that it does not force O_1 to be symmetric. In other cases, the ontologist may find it desirable to add axioms placing stronger restrictions directly on the class relations. For example, it seems plausible that no anatomical class A (even a non-discrete class, such as *Anatomical Entity* or *Blood*) is such that every instance x of A is a proper part of another instance of y of A.[15] If so, an axiom stating that for

[15] But notice that the following axiom may not be desirable: for any anatomical class A, $\sim PP_2(A, A)$. For example, it would seem that instance of *Blood* (i.e. any portion of blood) must have some instance of *Blood* (a smaller portion of blood) as a proper part.

any anatomical class A, ~PP_1(A, A) could be added to BIT+Cl. As another example, it seems plausible that whenever all instances of A overlap instances of B and all instances of B overlap instances of A, there is some class C consisting of those individuals which are the shared parts of A's and B's. If so an axiom stating

$$O_{12}(A, B) \rightarrow \exists C\ (P_{12}(C, A)\ \&\ P_{12}(C, B))$$

could be added to BIT+Cl.

4.2 Reasoning about Relations among Classes: Additional Logical Properties of Class Relations

In this subsection, we present important logical properties of the defined class relations which do not correspond directly to properties of the corresponding relations among individuals.

4.2.1 Logical Implications Involving Combinations of R_{12} and R_1 or R_{12} and R_2 Relations

One important property of the R_{12} class relations is that they always imply the corresponding R_1 and R_2 class relations. More precisely, let ***T*** again be any formal theory of relations on individuals and let R be any binary relation in ***T***. Then the following two implications hold:

$R_{12}(A, B) \rightarrow R_1(A, B)$

$R_{12}(A, B) \rightarrow R_2(A, B)$

For example, the following are theorems of BIT+Cl:

(ClT26-27) $PP_{12}(A, B) \rightarrow PP_i(A, B)$ $\quad$ i = 1, 2

(ClT28-29) $\text{Loc-In}_{12}(A, B) \rightarrow \text{Loc-In}_i(A, B)$ $\quad$ i = 1, 2

(ClT26)-(ClT29) allow us to substitute the stronger R_{12} relations for the weaker R_1 or R_2 relations in the antecedent of another implication. For example, it in combination with the transitivity theorems (ClT4) – (ClT9), (ClT26)-(ClT29) yield the following additional theorems.

(ClT30-31) $PP_i(A, B)\ \&\ PP_{12}(B, C) \rightarrow PP_i(A, C)$ $\quad$ i = 1, 2

(ClT32-33) $PP_{12}(A, B)\ \&\ PP_i(B, C) \rightarrow PP_i(A, C)$ $\quad$ i = 1, 2

(CIT34-35) $\text{Loc-In}_i(A, B)\ \&\ \text{Loc-In}_{12}(B, C) \rightarrow \text{Loc-In}_i(A, C)$ $\quad$ i = 1, 2

(ClT36-37) $\text{Loc-In}_{12}(A, B)\ \&\ \text{Loc-In}_i(B, C) \rightarrow \text{Loc-In}_i(A, C)$ $\quad$ i = 1, 2

For example, from PP_1(*Uterus*, *Pelvis*) (every uterus is a proper part of some pelvis) and PP_{12}(*Pelvis*, *Trunk*) (every pelvis is a proper part of some trunk and every trunk has a pelvis as a proper part) , it follows that PP_1(*Uterus*, *Trunk*) (every uterus is a proper part of some trunk). As another example, from PP_2(*Cartilage*, *Vertebra*) (every vertebra has some cartilage as a proper part) and PP_{12}(*Vertebra*, *Vertebral Column*) (every vertebra is a proper part of some vertebral column and every vertebral column has some vertebra as a proper part) , it follows that PP_2(*Cartilage, Vertebral Column*) (every vertebral column has some cartilage as a proper part).

(ClT26) - (ClT29) also yield important further theorems when combined with theorems (ClT13)-(ClT18). Each of the following can be derived in BIT+Cl:

(ClT38-39) $PP_{12}(A, B)\ \&\ \text{Loc-In}_i(B, C) \rightarrow \text{Loc-In}_i(A, C)$ $\quad$ i = 1, 2

(ClT40-41) $PP_i(A, B)\ \&\ \text{Loc-In}_{12}(B, C) \rightarrow \text{Loc-In}_i(A, C)$ $\quad$ i = 1, 2

(ClT42-43) $\text{Loc-In}_{12}(A, B)\ \&\ PP_i(B, C) \rightarrow \text{Loc-In}_i(A, C)$ $\quad$ i = 1, 2

(ClT44-45) $\text{Loc-In}_i(A, B)\ \&\ PP_{12}(B, C) \rightarrow \text{Loc-In}_i(A, C)$ $\quad$ i = 1, 2

For example, from PP_{12}(*Cervix of Uterus*, *Uterus*) (every cervix of a uterus is a proper part of some uterus and every uterus has a cervix of a uterus as a proper part) and Loc-In_1(*Uterus*, *Pelvic Cavity*) (every uterus is located in some pelvic cavity), it follows that Loc-In_1(*Cervix of Uterus*, *Pelvic Cavity*) (every cervix of a uterus is located in some pelvic cavity).

Because they are important for our discussion in Section 5 of parthood and containment relations in the FMA and GALEN, we represent theorems of BIT+Cl involving combinations of R_1, R_2, or R_{12} versions of the PP and Loc-In relations in the following table

The BIT+Cl theorems listed above are important for our discussion in Section 5 of parthood and containment relations in the FMA and GALEN. They are represented compactly along with theorems (ClT4) – (ClT9) and (ClT13) – (ClT18) in TABLE 2.

	PP_1(B, C)	PP_2(B, C)	PP_{12}(B, C)	Loc-In_1(B, C)	Loc-In_2(B, C)	Loc-In_{12}(B,C)
PP_1(A, B)	PP_1(A, C)		PP_1(A, C)	Loc-In_1(A, C)		Loc-In_1(A, C)
PP_2(A, B)		PP_2(A, C)	PP_2(A, C)		Loc-In_2(A, C)	Loc-In_2(A, C)
PP_{12}(A, B)	PP_1(A, C)	PP_2(A, C)	PP_{12}(A, C)	Loc-In_1(A, C)	Loc-In_2(A, C)	Loc-In_{12}(A, C)
Loc-In_1(A, B)	Loc-In_1(A, C)		Loc-In_1(A, C)	Loc-In_1(A, C)		Loc-In_1(A, C)
Loc-In_2(A, B)		Loc-In_2(A, C)	Loc-In_2(A, C)		Loc-In_2(A, C)	Loc-In_2(A, C)
Loc-In_{12}(A, B)	Loc-In_1(A, C)	Loc-In_2(A, C)	Loc-In_{12}(A, C)	Loc-In_1(A, C)	Loc-In_2(A, C)	Loc-In_{12}(A, C)

TABLE 2: Inferences from conjunctions of PP_i and Loc-In_j assertions

TABLE 2 tells us which relation between class A and class C can be inferred from a given assertion about the relation between class A and class B (listed in row headings) in conjunction with an assertion about the relation between class B and class C (listed in the column headings). For example, given PP_2(A, B) (row 2) and Loc-In_{12}(B, C) (column 6), it follows from the axioms of BIT+Cl that Loc-In_2(A, C) must also hold. (This is just theorem (ClT41).)

A blank cell in the table tells us that, unless additional information is given, we cannot derive any assertion of the form R_i(A, B) where R is one of the relations of BIT. For example, from Loc-In_1(A, B) (row 4) and PP_2(B, C) we cannot in general make any inference about the relation of class A and class C. To see this, consider the example. Loc-In_1(*Prostate*, *Pelvic Cavity*) (every prostate is located in a pelvic cavity) and PP_2(*Pelvic Cavity*, *Female Pelvis*) (every female pelvis has a pelvic cavity as a proper part) both hold, but R_i(*Prostate*, *Female Pelvis*) does not hold for any BIT relation R. In particular, *Prostate* stands in none of the relations PP_1, PP_2, PP_{12}, Loc-In_1, Loc-In_2, or Loc-In_{12} to *Female Pelvis*.

4.2.2 Logical Implications Involving R_1, R_2, R_{12} and Is_a

We can also derive many theorems describing the interaction between the R_1, R_2, and R_{12} relations and the Is_a relation. In theory $\boldsymbol{T}$ +Cl where R is any binary relation among individuals in $\boldsymbol{T}$, the following must hold for any classes A, B, and C.

R_1(A, B) & Is_a(B, C) $\rightarrow$ R_1(A, C)

R_1(A, B) & Is_a(C, A) $\rightarrow$ R_1(C, B)

R_2(A, B) & Is_a(A, C) $\rightarrow$ R_2(C, B)

R_2(A, B) & Is_a(C, B) $\rightarrow$ R_2(A, C)

R_{12}(A, B) & Is_a(A, C) $\rightarrow$ R_2(C, B)

R_{12}(A, B) & Is_a(C, A) $\rightarrow$ R_1(C, B)

R_{12}(A, B) & Is_a(B, C) $\rightarrow$ R_1(A, C)

R_{12}(A, B) & Is_a(C, B) $\rightarrow$ R_2(A, C)

BIT+Cl theorems for the PP_i relations corresponding to the schemata above are represented compactly in TABLE 3.

	Is_a(C, A)	Is_a(A, C)	Is_a(C, B)	Is_a(B, C)
PP_1(A, B)	PP_1(C, B)			PP_1(A, C)
PP_2(A, B)		PP_2(C, B)	PP_2(A, C)	
PP_{12}(A, B)	PP_1(C, B)	PP_2(C, B)	PP_2(A, C)	PP_1(A, C)

TABLE 3: Inferences from conjunctions of PP_i and Is_a assertions

The cells of TABLE 3 tell us i) which of the PP_i relations must hold between A and C when a given PP_i relation holds between A and B (listed in the row headings) and a given subsumption relation holds between B and C (listed in the column headings) and ii) which of the PP_i relations must hold between C and B when a given PP_i relation holds between A and B (row headings) and a given subsumption relations holds between A and C (column headings). For example, given PP_2(A, B) (row 2) and Is_a(C, B) (column 3), it follows that PP_2(A, C) must also hold. This corresponds to the BIT+Cl theorem:

$$PP_2(A, B)\ \&\ Is\_a(C, B) \rightarrow PP_2(A, C).$$

A blank cell indicates that, unless further information is given, no inference of the form R_i(A, C), R_i(C, A), R_i(B, C), or R_i(C, B) (with *R* a BIT relation) can be made. For example, from PP_1(A, B) (row 1) and Is_a(C, B) (column 3), we cannot in general make any inference about the relation of A to C. To see consider the example: PP_1(*Cell Nucleus*, *Cell*) (every cell nucleus is a proper part of a cell) and Is_a(*Platelet*, *Cell*) (a platelet is a cell), but no PP_i relation holds between *Cell nucleus* and *Platelet*.

TABLE 4 is analogous to TABLE 3 but represents inferences involving the $Loc\text{-}In_i$ relations rather than the PP_i relations.

	Is_a(C, A)	Is_a(A, C)	Is_a(C, B)	Is_a(B, C)
$Loc\text{-}In_1$(A, B)	$Loc\text{-}In_1$(C, B)			$Loc\text{-}In_1$(A, C)
$Loc\text{-}In_2$(A, B)		$Loc\text{-}In_2$(C, B)	$Loc\text{-}In_2$(A, C)	
$Loc\text{-}In_{12}$(A, B)	$Loc\text{-}In_1$(C, B)	$Loc\text{-}In_2$(C, B)	$Loc\text{-}In_2$(A, C)	$Loc\text{-}In_1$(A, C)

TABLE 4: Inferences from conjunctions of $Loc\text{-}In_i$ and Is_a assertions

For example, from $Loc\text{-}In_{12}$(*Ovary*, *Cavity of Female Pelvis*) and Is_a(*Cavity of Female Pelvis*, *Cavity of Pelvis*), it follows (row 3/column 4) that $Loc\text{-}In_1$(*Ovary*, *Cavity of Pelvis*). On the other hand, no assertion about the $Loc\text{-}In_i$ relation of *Ovary* to *Cavity of Male Pelvis* follows from $Loc\text{-}In_1$(*Ovary*, *Cavity of Pelvis*) and Is_a(*Cavity of Male Pelvis*, *Cavity of Pelvis*) (row 1/column 3).

Finally, we note that tables for the inverses of the PP_i and $Loc\text{-}In_i$ relations can be derived from TABLE 2 – TABLE 4 and theorems (ClT21) – (ClT24) tying these relations to their inverses. For example, TABLE 5 represents BIT+Cl inferences from conjunctions of $(Loc\text{-}In^{-1})_i$ assertions and Is_a assertions.

	Is_a(C, A)	Is_a(A, C)	Is_a(C, B)	Is_a(B, C)
$(Loc\text{-}In^{-1})_1$(B, A)		$(Loc\text{-}In^{-1})_1$(B, C)	$(Loc\text{-}In^{-1})_1$(C, A)	
$(Loc\text{-}In^{-1})_2$(B, A)	$(Loc\text{-}In^{-1})_2$(B, C)			$(Loc\text{-}In^{-1})_2$(C, A)
$(Loc\text{-}In^{-1})_{12}$(B, A)	$(Loc\text{-}In^{-1})_2$(B, C)	$(Loc\text{-}In^{-1})_1$(B, C)	$(Loc\text{-}In^{-1})_1$(C, A)	$(Loc\text{-}In^{-1})_2$(C, A)

TABLE 5: Inferences from conjunctions of $(Loc\text{-}In^{-1})_i$ and Is_a assertions

5 Parthood and Containment Relations in the FMA and GALEN

In this section we use the class relations introduced formally in BIT+Cl to analyze and compare class relations used in the FMA and GALEN. We here select two biomedical ontologies with significant anatomical content and focus on relations that roughly correspond to the PP_1, PP_2, PP_{12}, Loc-In_1, Loc-In_2, Loc-In_{12} and their inverses in BIT+Cl.

The Foundational Model of Anatomy instantiates nearly 1 million part relations among its more than 70,000 classes [24]. The FMA was developed over a ten year period by anatomists who, like the developers of most other biomedical terminologies, were essentially unaware of spatial theories and of the requirements of formal knowledge representation. Recent collaborations with theoreticians and knowledge engineers [12, 22, 24], of which the current communication is another example, provide opportunities for evaluating the FMA and for endowing it with formal mechanisms that can enforce consistency and eliminate ambiguity.

The OpenGALEN Common Reference Model (CRM) was developed over a nine year period as a clinical ontology resource. Like the FMA, GALEN's CRM (and in particular the CRM's anatomical component) was initially constructed by domain experts with no prior training in knowledge representation. The subsequent development of GALEN's CRM, particularly the CRM's high-level ontology, has benefited from theoretical work in ontology and knowledge representation [13, 14, 15].

OpenGALEN has a broader scope than the FMA, covering physiology, pharmacology, symptomatology, diseases and procedures in addition to human anatomy. The CRM anatomy sub-model is approximately 25% the size of the FMA, covering more or less the same breadth of content but at a coarser level of detail. However, most of the CRM assertions concerning class parthood and location relations are located this anatomical sub-model. In this paper, we consider only the CRM anatomy sub-model of OpenGALEN.

In collecting all data for this section, we used a version of the FMA dated from December, 2004 and the OpenGALEN Common Reference Model (Evaluation Edition) dated July 15, 2004.

5.1 Class Parthood in the FMA

The FMA has one general class parthood relation, part_of, which is divided into more specific sub-relations. For example, the FMA distinguishes between anatomical parts and arbitrary parts. For this paper, we will not attempt to distinguish these more specific class parthood relations. We focus exclusively on part_of and its inverse.

The FMA uses part_of as a proper parthood relation among anatomical classes, but does not (even with its more specific parthod relations) explicitly distinguish between PP_1, PP_2, and PP_{12} uses of part_of. The FMA's part_of corresponds in different contexts to PP_1, PP_2, or PP_{12}. For example, we find in the FMA:

	the FMA's part_of	BIT+Cl relation
1a	*Female Pelvis* part_of *Body*	PP_1
1b	*Male Pelvis* part_of *Body*	PP_1
2	*Cavity of Female Pelvis* part_of *Abdominal Cavity*	PP_1
3a	*Urinary Bladder* part_of *Female Pelvis*	PP_2
3b	*Urinary Bladder* part_of *Male Pelvis*	PP_2
4	*Cell* part_of *Tissue*	PP_2
5	*Right Ventricle* part_of *Heart*	PP_{12}
6	*Urinary Bladder* part_of *Body*	PP_{12}
7	*Nervous System* part_of *Body*	PP_{12}

TABLE 6: Assertions using of the FMA's part_of

Since, for example, every female pelvis is a proper part of some body but no male body has a female pelvis as a part, part_of is used in 1a in the sense of PP_1. On the other hand, since every female pelvis has a urinary bladder as a proper part, but some urinary bladders (those belonging to men) are not part of any female pelvis, part_of is used in 3a in the sense of PP_2. The FMA uses part_of as the stronger relation PP_{12} only in examples such as 5 - 7, where every instance of the first class (e.g. *Nervous System*) is a proper part of some instance of the second class (e.g. *Body*) and every instance of the second class has some instance of the first class as a proper part.

The FMA uses has_part as an inverse proper parthood relation among anatomical classes. Again, no explicit distinctions between $(PP^{-1})_1$, $(PP^{-1})_2$, and $(PP^{-1})_{12}$ are made. However, inspection reveals that, for any anatomical classes A and B, A has_part B is asserted in the FMA if and only if B part_of A is also asserted. Thus, in contexts where part_of corresponds to PP_1, has_part corresponds to the inverse of PP_1, which is $(PP^{-1})_2$. In contexts where part_of corresponds to PP_1, has_part corresponds to the inverse of PP_2, which is $(PP^{-1})_1$. In contexts where part_of corresponds to PP_{12}, has_part corresponds to the inverse of PP_{12}, which is $(PP^{-1})_{12}$. Examples of the has_part relation in the FMA are:

	the FMA's has_part	BIT+Cl relation
1a	*Body* has_part *Female Pelvis*	$(PP^{-1})_2$
1b	*Body* has_part *Male Pelvis*	$(PP^{-1})_2$
2	*Abdominal Cavity* has_part *Cavity of Female Pelvis*	$(PP^{-1})_2$
3a	*Female Pelvis* has_part *Urinary Bladder*	$(PP^{-1})_1$
3b	*Male Pelvis* has_part *Urinary Bladder*	$(PP^{-1})_1$
4	*Tissue* has_part *Cell*	$(PP^{-1})_1$
5	*Heart* has_part *Right Ventricle*	$(PP^{-1})_{12}$
6	*Body* has_part *Urinary Bladder*	$(PP^{-1})_{12}$
7	*Body* has_part *Nervous System*	$(PP^{-1})_{12}$

TABLE 7: Assertions using the FMA's has_part

Transitivity of part_of in the FMA

The FMA allows unrestricted transitivity reasoning with its part_of relation. Thus in many cases, the FMA concludes

A part_of C

from part_of assertions corresponding to

$$PP_i(A, B) \text{ and } PP_j(B, C)$$

where i and j may be different indices. As can be easily seen from the upper left corner of TABLE 2 in subsection 4.2, the conjunction above supports an inference to a parthood assertion $PP_k(A, C)$ (for k = 1, 2, or 12) only when either i) the indices i and j are identical or ii) at least one of i and j is the index 12.

In several cases, the FMA concludes A part_of C from a conjunction corresponding to $PP_2(A, B)$ and $PP_1(B, C)$, even though we cannot in general draw infer from this conjunction that one of the PP_k relations holds between A and C. That the FMA does not by this procedure reach false conclusions is explained by special circumstances. In each of these cases, there is a fourth class D such that Is_a(B, D) (B is subsumed by D), $PP_{12}(A, D)$, and $PP_{12}(D, C)$. Thus, the relations between D (the more general class) and each of A and C, guarantee that A part_of C (here, in the sense $PP_{12}(A, C)$).

The most common case of this type involves assertions about classes of sexually dimorphic structures. For example, the unrestricted transitivity of part_of in the FMA allows us to derive

Urinary Bladder part_of *Body*

in the following ways:

a) from	*Urinary Bladder* part_of *Female Pelvis* & *Female Pelvis* part_of *Body*

b) from	*Urinary Bladder* part_of *Male Pelvis* & *Male Pelvis* part_of *Body*

If we make the distinctions between PP_1, PP_2, and PP_{12} explicit, we have

$$PP_{12}\,(\textit{Urinary Bladder, Body})$$

and:

a*) from	PP_2*(Urinary Bladder, Female Pelvis)* & PP_1 (*Female Pelvis, Body)*
b*) from	PP_2*(Urinary Bladder, Male Pelvis)* & PP_1 (*Male Pelvis, Body)*

In this case, the following also holds: Is_ a(*Female Pelvis*, *Pelvis*), Is_a(*Male Pelvis*, *Pelvis*), PP_{12}(*Urinary Bladder*, *Pelvis*) , and PP_{12}(*Pelvis*, *Body*) (see Figure 2).[16]

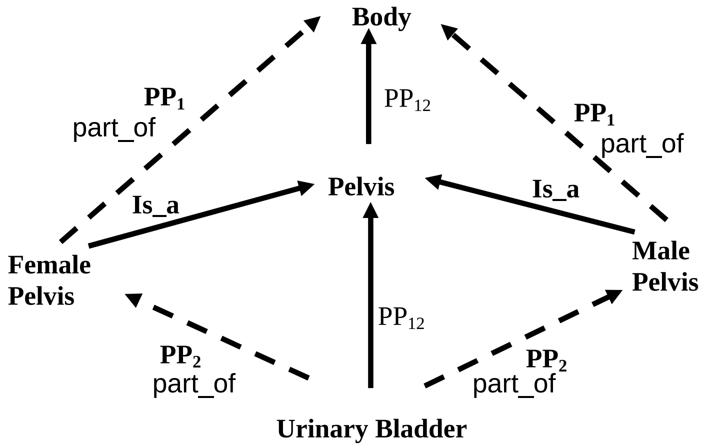

Figure 2: The FMA's part_of with Classes of Sexually Dimorphic Structures

Thus, the unrestricted transitivity of part_of yields in this case a true conclusion: *Urinary Bladder* part_of *Body* (where this can be understood as: PP_{12}(*Urinary Bladder, Body*)).

As far as we can see, the FMA's unrestricted transitivity inferencing for part_of does not generate false assertions. This is due partially to inherent features of human anatomy – e.g., that all human bodies are either male or female. However, the FMA's failure to distinguish the PP_1, PP_2, and PP_{12} meanings of the part_of relation makes assertions using part_of ambiguous and leaves the logical structure of the knowledge embodied in the FMA unclear.

Moreover, possibilities for expanding the FMA are limited unless distinctions between the different meanings of part_of are made explicit. This expansion might include either i) additional explicit assertions about relations between anatomical classes or ii) more sophisticated automated reasoning mechanisms. For i), there are many useful assertions about parthood relations among anatomical classes which not only cannot be unambiguously stated in terms of the part_of relation, but also would, if added to the FMA, lead to false conclusions. For example, the FMA currently asserts *Male Urethra* part_of *Urinary System*. If the assertion *Urinary System* part_of *Female Pelvis* (here in the sense PP_2(*Urinary System*, *Female Pelvis*)) were added, the unrestricted transitivity of part_of would yield the false conclusion: *Male Urethra* part_of *Female Pelvis*.

For ii), note that in all of the inference tables presented in subsection 4.2, the distinction between R_1, R_2, and R_{12} class relations is crucial for determining whether any inference can be made (and if so which one) from a

[16] Note that *Urinary Bladder* part_of *Pelvis* and *Pelvis* part_of *Body* are not asserted in the FMA.

conjunction involving these relations. Thus, automated assertion generation based on these tables can be implemented in the FMA only if PP_1, PP_2, and PP_{12} uses of part_of are explicitly distinguished.

We give a very simple example of how such automated reasoning might be advantageous for the FMA. The FMA includes the assertions *Ovary* part_of *Pelvis*, *Right Ovary* subclass_of *Ovary*, and *Left Ovary* subclass_of *Ovary* (where subclass_of is the FMA's Is_ a relation). No assertion is made about the relation of the classes *Right Ovary* and *Left Ovary* to *Pelvis*. An automated reasoning mechanism based on TABLE 3 could conclude both PP_1(*Right Ovary*, *Pelvis*) and PP_1(*Left Ovary*, *Pelvis*) from PP_1(*Ovary*, *Pelvis*), *Right Ovary* subclass_of *Ovary*, and *Left Ovary* subclass_of *Ovary*. On the other hand, no conclusion about parthood relations between C and B follows from PP_2(A, B) and Is_a(C, A). Thus, when we only have *Ovary* part_of *Pelvis* without explicit information about which sense part_of is used in, we cannot automatically infer anything about the relation of *Right Ovary* or *Left Ovary* to *Pelvis*.

In the subsection 5.5, we advocate that both the FMA and GALEN use distinguished versions of the relations PP_1, PP_2, and PP_{12}. There we sketch out further advantages of this approach.

5.2 Class Parthood in GALEN

According to the developers of GALEN, the GALEN version of a general class-level parthood relation is the relation InversePartitiveAttribute [16]. However, the logical properties of this relation are not clearly stipulated in GALEN. In particular, InversePartitiveAttribute is not required to be transitive. We will therefore focus instead on the relation isDivisionOf which is the most extensively used of InversePartitiveAttribute's two immediate sub-relations. GALEN stipulates that isDivisionOf is transitive. It is distinguished from makesUp, the other immediate sub-relation of InversePartitiveAttribute, by holding between classes of anatomical structures [16]. By contrast, makesUp, but not isDivisionOf, may hold between classes of substances – e.g. *Plasma* makesUp *Blood*. isDivisionOf is in this sense less general than the class-level proper parthood relations, PP_1, PP_2, PP_{12}, of BIT+Cl, since, e.g., PP_{12}(*Plasma*, *Blood*). However, this particular discrepancy between the BIT+Cl class parthood relations and isDivisionOf will not affect the discussion below since we consider only examples involving classes of anatomical structures.

As with the FMA's part_of, isDivisionOf has more specific sub-relations. These include: isSurfaceDivisionOf, isSolidRegionOf, isLinearDivisionOf, isStructuralComponentOf, and isArbitraryComponentOf. We will not attempt to distinguish between these sub-relations but will focus instead on their common super-relation isDivisionOf.

An inspection of GALEN reveals that isDivisionOf is generally used as a restricted version of (i.e. a sub-relation of) PP_1. That is, in most contexts, if A isDivisionOf B is asserted in GALEN, then PP_1(A, B) also holds – every instance of A is a proper part of some instance of B. For example, GALEN asserts: *Female Pelvic Cavity* isDivisionOf *Pelvic Part of Trunk*, *Prostate Gland* isDivisionOf *Genito-Urinary System*, *Prostate Gland* isDivisionOf *Male Genito-Urinary System*, and *Left Heart Ventricle* isDivisionOf *Heart*.

The GALEN relation hasDivision is generally used as a restricted version of $(PP^{-1})_1$. That is, in most contexts, if A hasDivision B is asserted in GALEN, then $(PP^{-1})_1$(A, B) holds – every instance of A has some instance of B as a proper part. For example, *Pelvic Part of Trunk* hasDivision *Hair* and *Male Genito-Urinary System* hasDivision *Prostate Gland*.

Recall that $(PP^{-1})_1$ is NOT the inverse of PP_1. Rather, $(PP^{-1})_1$ is the inverse of PP_2. (See Subsection 4.1.5.) GALEN's hasDivision is, correspondingly, NOT the inverse of isDivisionOf. In many cases, A isDivisionOf B is asserted in GALEN, but B hasDivision A is not asserted. For example, *Genito-Urinary System* hasDivision *Prostate Gland* and *Pelvic Part of Trunk* hasDivision *Female Pelvic Cavity* are not asserted. In other cases (but less often), B hasDivision A is asserted and A isDivisionOf B is not asserted. For example, *Hair* isDivisionOf *Pelvic Part of Trunk* is not asserted.

GALEN generally asserts both A isDivisionOf B and B hasDivison A when the stronger relation PP_{12} holds between A and B. For example, both *Prostate Gland* isDivisionOf *Male Genito-Urinary System* and *Male Genito-Urinary System* hasDivision *Prostate Gland* are asserted. But hasDivision seems to be less regularly used in GALEN than isDivisionOf. Thus, in several cases in which PP_{12}(A, B) holds only A isDivisionOf B is asserted. For example, *Urinary Bladder* isDivisionOf *Genito-Urinary System* is asserted, but *Genitio-Urinary System* hasDivision *Urinary Bladder* is not asserted.

Finally, in a few contexts, isDivisionOf and hasDivision are used in a way that does not correspond to any of the BIT+Cl class relations. For example, GALEN asserts *Pericardium* isDivisionOf *Heart*, as well as *Heart* hasDivision *Pericardium*. But of the three classes of membranes which are subclasses of *Pericardium* only one, *Visceral Serous Pericardium* (also called "epicardium") has instances which coincide partially with instances of *Heart*. The other two classes, *Parietal Serous Pericardium* and *Fibrous Pericardium*, have no instances which even partially coincide with instances of *Heart*. Thus, not only the PP_i relations, but also the much weaker $PCoin_i$ relations, fail to hold between *Pericardium* and *Heart*.

TABLE 8 summarizes different uses of GALEN's isDivisionOf and hasDivision.

GALEN's isDivisionOf assertion	BIT+Cl relation	GALEN's hasDivision	BIT+Cl relation
Female Pelvic Cavity isDivisionOf *Pelvic Part of Trunk*	PP_1	none	
Prostate Gland isDivisionOf *Genito-Urinary System*	PP_1	none	
none		*Pelvic Part of Trunk* hasDivision *Hair*	$(PP^{-1})_1$
LeftHeartVentricle isDivisionOf *Heart*	PP_{12}	*Heart* hasDivision *LeftHeartVentricle*	$(PP^{-1})_{12}$
Prostate Gland isDivisionOf *Male Genito-Urinary System*	PP_{12}	*Male Genito-Urinary System* hasDivision *Prostate Gland*	$(PP^{-1})_{12}$
Urinary Bladder isDivisionOf *Genito-Urinary System*	PP_{12}	none	
Pericardium isDivisionOf *Heart*	none	*Heart* hasDivision *Pericardium*	none

TABLE 8: Assertions using GALEN's isDivisionOf and hasDivision

5.3 Class Containment in the FMA

The FMA uses the relation contained_in as a class-level location relation. This relation is restricted so that

A contained_in B

may hold only when A is a class of material individuals and B is a class of immaterial individuals. In the FMA's terms, A must be a subclass of *Material Physical Anatomical Entity* and B must be a subclass of *Anatomical Space*. Subclasses of *Material Physical Anatomical Entity* can be subclasses of either *Anatomical Structure* (e.g. *Heart*) or subclasses of *Anatomical Substance* (e.g. *Blood*). Examples of subclasses of *Anatomical Space* include *Pelvic Cavity*, *Cavity of Stomach*, and *Lumen of Esophagus*.

Because material individuals are never parts of immaterial individuals, A contained_in B and A part_of B cannot both hold in the FMA. The mutual exclusivity of the FMA's contained_in and part_of relations contrasts with the inclusivity of the BIT+Cl relations $Loc\text{-}In_1$, $Loc\text{-}In_2$, and $Loc\text{-}In_{12}$. By theorems (ClT10) – (ClT12), $Loc\text{-}In_i$(A, B) must also hold whenever PP_i(A, B) holds. For example, both PP_{12}(*Right Ventricle*, *Heart*) and $Loc\text{-}In_{12}$(*Right Ventricle*, *Heart*) hold in BIT+Cl, whereas only *Right Ventricle* part_of *Heart* holds in the FMA.

The relation contains is used throughout the FMA as the inverse of contained_in. Thus, A contains B can hold only when A is a subclass of *Anatomical Space* and B is a subclass of *Material Physical Anatomical Entity*.

The FMA uses contained_in in different contexts as a sub-relation of Loc-In_1, a sub-relation of Loc-In_2 or a sub-relation of Loc-In_{12}. Examples of these different uses of contained_in are given in TABLE 9.

	the FMA's contained_in	BIT+Cl relation
1	*Right Ovary* contained_in *Abdominopelvic Cavity*	Loc-In_1
2a	*Urinary Bladder* contained_in *Cavity of Female Pelvis*	Loc-In_2
2b	*Urinary Bladder* contained_in *Cavity of Male Pelvis*	Loc-In_2
3	*Blood* contained_in *Cavity of Cardiac Chamber*	Loc-In_2
4	*Urinary Bladder* contained_in *Pelvic Cavity*	Loc-In_{12}
5	*Uterus* contained_in *Cavity of Female Pelvis*	Loc-In_{12}
6	*Prostate* contained_in *Cavity of Male Pelvis*	Loc-In_{12}
7	*Heart* contained_in *Middle Mediastinal Space*	Loc-In_{12}
8	*Blood* contained_in *Lumen of Cardiovascular System*	Loc-In_{12}
9	*Bolus of Food* contained_in *Lumen of Esophagus*	none

TABLE 9: Assertions using the FMA's contained_in

In example 7, every heart is located in some middle mediastinal space and every middle mediastinal space has a heart located in it. By contrast, (example 1) although every right ovary is located in some abdominopelvic cavity, some abdominopelvic cavities (those belonging to males) do not contain a right ovary. Thus, only Loc-In_1(*Right Ovary*, *Abdominopelvic Cavity*) holds. In example 3, every cavity of a cardiac chamber contains some portion of blood, but not every portion of blood is located (at a specific time) in the cavity of a cardiac chamber (some blood is instead in the lumen of the blood vessels). Thus, only Loc-In_2(*Blood*, *Cavity of Cardiac Chamber*), holds.

We note briefly that in a few examples involving anatomical substances, contained_in is not used as a sub-relation of any of the BIT+Cl relations. For example 9, it is not the case that either i) every bolus of food is located in the lumen of some esophagus or ii) every lumen of an esophagus has (at a given time) as bolus of food located in it. In other words, neither Loc-In_1(*Bolus of Food*, *Esophagus*) nor Loc-In_2(*Bolus of Food*, *Esophagus*) (as well as the stronger assertion Loc-In_{12}(*Bolus of Food*, *Esophagus*)) holds. The assertion A contained_in B seems in this and similar cases to mean that i) every instance of A is *at some time* located in some instance of B and ii) every instance of B *at some time* has an instance of B located in it. This is a much more complicated class relation than any considered in this paper since it assumes a time-dependent location relation among individuals and requires quantification over times.

As with the part_of relation, an explicit distinction between the different uses of contained_in is essential for disambiguating the FMA's assertions. Different relations hold between the anatomical classes in examples 1, 2a, 4, and 9 above, but these differences are not made explicit in the FMA's assertions.

Also as with part_of, a clear distinction between the different uses of the contained_in relation is necessary for implementing automated reasoning over containment assertions. Currently, the FMA has no automated reasoning for the contained_in and contains relations. Note that, although contained_in is transitive, transitivity reasoning over contained_in does not generate additional assertions. This is because the argument restrictions on contained_in do not allow classes A, B, and C such that

A contained_in B & B contained_in C.

Since B cannot be both a class of immaterial individuals (as the second argument of contained_in in the first conjunct) and a class of material individuals (as the first argument of contained_in in the second conjunct), the conjunction above cannot hold. Thus, the antecedent of the transitivity implication is never satisfied and we cannot generate additional assertions from the transitivity of contained_in.

But other of the BIT+Cl theorems embodied in Table 2 and Table 4 would be useful for generating further assertions, if the Loc-In$_1$, Loc-In$_2$, and Loc-In$_{12}$ uses of contained_in as well as the PP$_1$, PP$_2$, and PP$_{12}$ uses of part_of were clearly distinguished. For example, the FMA asserts

Heart contained_in *Middle Mediastinal Space*

and

Middle Mediastinal Space part_of *Thoracic Cavity*.

Since Loc-In$_{12}$(*Heart*, *Middle Mediastinal Space*) and PP$_{12}$(*Middle Mediastinal Space*, *Thoracic Cavity*), we can use Table 2 (Row 6, Column 3) to infer: Loc-In$_{12}$(*Heart*, *Thoracic Cavity*). Since, in addition, *Thoracic Cavity* is a subclass of *Anatomical Space*, *Heart* contained_in *Thoracic Cavity* (with contained_in used as a sub-relation of Loc-In$_{12}$) should hold as well, but is not currently asserted in the FMA. See Figure 3.

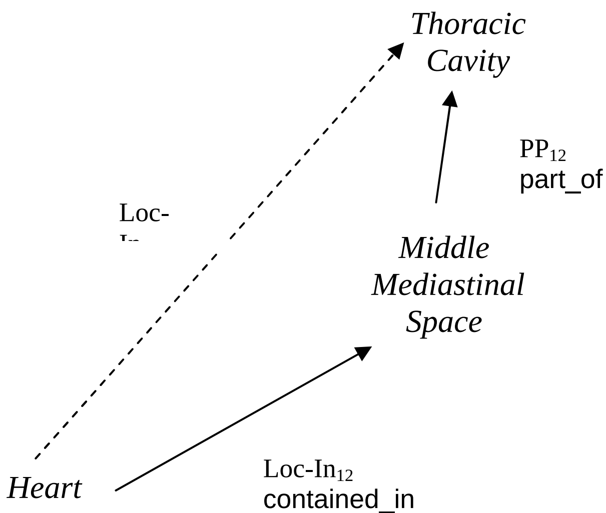

Figure 3: Potential for reasoning about parthood and containment in the FMA

As another example, the FMA includes the assertions *Lung* contained_in *Thoracic Cavity* and *Right Lung* subclass *Lung*. Since, Loc-In$_{12}$(*Lung*, *Thoracic Cavity*), we can use Table 4 to derive Loc-In$_{12}$(*Right Lung*, *Thoracic Cavity*). As a subclass of *Lung*, *Right Lung* must also be a subclass of *Material Physical Anatomical Entity*. Thus, *Right Lung* contained_in *Thoracic Cavity* (with contained_in is used as a sub-relation of Loc-In$_{12}$) should also hold, but is not currently asserted in the FMA. See Figure 4.

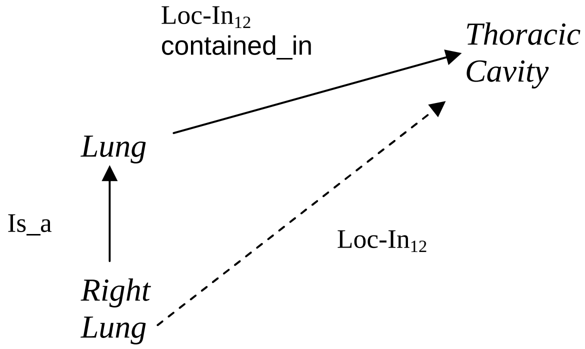

Figure 4: Potential for reasoning about class subsumption and containment in the FMA

In general, BIT+Cl theorems concerning class location relations can be used to generate additional containment assertions in the FMA as long as i) R_1, R_2, and R_{12} relations are distinguished and ii) if necessary, an extra step is taken to check that the arguments of the derived BIT+Cl location assertion satisfy the FMA's restrictions on the arguments of contained_in.

5.4 Class Containment in GALEN

GALEN's most general location relation is isContainedIn. Like isDivisionOf, isContainedIn has several sub-relations. isPartitivelyContainedIn and isNonPartitivelyContainedIn are its two immediate sub-relations, which are, in turn, each divided into several sub-relations. For the most part, the distinctions between the different sub-relations of isContainedIn are not relevant to our discussion and will be ignored. However, we will briefly mention below the special use of isPartitivelyContainedIn, since this sub-relation highlights one important distinction between GALEN's and the FMA's containment relations.

Table10 lists examples of GALEN assertions using isContainedIn and its counterpart Contains.

In most—but not all—contexts, isContainedIn is used as a restricted version of Loc-In_1. For example, GALEN asserts *Ovarian Artery* isContainedIn *Pelvic Cavity*, *Uterus* isContainedIn *Pelvic Cavity*, *Uterus* isContainedIn *Female Pelvic Cavity*, and *Mediastinum* isContainedIn *Thoracic Space*.

The relation Contains is used in most contexts as a restricted version of $(\text{Loc-In}^{-1})_1$. For example, *Venous Blood* Contains *Haemoglobin*, *Male Pelvic Cavity* Contains *Urinary Bladder*, *Female Pelvic Cavity* Contains *Uterus*, and *Thoracic Space* Contains *Mediastinum*. However, we have also found one context in which Contains is used instead as a restricted version of $(\text{Loc-In}^{-1})_2$ — GALEN asserts *Pelvic Cavity* Contains *Ovarian Artery*, *Pelvic Cavity* Contains *Uterine Artery*, and *Pelvic Cavity* Contains *Vaginal Artery*.

Just as $(\text{PP}^{-1})_1$ is not the inverse of PP_1, $(\text{Loc-In}^{-1})_1$ is not the inverse of Loc-In_1. (See Subsection 4.1.5.) Thus, as with isDivisionOf and hasDivision, isContainedIn and Contains are not inverses. For example, GALEN asserts *Uterus* isContainedIn *Pelvic Cavity*, but not *Pelvic Cavity* Contains *Uterus*. Also, GALEN asserts *Venous Blood* Contains *Haemoglobin*, but not *Haemoglobin* isContainedIn *Venous Blood*.

Typically— but again not always — both A isContainedIn B and B Contains A are asserted when the stronger Loc-In_{12} relation holds between A and B. For example, GALEN asserts *Uterus* isContainedIn *Female Pelvic Cavity* and *Female Pelvic Cavity* Contains *Uterus*, as well as *Mediastinum* isContainedIn *Thoracic Space* and *Thoracic Space* Contains *Mediastinum*. But note that *Ovarian Artery* isContainedIn *Pelvic Cavity* and *Pelvic Cavity* Contains *Ovarian Artery* are both asserted even though Loc-In_{12}(*Ovarian Artery*, *Pelvic Cavity*) does NOT hold (instead only Loc-In_2(*Ovarian Artery*, *Pelvic Cavity*) holds).

As additional exceptions to the typical behavior of isContainedIn and Contains, GALEN includes a significant number of assertions of the form A isContainedIn B or B Contains A where none of the BIT+Cl relations holds between A and B. For example, GALEN asserts *Lung* isContainedIn *Pleural Membrane* (as well as *Pleural Membrane* Contains *Lung*). But no lung stands in either the relation Loc-In or the weaker relation PCoin to any pleural membrane. GALEN seems to use isContainedIn in this and similar cases to indicate that members of one anatomical class are surrounded by or enclosed within members of another anatomical class. This type of spatial relation is much more complex than those introduced in BIT+Cl since it is based not just in topological structure but also requires, at a minimum, some mechanism for distinguishing convex and non-convex structures (since only non-convex individuals can surround other individuals). A slightly different example is the GALEN assertion *Tooth* isContainedIn *Tooth Socket* (and also *Tooth Socket* Contains *Tooth*). Note that the relation between a tooth and its socket is significantly weaker than the relation between a lung and its pleural membrane – a tooth socket only partially surrounds its tooth.

Finally, we have found a small group of erroneous assertions which seem to appear in GALEN as a result of improper automated reasoning over the Contains relation. GALEN implements unrestricted transitivity reasoning on both isContainedIn and Contains. GALEN also seems to implement reasoning, corresponding roughly to inferences represented in Tables 4 and 5, over conjunctions of isContainedIn and SubclassOf assertions or conjunctions of Contains and SubclassOf assertions. As we have already seen, these kinds of inferences can lead to false conclusions if the R_1, R_2, and R_{12} versions of class relations are not explicitly distinguished.

A failure to tailor automated reasoning to the different properties of Loc-In_1, Loc-In_2, Loc-In_{12}, and their sub-relations seems to be the reason for erroneous GALEN assertions such as *Male Pelvic Cavity* Contains *Ovarian Artery*, *Male Pelvic Cavity* Contains *Uterine Artery*, and *Male Pelvic Cavity* Contains *Vaginal Artery*. The assertion *Male Pelvic Cavity* Contains *Ovarian Artery* seems to have been generated from the GALEN assertions

Pelvic Cavity Contains *Ovarian Artery*

and

Male Pelvic Cavity SubclassOf *Pelvic Cavity*.

These assertions correspond to the following BIT+Cl assertions:

$(\text{Loc-In}^{-1})_2$(*Pelvic Cavity*, *Ovarian Artery*)
(every ovarian artery is located in some pelvic cavity)

and

Male Pelvic Cavity Is_a *Pelvic Cavity*
(every male pelvic cavity is a pelvic cavity).

See Figure 5.

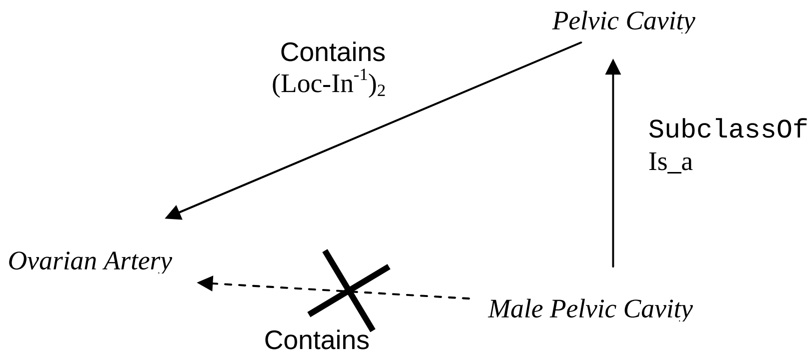

Figure 5: Reasoning about containment and subclass relations in GALEN

As can been seen from Table 5 (row 2, column 3), no conclusion about location relations between classes B and C can be derived from the conjunction $(\text{Loc-In}^{-1})_2$(A, B) & Is_a(C, A).Thus, the inference from *Pelvic Cavity* Contains *Ovarian Artery* and *Male Pelvic Cavity* SubclassOf *Pelvic Cavity* to *Male Pelvic Cavity* Contains *Ovarian Artery* is invalid.

	GALEN's isContainedIn	BIT+Cl relation	GALEN's Contains	BIT+Cl relation
1	*Ovarian Artery* isContainedIn *Pelvic Cavity*	Loc-In_1	*Pelvic Cavity* Contains *Ovarian Artery*	$(\text{Loc-In}^{-1})_2$
2	*Uterus* isContainedIn *Pelvic Cavity*	Loc-In_1	none	
3	none		*Venous Blood* Contains *Haemoglobin*	$(\text{Loc-In}^{-1})_1$

4	*none*		*Male Pelvic Cavity* Contains *Urinary Bladder*	$(\text{Loc-In}^{-1})_1$
5	*Uterus* isContainedIn *Female Pelvic Cavity*	Loc-In_{12}	*Female Pelvic Cavity* Contains *Uterus*	$(\text{Loc-In}^{-1})_{12}$
6	*Mediastinum* isContainedIn *Thoracic Space*	Loc-In_{12}	*Thoracic Space* Contains *Mediastinum*	$(\text{Loc-In}^{-1})_{12}$
7	*Larynx* isContainedIn *Neck*	Loc-In_{12}	*Neck* Contains *Larynx*	$(\text{Loc-In}^{-1})_{12}$
8	*Lung* isContainedIn *Pleural Membrane*	none	*Pleural Membrane* Contains *Lung*	none
9	*Tooth* isContainedIn *Tooth Socket*	none	*Tooth Socket* Contains *Tooth*	none
10	none		*Male Pelvic Cavity* Contains *Ovarian Artery*	none

TABLE 10: Assertions using GALEN's isContainedIn and Contains

Examples in Table 10 highlight some important distinctions between the FMA's and GALEN's containment relations.

Examples 6 and 7 show that GALEN's class containment relation does not, like that of the FMA, exclude class parthood relations. GALEN uses the relation isPartitivelyContainedIn as a sub-relation of both isContainedIn and isDivisionOf. Analogously, PartitivelyContains is in GALEN a sub-relation of both Contains and hasDivision. These stronger relations hold between the pairs of anatomical classes in examples 6 and 7. Thus, GALEN asserts both *Mediastinum* isContainedIn *Thoracic Space* and *Mediastinum* isDivisionOf *Thoracic Space*, as well as both *Larynx* isContainedIn *Neck* and *Larynx* isDivisionOf *Neck*. Also, GALEN asserts both *Thoracic Space* Contains *Mediastinum* and *Thoracic Space* hasDivision *Mediastinum*, as well as *Neck* Contains *Larynx* and *Neck* hasDivision *Larynx*.

But note that GALEN's isDivisionOf is not a sub-relation of isContainedIn . We have seen that in BIT+Cl, $PP_i(A, B)$ implies $\text{Loc-In}_i(A, B)$. By contrast, GALEN often asserts that A isDivisionOf B without also asserting A isContainedIn B.[17] For example, GALEN asserts *Urinary Bladder* isDivisionOf *Lower Urinary Tract* but not *Urinary Bladder* isContainedIn *Lower Urinary Tract*. Also GALEN asserts *Left Side Of Heart* isDivisionOf *Heart*, but not *Left Side Of Heart* isContainedIn *Heart*. Similarly, Contains is not a sub-relation of hasDivision. For example, *Lower Urinary Tract* hasDivision *Urinary Bladder* and *Heart* hasDivision *Left Side Of Heart* are asserted but not *Lower Urinary Tract* Contains *Urinary Bladder* and *Heart* Contains *Left Side Of Heart*. It is not clear, however, exactly what principle GALEN uses to distinguish cases of class parthood which are also cases of class containment from cases of class parthood which are not cases of class containment.

Examples 6 and 7 (as well as examples 8 and 9) also demonstrate that GALEN does not, as the FMA does, restrict the arguments of its containment relation so that the first must be a class of material individuals and the second must be a class of immaterial individuals. In GALEN, *Mediastinum* (the first argument in example 6) is a subclass of *Body Space* and *Neck* (the second argument in example 7) is a subclass of *Muscle Tissue Structure*.

In sum, we have seen that GALEN's failure to distinguish between $(\text{Loc-In}^{-1})_1$ and $(\text{Loc-In}^{-1})_2$ uses of Contains has led in one case to ambiguous and false assertions and invalid inference mechanisms. Also, the root spatial meaning of GALEN's general containment relation is unclear. In particular, it is not clear what exactly (in the

[17] Of course, in these cases a sub-relation of isDivisionOf other than *isPartitivelyContainedIn* is used.

spatial configurations the relevant individuals) is supposed to distinguish the isDivisionOf and isContainedIn relations. In addition, isContainedIn and its sub-relations are used in some cases, not as a class-level location relations (like BIT+Cl's Loc-In_i relations or the FMA's contained_in), but rather as class-level *surrounds* relations. The spatial relation between my urinary bladder and my pelvic cavity is very different from the spatial relation between a tooth and its socket. My urinary bladder occupies part of my pelvic cavity, while my tooth is partially surrounded by its socket. Yet the same sub-relation of isContainedIn -- isNonPartitivelyContainedIn – is used in the GALEN assertions about the corresponding classes: *Urinary Bladder* isNonPartitivelyContainedIn *PelvicCavity* and *Tooth* isNonPartitivelyContainedIn *Tooth Socket*.

5.5 Using BIT+Cl to Improve Anatomical Representation and Reasoning in Biomedical Ontologies

We recommend that all biomedical ontologies link their spatial terms to the relations of a formal theory, such as BIT+Cl or (for more complex relations) an extension of BIT+Cl. We particularly urge that relations which are distinct in the formal theory be linked to different relational terms in the biomedical ontology. This will greatly improve the clarity of the information contained in the biomedical ontology – the user will know, e.g., that the class parthood relation holding between *Male Pelvis* and *Body* is different from the class parthood relation holding between *Urinary Bladder* and *Male Pelvis*. It will also allow for expanded automated assertion generation through the consistent implementation of reasoning based on theorems of the formal theory. The automated generation of assertions will, in turn, decrease the need for manual input into the ontology and, if consistently implemented, decrease number of erroneous assertions mistakenly entered into the ontology.

We have focused in Sections 4 and 5 on the need to explicitly distinguish R_1, R_2, and R_{12} types of class relations. We now briefly sketch how a biomedical ontology which clearly distinguishes the PP_1, PP_2, and PP_{12} relations might operate. For such an ontology, assertions involving the PP_1 and PP_2 relations could be generated automatically from PP_{12} assertions and Is_a assertions. In addition, the transitivity of PP_{12} can be used to automatically generate PP_{12} assertions from a (relatively) small collection of manually entered PP_{12} assertions. For example, given the following inputs:

PP_{12}(*Pelvis*, *Body*)
PP_{12}(*Urinary Tract*, *Pelvis*)
PP_{12}(*Urinary Bladder*, *Urinary Tract*)

transitivity reasoning on PP_{12} generates:

PP_{12}(*Urinary Tract*, *Body*)
PP_{12}(*Urinary Bladder*, *Body*)
PP_{12}(*Urinary Bladder*, *Pelvis*).

Given also the Is_a assertions:

Is_a(*Female Pelvis*, *Pelvis*)
Is_a(*Male Pelvis*, *Pelvis*)

the theorems represented in Table 3, generate:

PP_2(*Urinary Tract*, *Female Pelvis*)
PP_2(*Urinary Tract*, *Male Pelvis*)
PP_2(*Urinary Bladder*, *Female Pelvis*)
PP_2(*Urinary Bladder*, *Male Pelvis*)

See Figure 2, Subsection 5.1.

Note that the strong PP_{12} relations can link to *Pelvis* or *Body* only classes, like *Urinary Bladder*, whose instances are parts of all pelvises and bodies. But the PP_{12} relation can link classes of sexually dimorphic structures to either *Female Pelvis* or *Male Pelvis* (or *Female Body* or *Male Body*). From inputs such as

PP_{12}(*Uterus*, *Female Pelvis*)
PP_{12}(*Prostate Gland*, *Male Pelvis*)

PP_1 assertions linking *Pelvis* (or *Body*) to the classes of sexually dimorphic structure can be generated via Table 3:

PP_1(*Uterus*, *Pelvis*)
PP_1(*Prostate Gland*, *Pelvis*).

Thus, given this kind of mechanism for automatically generating PP_1 and PP_2 assertions from PP_{12} and Is_a assertions and given also a rich enough classification system[18], the curators of a biomedical ontology need only manually input a portion of its PP_{12} and Is_a assertions to derive a full range of distinct PP_1, PP_2, and PP_{12} assertions.

Of course, displaying at once *all* PP_1, PP_2, and PP_{12} assertions involving a given class is probably impractical. It would also be redundant since for each assertion of the form PP_{12}(A, B), we have also (via theorems (ClT26) – (ClT27)) both PP_1(A, B) and PP_2(A, B). (For example, PP_{12}(*Urinary Bladder*, *Pelvis*) entails the weaker assertions: PP_1(*Urinary Bladder*, *Pelvis*) and PP_2(*Urinary Bladder*, *Pelvis*).) We suggest that PP_1, PP_2, and PP_{12} assertions be displayed in separate (and clearly distinguished) modalities of the interface's parthood graphs or tables of assertions. Examples illustrating some differences in the kind of information that would be embodied in separate PP_{12}, PP_1, and PP_{12} graphs are given in Figure 6.

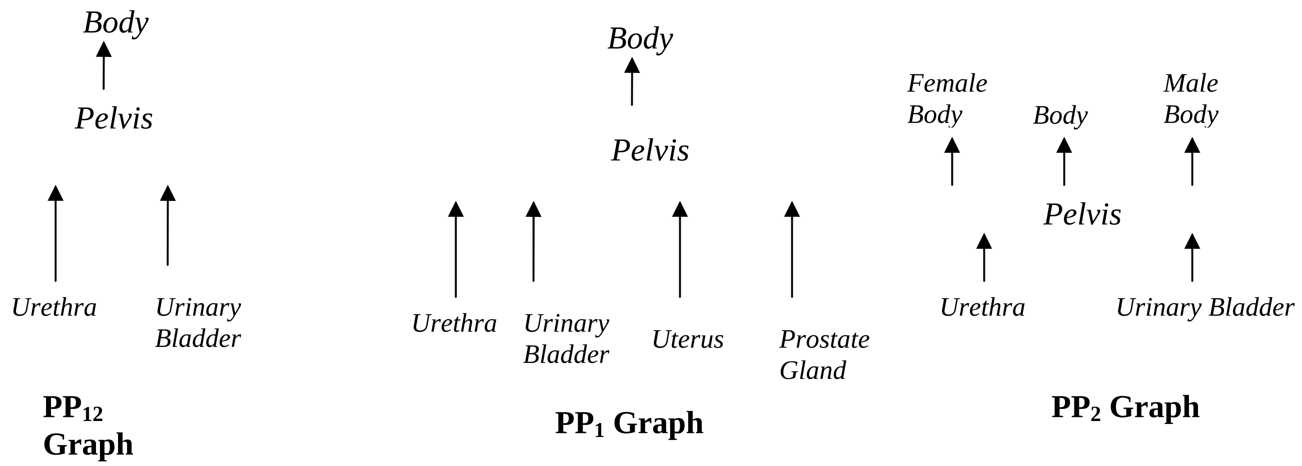

Figure 6: Separate graphs for the PP_{12}, PP_1, and PP_2 relations

The same kind of strategy can be used to input, derive, and display assertions involving R_1, R_2, and R_{12} class relations for other underlying relations R. For example, it can be used for assertions involving the broad BIT+Cl location relations, Loc-In_1, Loc-In_2, and Loc-In_{12}, or for assertions involving clearly distinguished versions of either the FMA's or GALEN's containment relations. With a wide collection of class relations, more complex inference rules can be implemented for automatically generating assertions. For example, Table 2 can be used to generate further assertions from combinations of class parthood and class location assertions.

We have focused in this section on the advantages to be gained and the problems to be avoiding by including clearly distinguished R_1, R_2, and R_{12} versions of parthood and location relation in a biomedical ontology. But we have also seen other kinds of ambiguities in the FMA's and GALEN's uses of their parthood and containment relations. For example, we saw that GALEN uses the same relation, isNonPartativelyContainedIn, both as a class-level surround relation and as class-level location relation (in the sense of the Loc-In_i). We have also seen that in some cases the FMA seems to use contained_in to mean: is-at-some-times-contained-in (as in *Bolus of Food* contained_in *Lumen of Esophagus*). These kinds of ambiguities are undesirable and may, like the

[18] More precisely, the classification needs to satisfy the following two conditions: i) whenever PP_1(A, B) holds but PP_{12}(A, B) does NOT hold, there is either some class C such that either C Is_A B and PP_{12}(A, C) or A Is_a C and PP_{12}(C, B); ii) whenever PP_2(A, B) holds but PP_{12}(A, B) does NOT hold, the is some class D such that either B Is_a D and PP_{12}(A, D) or D Is_a A and PP_{12}(D, B).

R_1, R_2, R_{12} ambiguities, obstruct the development of robust reasoning mechanisms. A more complex extension of BIT+Cl can be used to disambiguate these uses of the containment relations and also to analyze other types of relations (e.g. adjacency and continuity) which are used in the FMA and GALEN. Such an extension of BIT+Cl must have a temporal component as well as a wider range of spatial relations. It could be used to render the meanings of the biomedical ontologies' relational terms more precise and to support reasoning over a wide range of class relations.

Finally, we note that some of the BIT+Cl relations have no counterparts in the FMA or GALEN. We suggest that biomedical ontologies consider expanding their collection of spatial inclusion relations so that they can contain more anatomical information. For example, with PCoin_{12}, the ontologies could assert:

PCoin_{12}(*Esophagus*, *Superior Mediastinal Space*)
(every esophogus partially coincides with some superior mediastinal space and every superior mediastinal space partially coincides with some esophagus)
PCoin_{12}(*Esophagus*, *Posterior Mediastinal Space*)
(every esophogus partially coincides with some posterior mediastinal space and every posterior mediastinal space partially coincides with some esophagus)

and so on. With O_{12}, the ontologies could assert:

O_{12}(*Bony Pelvis*, *Vertebral Column*)
(every bony pelvis overlaps some vertebral column and every vertebral column overlaps some bony pelvis)

Adding these particular relations to the ontologies would be especially advantageous since they have strong inferential ties to the PP_1, PP_2, PP_{12}, Loc-In_1, Loc-In_2, and Loc-In_{12} relations which correspond roughly to the FMA's and GALEN's parthood and containment relations. Thus, for example, the assertion O_{12}(*Bony Pelvis, Vertebral Column*) could be inferred from information already in the FMA and GALEN once the different versions of their parthood relations are clearly distinguished. The FMA already includes the assertions *Sacrum* part_of *BonyPelvis* and *Sacrum* part_of *Vertebral Column*. GALEN includes analogous assertions using its isDivisionOf relation.[19] Given that the parthood relations in this case are the strong PP_{12} assertions, O_{12}(*Bony Pelvis*, *Vertebral Column*) can be inferred. Also, PCoin_{12}(*Esophagus*, *Superior Mediastinal Space*) can be derived in BIT+Cl from PP_{12}(*T4 Segment of Esophagus*, *Esophagus*) and Loc-In_{12}(*T4 Segment of Esophagus, Superior Mediastinal Space*). Analogous inferences generate PCoin_{12}(*Esophagus, Posterior Mediastinal Space*) and other PCoin_{12} assertions for *Esophagus*. Thus, with strong automatic assertion generation capabilities and unambiguous class parthood and location relations, assertions such as O_{12}(*Bony Pelvis, Vertebral Column*), PCoin_{12}(*Esophagus*, *Superior Mediastinal Space*), and PCoin_{12}(*Esophagus*, *Posterior Mediastinal Space*) would not require additional manual input into the ontologies.

6. Conclusions and Further Work

A central goal in artificial intelligence is to create ontologies which encode the general background knowledge needed for organizing and using data in a specific domain such as medicine, biology, or geography. For these domain ontologies to function as general references, they must be robust in the sense that they can be used in different contexts by users with different kinds of expertise and different objectives. In particular, it should be possible for users to integrate data organized in terms of a domain ontology with data organized according to a different system. The domain ontologies should also be expandable – we should be able to add content or stronger inference mechanisms without having to restructure the entire ontology.

To achieve these goals, it is crucial that the creators of an ontology organize the terms in their ontology in a clear and systematic way and that all relational terms are linked to a formal theory which makes the logical properties of the relations explicit. Our investigation has shown that the spatial relational terms used to organize

[19] Note that GALEN uses the term "*SpinalColumn*" instead of "*VertebralColumn*".

the anatomical content of the FMA and GALEN are not clearly defined and that often the same relational term is used for relations with significantly different logical properties. As a result, some assertions in these ontologies are ambiguous and it is not obvious how to integrate anatomical information from the FMA with anatomical information in GALEN.[20] We have also seen that the failure to distinguish different class-level relations obscures the logical structure of the information embodied in these ontologies and limits possibilities for consistent automated reasoning.

We have proposed Basic Inclusion Theory for Class (BIT+Cl) as a first-order logical theory in which different class-level parthood and location relations can be clearly distinguished. The theory we develop here builds on previous work [9, 19, 22]. We go beyond this earlier work in distinguishing an interconnected group of parthood and location relations among individuals which are used to formally define corresponding class relations. We have also investigated in much greater detail the logical properties of the relations introduced in our formal theory and their correspondence with the relational terms of the FMA and GALEN.

Our approach can, in turn, be extended by strengthening the spatial component (BIT) of BIT+Cl. BIT can be strengthened either through the addition of further restrictions on the relations already included in BIT (along the lines suggested in Subsection 2.3 of this paper) or through the introduction of further relations. Further formal relations are necessary for giving a full analysis of both the FMA's and GALEN's containment relations as well as an analysis of other relations such as continuous_with or boundary_of. Another important area for further research is the introduction of time dependent spatial relations (along the lines sketched in [4]) which can be used in, e.g. developmental anatomy, to describe intermittent or evolving spatial relations between the instances of two classes.

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[20] Note that obstacles to integration stemming from the use of unclear class-level relations are compounded by the mutually inconsistent classification schemes adopted by these ontologies. For example, in the FMA *Mediastinum* is a subclass of *Material Physical Anatomical Entity* and in GALEN *Mediastinum* is a subclass of *Body Space*.

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