A Reference Model for Biomedical Ontology Evaluation: The Perspective of Granularity

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Abstract

There have been many attempts using ontologies to develop systems that integrate data from the domains of medicine and biology, across levels of gravity. Such integration systems have not gained wide adoption and reuse. This is largely due to a lack of an approach with metrics as frame of reference to enable users evaluate these systems for their representation of biomedical structure, accross levels of granularity. In this paper a reference ontology against which such evaluation of biomedical ontologies may be conducted is presented. Requirements for the reference ontology were validated in a descriptive study. Basic formal ontology with its support for representing biomedical structure across levels of granularity is adopted as the underlying theory for deriving the reference ontology. Metrics for determining the suitability of an ontology to integrate biomedical data across levels of granularity are derived using the reference ontology. The utility of the reference ontology was tested by a prototype tool that was used to evaluate the infectious disease ontology. The results were validated in a questionnaire based study with users.

Categories and Subject descriptors: H.1.1 [**Models and Principles**]: Systems and Information theory – General Systems Theory; J.3 [**Life and Medical Science**s]: Medical Information Systems, Biology and Genetics

General terms: Reference Ontology; Biomedical Ontology; Ontology Evaluation; Biomedical Data Integration; Granularity; Additional key words and phrases: Levels of Granularity; Biological data; Clinical data.

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1. INTRODUCTION

Biomedical Ontologies [BOs] are used to integrate data from disparate biological and clinical databases [Kumar et al. 2006; 2006; Rey-Perez et al. 2006; Sioutos et al. 2006]. However, their reuse and wide adoption in distributed computing environments remains constrained by the lack frameworks with metrics for users to assess their suitability in specific applications [EON 2006]. To integrate data from the domains of clinical medicine and biology BOs have to address the problematic issue of treatment of granularity across biomedical

structures [Yu 2006]. This problem continues to undermine efforts to develop frameworks for their evaluation and underlies the difficulty of selecting an ontology for use during data integration [Alani and Brewster 2006].

The challenge of evaluating and selecting ontologies to be used in biomedical applications therefore remains an important research and development endeavor, especially for distributed computing environments [Kalfoglou and Schorlmer 2006]. Existing approaches largely assess an ontology based on its taxonomy, and not the ability to integrate across levels of granularity commonly found in biomedical structure. This makes them unsuitable for assessing the suitability of an ontology for use in a biomedical data integration task. The result has been the proliferation of ontologies whose reuse and wide adoption in ontology-based biomedical data integration systems by industry has, like with other domains not yet been realized [Gangemi et al. 2005; EON 2006].

In this paper the results of a study to develop a reference ontology for biological and clinical data integration, as a frame of reference for assessing biomedical ontologies are presented. The reference ontology represents the essence of a biological and clinical data integration system. The properties of the reference ontology as identified from the literature were validated in a descriptive questionnaire based field study.

The rest of this paper is organized as follows. Section 2 discusses the role of biomedical ontologies for data integration. Section 3 explores current approaches to ontology evaluation, while section 4 explains how a reference ontology and metrics for biomedical ontology evaluation are derived. Section 5 presents the validation of the reference ontology. Conclusions are made in section 6.

2.0 BIOMEDICAL ONTOLOGY

Integrating data from the domains of biology and clinical medicine using ontologies is important for biomedical knowledge representation [Hongzhan et al. 2004]. Existing bio-ontologies are challenged when it comes to representing biomedical data due to its complexity, differences between and within disciplines and research groups [Keet 2003]. The vast amounts of data generated from biology and clinical medicine require integration systems to represent semantically heterogeneous data sources across levels of granularity and biomedical processes. There is therefore continuing development of new ontologies for biomedical data integration systems, and rapid evolution of existing ones involving many researchers [Perez-Rey et al. 2006; 2006; Kumar et al. 2006]. Despite these models, the lack of a unifying ontology based approach for integrating biomedical data persists [Grenon et al. 2004; Yu 2006].

Attempts to standardize data integration on a large scale have used upper level ontology theories [SUMO 2008; Gangemi et al. 2005; Grenon et al. 2004]. These ontologies have an unbounded universe of discourse, are built using different tools and theories and differ in their theoretical representation of processes, temporality, granularity, spatiality and structure [Grenon et al. 2004]. These differences become important for selecting an ontology based theory for to support data integration and knowledge representation in all fields including biomedicine [Alani and Brewster 2006].

Whatever the data integration approach used, for ontology based systems to gain wide acceptance and reuse, they need to be evaluated. Integrating biomedical data structures, function, processes across levels of granularity using ontologies therefore remains challenging, with no unifying approach against which the integrated systems can be assessed by users. This lack of a standard integration model presents a challenge for biomedical ontology evaluation. Comparing the performance of different ontology based integration systems in use thus remains problematic due to the lack of standard approaches and metrics [Kalfoglou and Schorlermmer 2003].

2.1 Importance of Granularity for Biomedical Data Integration

Granularity, the ability to represent and operate at different levels of detail in data, is indispensable for managing and analyzing huge amounts of data found in biological databases and ontologies [Keet 2008]. Granularity articulates something hierarchically according to some criteria - the granular perspective [ibid]. There is no single unifying perspective for articulating granularity. Thus Keet [2008] identify perspectives of granularity as: i) arbitrary scale versus non scale dependent; ii) how levels, and its contents, in a perspective relate to each other; iii) difference in emphasis, i.e. being entity, relation, or criterion-focused; and iv) representation based on set theory or mereology.

Other granular perspectives consider range size and collectivity dealing with aggregations of individuals into collections have also been proposed [Kumar et al. 2005; Rector et al. 2006]. There is a distinction between the notions of collectivity and size range as the two dimensions of granularity [Rector et al. 2006]. The notion of collectivity is pervasive across size ranges, and is key to providing an account of whether the *part_whole* relation is, or is not transitive in biomedicine [ibid].

Health care workers require data on structures, processes and functions of organisms at the coarser levels of granularity, while for molecular biologists it is at the finer levels. This underlies the need for biomedical ontology models that integrate data across levels of granularity [Kumar et al. 2005; Rector *et al*., 2006]. For instance, the Gene Ontology with the cell as its highest level of granularity does not offer a good framework for representation of biological processes that occur at coarser levels [Kumar et al. 2005]. Good representation of granularity in a model enables tracking of entities and attributes across levels, leading to building of better data integration systems [Kumar et al. 2006].

2.2 Issues for Ontology-based Biomedical Data Integration

Integrating biomedical data using ontologies is challenging for several reasons. There is need to overcome problems of semantic heterogeneity and bridge across levels of granularity between data sources. Biological and clinical data is to be found at different levels of detail [Smith et al. 2006; Rector et al. 2006]. Biomedical data is diverse, rapidly changing, and stored in autonomous sources that can freely modify their design, change or block access to data without notice [EMBL, 2005]. Ontologies for biomedical data integration also have to address issues of changing structure, function and processes presented by the different data sources [Kumar et al. 2005; Rector et al. 2006].

Biomedical data integration ontologies also vary in scope (purpose and users). They range from single domain (domain dependent) to generic (domain independent) models. The latter are used to integrate data across domains in the life sciences. Many approaches to ontology based integration of biomedical data have been attempted [Perez-Rey et al. 2006; 2006; Kumar et al. 2006]. However, the lack of a single unifying strategy to the problem of biomedical data integration across scope, granularity and heterogeneous data sources persists [Davidson et al. 1995; Ding and Foo, 2002].

3.0 APPROACHES TO ONTOLOGY EVALUATION

There is no unifying definition of ontology evaluation. It is a technical judgment of the contents of an ontology with respect to requirements specifications, competency questions, or a reference ontology as frame of reference [Gangemi et al. 2005; Gomez-Perez 2004]. Evaluation determines the quality and adequacy of an ontology for use in a specific context and goal [Fernández et al. 2006]. There is no unifying approach with metrics for evaluating an ontology across contexts. This remains an obstacle for their reuse and wide adoption by industry and the wider web community [Alani and Brewster 2006; Kalfoglou and Schorlmer 2006]. The result has been a multiplicity of proposed approaches for ontology evaluation based on either: i) the level of complexity of an

ontology; ii) the use of multiple criteria, and iii) the use of approaches based on semiotic theory to evaluate an ontology.

3.1 Level Based Approaches to Ontology Evaluation

Various contexts are used to conduct ontology evaluation at different levels of complexity. A taxonomy of evaluation approaches based on type and purpose and adopting levels of vocabulary, taxonomy, semantic relations, application, syntax, structure and design is provided by Brank et al. [2005], as shown in table 1.

Table 1: A level based Taxonomy of Ontology Evaluation approaches [Brank et al. 2005]

	Evaluation approach			
Evaluation level	Golden standard	Application based	Data or corpus driven	Human assessment
Lexical, vocabulary	X = applied	X	X	X
Hierarchy	X	X	X	X
Semantic relations	X	X	X	X
Content application	X	X	Not applied	X
Syntactic relations	X	Not applied	X	X
Structure, architecture, design	Not applied	Not applied	Not applied	X
Process, function, granularity	Not applied	Not applied	Not applied	Not applied

This level based taxonomy categorizes existing ontology evaluation approaches into: i) golden standard approaches that compare an ontology to a gold standard [Gomez-Perez 1994; Hovy 2001]; ii) task based approaches that assess results after using the ontology in an application [Porzel and Malaka 2004]; iii) data or corpus driven approaches that compare the fit of an ontology to domain texts [Brewster et al. 2004]; iv) human assessment against some predefined criteria [Lozano-Tello and Gomez-Perez 2004; Supekar 2005]. Table 1 illustrates the lack of a unifying approach for conducting ontology evaluation across all levels of complexity.

3. 2 Ontology Evaluations Based on Semiotic Theory

Based on Semiotic theory, an ontology is a semiotic object with three evaluation levels of structure, function and usability. The structural level assesses the ontology syntax and formal semantics; the functional level assesses the ontology's cognitive semantics while the usability-related level for assesses its pragmatics [Dividino and Sonntag 2008]. Based on semiotic theory, metrics for ontology evaluation therefore consider its syntactic, semantic, and pragmatic aspects. As an application of this theory, the Semiotic-based tool [S-OntoEval] has been proposed and used to evaluate the Ontology of the Smart Web project – SWIntO, using metrics for each semiotic ontology level [ibid]. At the structural level it checks the logical consistency of an ontology model and graph theory measures e.g. depth. The functional level is a task-based evaluation approach

measuring the quality of the ontology, and [iii] on the usability-profiling level a quantitative analysis of the amount of annotation is applied [Dividino and Sonntag 2008].

Similar to the semiotic based ontology evaluation, a framework with metrics to evaluate the structure, usability and function of an ontology is described by Gangemi et al. [2005]. Functional measures assess the intended use of an ontology. Usability-profiling measures use its level of annotation to assess user-satisfaction, completeness and reliability [ibid].

3.3 Multi-Criteria Based Approaches to Ontology Evaluation

Multiple criteria approaches deal with the problem of selecting a good ontology from a given set based on defining several decision criteria or attributes. For each criterion, the ontology is evaluated and given a numerical score and an overall score computed as a weighted sum of its per-criterion scores [Lozano-Tello and Gomez-Perez 2004]. While this approach requires a lot of manual involvement by human experts, it allows a combination of criteria at many levels [ibid].

3.4. The Role of Classes and Relations for Ontology Evaluation Metrics

Classes and properties are used to describe the structure, function, knowledge representation and level of integration of an ontology and so play an important role in deriving metrics for their evaluation. Metrics provide a way to assess an ontology during its engineering and application and have been classified according to what they measure i.e. structure, function, use and semantics. The structural topology [depth and breadth] or inheritance richness, which determines the distribution of information in an ontology has been used to derive ontology evaluation metrics [Dasgupta et al 2007]. Structure and coverage metrics rank ontologies using both the ratio of class to property definitions, and the level of integration [connectedness] between ontologies [Buitelaar et al 2007].

Based on structure, Alani and Brewster [2006] describe the Class Match Measure [CMM], the Density measure [DM], Semantic similarity [SS] and Betweenness [BM] measures for ranking ontologies. The CMM assesses the coverage of an ontology for a given search term. The Density Measure estimates information-content and level of knowledge detail of classes. Structural similarity determines how close the classes that match search terms are in an ontology. Betweenness determines classes that are central to an ontology. The ratio of non *is_a* relations to the total number of relations [relational richness] is another structure based metric for comparing ontologies [Tartir et al 2005].

3.5 The Challenge for Biomedical Ontology Evaluation

Current approaches largely evaluate an ontology based on the technical aspects of design, taxonomy, content and knowledge representation and so are useful for ontology evaluation from the designer's viewpoint. The need therefore remains for studies to determine; i] the properties users require when judging the suitability of an ontology [Alani and Brewster 2006]; and [ii] a holistic evaluation strategy with a greater role and participation of user communities in the evaluation process [Kalfoglou and Hu 2006].

The literature shows that for ontology evaluation metrics, emphasis has been placed on defining structural metrics on the basis of concepts while ignoring relations between concepts and their semantics [Buitelar et al. 2007; Dasgupta et al. 2007; Tatir et al. 2005; Vrandecic and Sure 2007]. This is a major limitation since relations provide valuable information in the search for the right ontologies, at the correct level of granularity [Sabou et al 2006].

For comparing and evaluating biomedical ontology [BO] integration systems from the user's perspective, the existing approaches remain unsuitable. BOs also need to be assessed for their suitability to represent structure it differing levels of granularity. Their evaluation is related to, but can therefore not entirely be conducted solely using existing approaches. The lack of a unifying framework for evaluating biomedical ontologies therefore remains an obstacle for their reuse and adoption by industry [Alani and Brewster 2006; Fernandez et al. 2006].

The approaches and metrics presented in this paper have found use in evaluating the structure of an ontology as represented by its taxonomy. They however remain inadequate for evaluating biomedical ontologies. This is attributed to the need to conduct evaluations on both: 1] the quality and adequacy of the structure and knowledge representation in an ontology; 2] the need to model [represent] dynamic processes, function and granularity presented by biomedical ontology, in the absence of a unifying frame of reference against which such evaluation can be conducted.

4. DERIVING A REFERENCE MODEL FOR BIOMEDICAL ONTOLOGY EVALUATION

Reference or Top domain ontologies have general core classes of a given domain. These core classes interface with both top and domain ontologies. They are general purpose resources designed to generalize to other domains and offer support to a range of different types of research and clinical applications [Stenzhorn et al. 2008]. The reference model presented here is the result of a study to develop a target model as frame of reference for evaluating and selecting an ontology for use to integrate biomedical data, from among alternatives. The model presents core classes and relations that are instantiated with biomedicine as the universe of discourse. It captures and represents the essence of a biomedical ontology and together with its derived metrics are part of a framework against which other ontologies for use in integrating biomedical data may be assessed.

The reference ontology was derived using the following major steps were followed: i] description of requirements from the literature sources and their validation using a descriptive survey; ii] informal specification of the model using the requirements; iii] examining theories to fit and explain these requirements; iv] using requirements and the informal specifications to extend an existing ontology theory.

4.1 Determining Requirements for the Reference Ontology

The literature review guided the description of the scope, structure and properties of a theoretical model for biomedical data integration. A questionnaire based descriptive survey was used to validate the theoretical reference ontology with users (biologists & medical doctors) of the model. The descriptions of the theoretical model guided framing of the data collection questions on evaluating a biomedical data integration model along the themes of scope (users and use cases) and properties of a biomedical data integration model, and its representation of granularity. The descriptive survey tested the level of agreement by respondents to proposed characteristics of the reference model. The questionnaire, pretested on twenty (20) medical doctors and five (5) biologists was used to collect data and clarify requirements for the model. The study population had six hundred thirty (630) randomly selected biomedical workers (580 medical doctors and 50 biologists). Completed questionnaires were returned by four hundred four (404) medical doctors and forty six (46) biologists. The statistical package for social sciences (SPSS) was used to analyze the data and determine the level of respondent's agreement with the theoretical integration model. The resulting requirements for the integration model and its informal specification are presented in Tables 2, 3 and 4.

Table 2: Requirements for a Biomedical Data Integration Model

User category	Biologists		Medical Doctors	
	No. of responses	Agreement Level [%]	No. of responses	*Agreement Level [%]*
Model Genericity	46	94	404	*77*
Model Flexibility	46	94	404	*78*
Adequacy of Detail	46	87	404	*75*
Represent Aggregation	46	88	404	*68*
Supporting Meta Meta Language (theory)	46	72	404	*53*

The results in Table 2 confirm that a biomedical data integration model should be: i) generic in scope to cater for different biomedical data sources; ii) flexible to accept input of new biological and clinical models and formats from different sources; iii) detailed enough for users to easily recognize the important properties that make it suitable for their task; iv) represent biomedical data from sources across levels of aggregation (granularity); v) supported by a theory or language for good knowledge representation for clinical and biological concepts.

4.2. Informal specification of the Reference Ontology from Use Cases

The results in Table 3 provide respondents perspectives on the use cases for a biomedical data integration system from the descriptive survey. A use case corresponds to a requirements model and summarizes the scenarios for a single biomedical integration task or goal. Table 3 presents use cases as functional requirements a biomedical data integration model. These use cases are adopted and used to further scope the model by revealing classes and relations to be represented in the informal specification of the reference ontology structure as presented in Table 4. The requirements specifications and general properties of the reference model were derived from analyzed data from the survey. In the absence of a single unifying methodology for building ontologies, the method outlined combines aspects of several existing methodologies [Fernández López 1999; Gruninger and Fox 1995; Uschold and Gruninger 1996].

Table 3: Use cases [Competence areas] for a Biomedical Integration System

	MOLECULAR BIOLOGIST	***MEDICAL DOCTORS***

USE CASES [COMPETENCE AREA]	*Number of respondents*	*Agreement Level[%]*	*Number of respondents*	*Agreement Level[%]*
Relate a genetic profile to a patient	46	90	404	91
Relate clinical history to a patient	46	97	404	97
Relate patient gene profile to a disorder	46	92	404	94
Relate a person's trait to a genetic profile	46	95	404	91
Relate genetic profile to characteristics	46	92	404	93
Relate role of genes in develop. of proteins tissues and organs	46	96	404	91
Relate tissues to a genetic disorder	46	85	404	85
Relate gene prevalence to population	46	87	404	88
Determine disorder prevalence in population	46	90	404	90

Use cases in table 3 were used to informally specify requirements for the reference ontology presented in Table 4. Deriving the informal specification of the reference ontology was guided by methodologies for ontology construction that emphasize flexibility in formalizing knowledge and use of competency areas [Uschold and Gruninger 1996]. Competence areas [in Table 3] were used to re-scope the reference-ontology by identifying its main motivating scenarios and applications. Motivating scenarios are used to extract the main concepts and relations of the reference-ontology, and the resulting description taken as requirements specification against which an ontology can be assessed [Gomez-Perez 2004].

Analysis of the statements presented by these scenarios enabled biological and clinical concepts, and their corresponding relationships for the reference-ontology to be derived. These concepts and relationships between biological and clinical types derived from use case statements are given as informal specification in table 4. These concepts [objects] and relations are the basis for the derived informal specification of the reference-ontology for biomedical data integration.

Table 4: Informal specification of the Reference-ontology

COMPETENCE SCENARIO	BIOLOGICAL OBJECTS	CLINICAL OBJECTS	OBJECT RELATIONS
Genetic profile of a patient	Genetic profile	Patient	Patient ***has*** genetic profile
Clinical history of a patient		Clinical-history, Patient	Clinical history ***has_participant*** Patient

Patient gene profile to disorder or disease	Genetic profile	Patient, Disease, Disorder	Patient ***has*** gene profile; Gene ***participate_in*** disorder
Persons genetic trait to a genetic profile	Gene trait, Genetic profile	Person	Person ***may have*** trait Genetic profile ***cause of*** trait
Role of genes in develop. of proteins tissues and organs	Gene, Protein dev, Protein, Tissue, Organ		Gene ***participates_in*** Protein-dev. ; Protein ***part of*** tissue Tissue ***par_ of*** organ
Tissues or organs affected by a genetic disorder	Tissues, Organs	Disorder, Disease	Organ ***participates_in*** disorder.
Prevalence of genetic disorder in population	Gene	Population, disorderPrevalence	Population ***may have*** disorder prevalence

Table 4 reveals classes and relations in the informal specification that are used to derive the biomedical reference ontology. Classes like disease and disorder are revealed as processes, while others [e.g. organ] are shown as non process distinct types for structuring knowledge during biomedical data integration.

Intra and *trans_domain* relationships within and between biological and clinical classes are also revealed. Intra domain relationships are identified between biological objects [e.g. Gene *participates_in* Protein development], or clinical objects [e.g. Clinical history *has_participant* Patient] of the same hierarchy. Trans domain relations between different hierarchies are also revealed between clinical and biological objects. Trans domain relations are also seen to model biomedical objects at different levels of aggregation [e.g. Patient *has* gene]. Relations between processes and non-processual types are also revealed [e.g. Organ *may_have* Disorder].

The informal specification in table 6 provides concepts and relations to be represented in the structure of the biomedical Reference ontology. Examining table 6 also revealed that the proposed biomedical reference-ontology represented in the specification models via its relations: 1] structure and processes for clinical and biological data integration; 2] biological and clinical data types across levels of granularity. Biomedical structure [objects and relations], processes and representation of granularity are therefore properties that need to be captured in the design of a biomedical integration reference-ontology. The choice of an ontology theory to reuse and extend is therefore informed by its fit to these requirements. The informal specification [Table 6] is therefore considered in the selection of the ontology theory to reuse and in the design of the reference or target biomedical reference-ontology [TaMO].

4.3. The Role of Basic Formal Ontology in Deriving Model

Basic formal ontology [BFO] with its modular framework has been used to model biomedical reality. It is a bi-ontological theory having the Snap [continuant] and Span [occurrent] sub ontologies. The snap sub ontology

models independent entities and function, while the span sub ontology models processual entities [BFO, 2008; Grenon et al. 2004]. The two complementary sub ontologies provide a framework for modeling biomedical structure, function and processes. BFO's structure supports both *intra* ontological relations [e.g. *is_a, has_ part, contained_in*] between classes in the same ontology and *trans* ontological relations [e.g. *participates_in*] between classes of different ontologies [Grenon et al. 2004]. These relations provide the basis to model BFO's universal classes as the mereological sum of its objects [e.g. ObjectAggregate] or processes [e.g. ProcessAggregate]. These mereologically defined universal classes together with the *intra* and *trans* ontological relations offer a suitable framework for multiple representation of granularity by BFO. The ability to represent structure, function, processes and granularity justify the adoption of BFO as a suitable upper level ontology theory for modeling biomedical reality. It provides a suitable framework for representing the requirements of the biomedical reference-ontology. It was thus adopted in this study as the underlying baseline theory for developing a reference ontology for biomedical data integration. The informal specification (Table 4) with its newly defined biological and clinical classes was therefore used to extend selected universal classes of BFO in order to derive the reference ontology model.

4.4 The Reference Ontology

From the informal specification descriptions, the reference-ontology was implemented using the Web Ontology Language [OWL DL] in protégé. OWL DL is supported by description logics that offer a good formal foundation plus automated reasoning to check the classification hierarchy of the taxonomy and its consistency. Protégé, is a First Order Logic based, OWL compatible stand alone ontology development and editing tool. It supports ontology browsing, documentation, import and export to and from different formats. BFO OWL files were imported into Protégé and extended to generate the biomedical reference-model. The resulting reference-model extends BFO via *its object, objectAggregate, quality, role* and *process* universals. Selection of the appropriate universal to extend was based on their theoretical definitions as provided by BFO [Grenon et al. 2004]. The resulting reference-model is illustrated in figure 1 as an OWL file of Protege' using the OWL Viz plug in tool.

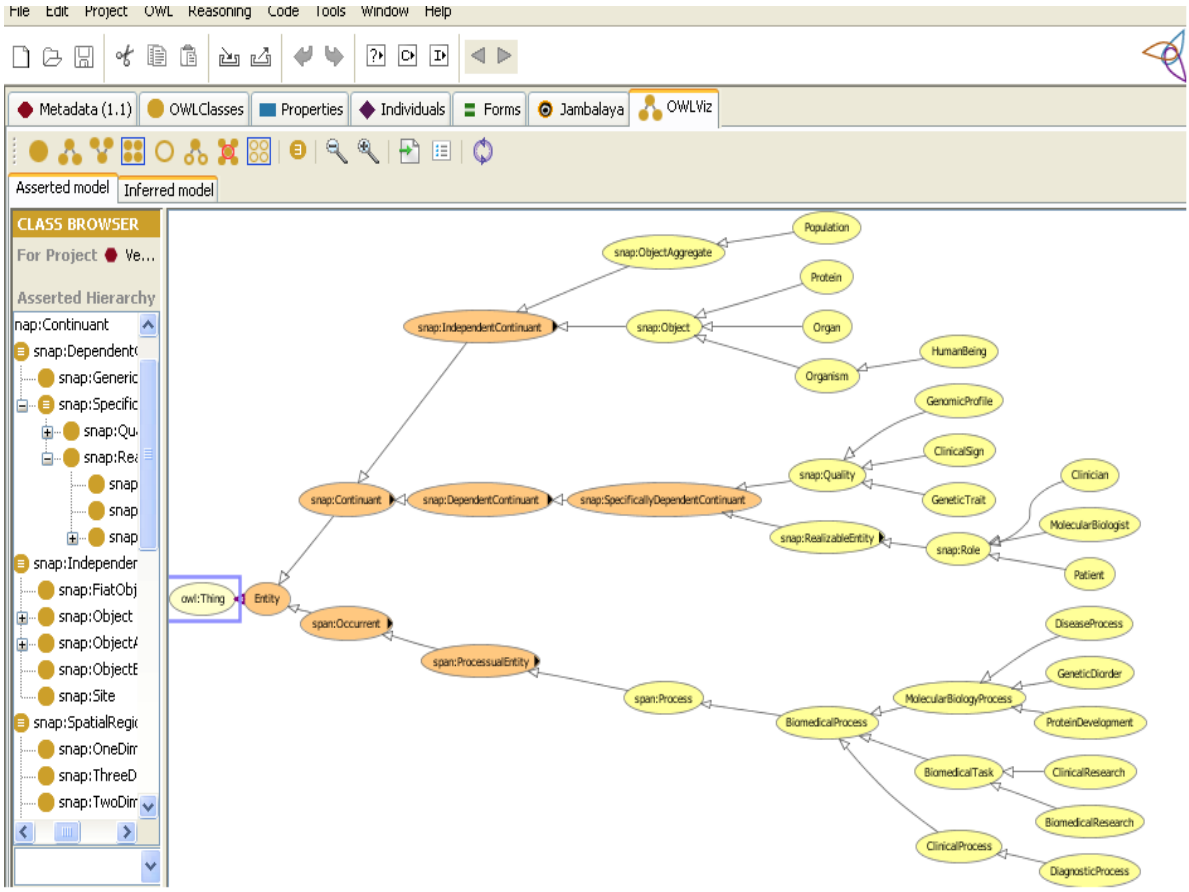

Fig. 1. The Reference Ontology extending a BFO file in Protégé, shown using OWL Viz.

The reference ontology [Figure.1] models biomedical structure across levels of granularity; important properties required for selection of a biomedical data integration model. By modeling biomedical structure and granularity, the reference ontology provides the basis for their use to define metrics useful in evaluating these properties.

4.5. A Metric for Measuring Representation of Granularity [Granular Density]

The metric defined for representation of granularity using the model provides an evaluation measure from properties agreed on by users. The metric is derived from biomedical relations by adopting the principles of mereology. To define metrics for use in selecting a suitable ontology for representing biomedical structure across levels of granularity, relations as defined in BFO and the relational ontology are used [Smith *et al.*, 2005]. The OBO relational ontology [RO] provides consistent and unambiguous formal definitions of the relational expressions used in OBO library ontologies, [ibid].

In the reference ontology [Figure 1], granularity is articulated using descriptions of relations of class aggregations e.g. *part_of* and *contained_in*. The part_of relation is both *intra* and *trans* ontological as it can be

used to model relationships between biological and clinical classes e.g. the relation *human being part_of population*. This is an aggregation relationship in which population is a collection of human beings. Another example is *object contained_in objectAggregate* that articulates granularity based on size. By describing different relationships between objects and packages, the reference ontology supports multiple perspectives of granularity according to size and collectives.

This perspective of granularity as collectives linked by relations is used to derive a metric that assesses the representation of biomedical data across levels of granularity in an ontology. *Intra* and *trans* ontological relations in the reference ontology are used to define the metric. Trans ontological relations like *part_of*, *has_part* and *contained_in* model collectives. Their density in an ontology is therefore an indicator of its ability to model collectives. A metric for measuring the level to which an ontology models granularity in the ontology is therefore expressed as, the ratio of trans ontological relations that model collectives to all trans ontological relations present in the ontology. This ratio or the granular density is derived as follows.

Deriving Granular Density [G_d].

Let R_{co} represent a trans ontological relation modeling collectives per node in an ontology. Suppose the number of nodes which have the $R_{co\ is}$ K,

All R_{co} will be given by $\sum_{i=1}^{k} Rco$

Let R_{to} represent a trans ontological relations per node in an ontology, and let the nodes in an entire ontology be n.

All R_{to} will be given by $\sum_{i=1}^{n} Rto$;

where $<k \leq$ n; and k is a subset of n.

Then the Granular density G_d is given by: $\frac{\sum_{i=1}^{k} Rco}{\sum_{i=1}^{n} Rto}$ [Equation 4.7]

An ideal ontology should have a G_d ratio of 1.0 for a given integration task. A G_D ratio of 0 [zero] denotes a lack of relations to represent granularity. The higher the G_d ratio, the better an ontology is for modeling granularity. This metric provides a basis for selecting the most suitable ontology for integrating biomedical data across levels of granularity that are common in biomedicine.

5. VALIDATION OF THE REFERENCE MODEL APPROACH

The utility of the Reference-model approach was demonstrated by a tool developed as part of a flexible user centered framework for evaluating biomedical ontologies [Maiga and Williams 2008]. The tool was implemented in the visual studio 2005 integrated development environment, in C# and SqlExpress2005 database management system. The tools database consisted of summaries of the human phenotypic ontology [HPO] and the infectious disease ontology [IDO], selected from the open biomedical ontologies [OBO] library [Smith et al 2007].

The tool based on the algorithm in figure 2 allows different users the flexibility to iteratively search through an ontology library using multiple criteria. This is more likely to result into the selection of a suitable ontology for a given task, or re-specification of new requirements for an ontology to fit the task. The prototype tool

developed using this algorithm enables a user to select a biomedical ontology that supports development of a suitable application for their integration using Granular density as one of the metrics applied.

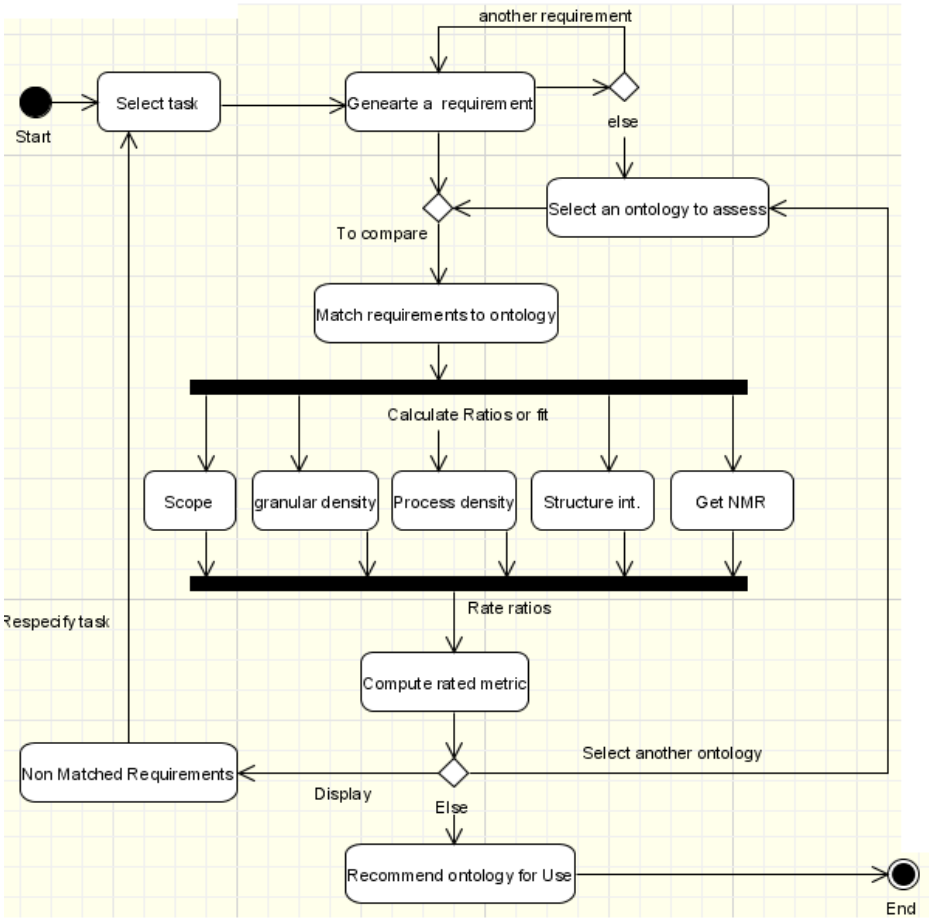

Figure 2: The Assessment Tools Algorithm as a UML Activity Diagram

5.2 Evaluating the infectious disease Ontology [IDO]

Previous attempts to validate ontology evaluations have used tools that either: i) compared the results of assessing an ontology in experiments using the tool to those by other approaches as controls or ii) compared the results of assessing an ontology using the tool to human assessment by expert users, ontology consumers and domain experts [Tartir et al. 2005; Alani and Brewster 2006; Cross and Pal 2006]. The first approach is ideal for mature ontologies that have previously been evaluated by other tools using similar or related metrics, with data available for comparison. For IDO, no such data was available. The tool was used to assess the ability of IDO to match requirements for a selected biomedical data integration task. IDO is a set of interoperable ontologies that provide coverage of the infectious disease domain. They define general entities relevant to biomedical and clinical aspects of infectious diseases. Experiments using the tool compared the ontology for their ability support different use case scenarios of biomedical data integration applications. Use case scenarios differed by the integration task selected, the requirements generated as a set of search terms and by the relative importance

of these requirements or search terms for the users task. The output of using the tool to assess the IDO ontology for the different use case scenarios as illustrated in Figure. 3

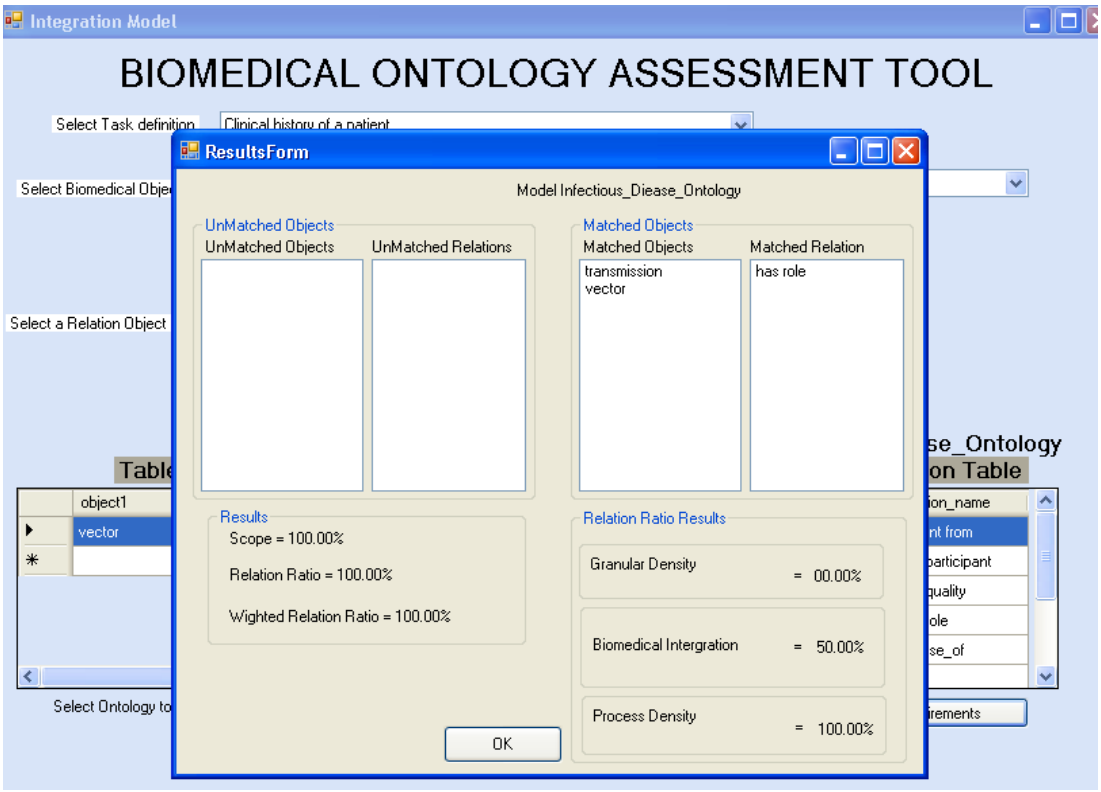

Figure.3. The Tool's Results Interface

The results displayed as scores of scope, process density, granular density and biomedical integration. Scope indicates of how well an ontology's classes represent requirements for an integration task. For the tool, it is expressed as the number of objects [% search terms] in the requirements that are present or found in the ontology model. These scores are basis for a user to select the ontology, re-specify requirements or select another ontology to rate. The result also displays any unmatched requirements [search terms].

5.8. The Pearson Correlation

The results of assessing IDO with the tool [TA] were compared to those by a questionnaire based human assessment [HA] study using a Pearson correlation [r] for significance. A random selection of 32 biomedical workers [18 medical doctors and 14 biologists] was used for this test. The questionnaire had a screen shot of the IDO model, two tables with six use case scenarios for applying the model and instructions on how to fill in the tables. For each scenario, a question was asked about the models [IDO] ability to represent biomedical processes and representation of levels of granularity. Answers to these questions were used to calculate the

granular and process density ratios. The tool results [TA] of assessing IDO and corresponding ones from a questionnaire based human assessment [HA] for the different use case scenarios were compared and the corresponding Pearson correlation coefficients are given in table 6.

Metric scored	The Pearson correlation [r]	Valid metric?
Granular density	0.968	Yes
Process density	0.657	Yes

Table 6: Pearson Correlation [r] of Tool Scores against Human Assessments for IDO

The r values from the tool and corresponding ones from the questionnaire based human assessment show a moderate to strong positive correlation between the two sets [r = 0 means zero correlation; r = 1 means strong positive correlation; r = -1 means strong negative correlation].

The strong positive correlation between TA and HA is an indication of the success of the tool used, and the validity of our approach.

6. CONCLUSIONS

This paper presents a reference ontology as frame of reference for user evaluations of ontologies for biomedical data integration. The reference ontology is neither a top level nor a domain [or application] ontology. It is an interface between the two, making it a top domain ontology. Requirements for the model from a field study were used to derive the core classes of the reference ontology that are used to extend Basic formal ontology [BFO] as a meta theory to support the model. Core classes of the reference ontology extend five BFO classes of Object, Quality, ObjectAggregate, Role and Process. Relations between these core classes are used to derive metrics for assessing structure, process and granularity as dimensions against which biomedical ontology evaluations may be performed. The metrics provide a theoretical basis for evaluating biomedical ontologies.

The strength of this model is underlined by: [i] the theoretical support offered by the basic formal ontology in representing biomedical structure, processes and multiple aspects of granularity; [ii] the flexible and extensible nature of the model since new objects, processes and relations can be added to it, [iii] providing theoretical metrics to be used for biomedical ontology evaluation based on the principles of mereology; [iv] providing the design of an easy to use evaluation tool.

The reference ontology is both flexible and extensible. New objects can be added to the model. New relations can also be described to support emergent classes a definite advantage as it allows for description of objects, new processes and definition of multiple perspectives of granularity within the same model. The reference model is therefore adaptable to other domains that integrate data across levels of granularity and processes.

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References

ALANI, H. & BREWSTER, C. 2006. Metrics for Ranking Ontologies. In *Proceedings of the 4th International Conference on Evaluation of Ontologies for the Web.* EON Workshop Edinburgh International Conference Center. Edinburgh UK. May 22nd 2006.

BFO. 2008. Basic formal Ontology. *Available http://www.ifomis.org/bfo/*. Accessed December 2nd 2008.

BOARDMAN, R. 2004. Improving Tool Support for Personal Information Management. PhD Thesis.

BRANK, J., GROBENLINK, M. AND MLADENIC, D. 2005. A Survey of Ontology Evaluation Techniques. *At the conference on Data Mining and Data Warehouses* SiKDD.

BUITELAAR, P.,EIGNER, T. 2007. Evaluating Ontology Search. *In proceedings of the 6th International Semantic Web Conference and Second Asian Semantic Web conference*, 11-15th November, 2007, BEXCO Busan, Korea.

CROSS, V. AND PAL, A. ONTOCAT: 2006. An Ontology Consumer Analysis Tool and Its Use on Product Services Categorization Standards. Available: http://protege.stanford.edu/conference/2006/submissions/abstracts/

DASGUPTA, S., DINAKARPANDIAN, D., LEE, Y. 2007. A Panoramic Approach to Integrated Evaluation of Ontologies in the Semantic Web. *In proceedings of the 6th international semantic web Conference and second Asian Semantic Web conference*

D'AQUIN, M. SABOU, M. DZBOR, C. BALDASSARRE, L. GRIDINOC, S. ANGELETOU, & E. MOTTA. 2007. WATSON: A Gateway for the next Generation Semantic Web Applications. *ESWC 2007*

EON. 2006. Evaluation of Ontologies for the Web, *4th International EON Workshop* located at the 15th International World Wide Web Conference, Edinburgh International Conference Center, Edinburgh, United Kingdom, *Available: http://km.aifb.uni-karlsruhe.de/ws/ eon2006*. Accessed May 25th, 2006.

FAYAD, E.M., SCHMIDT, D.C., AND JOHNSON, R. 1999. Chapter 1 in Building Application Frameworks: Object-Oriented Foundations of Framework Design. New York: John Wiley & Sons, September 1999

FERNANDEZ, M., CANTADOR, I., & P CASTELLS. 2006. CORE: A Tool for Collaborative Ontology Reuse and Evaluation.

FOWLER, M. & SCOTT, K. 1997. UML Distilled. Applying the Standard Object Modeling Language. *Addison-Wesley*, Reading

GANGEMI, A., CATENACCI, C., CIARAMITA, M. & LEHMANN, J. 2005. A theoretical framework for ontology evaluation and validation. *In Proceedings of SWAP 2005* .

GOMEZ-PEREZ, A. 1994. Some ideas and Examples to Evaluate Ontologies. Technical Report KSL-94-65. Knowledge System Laboratory. Stanford University. Also in Proceedings of the 11 the

Conference on Artificial Intelligence for Applications, CAIA94.
GUARINO, N. & WELTY, C. 2002. Evaluating Ontological Decisions with OntoClean. *Communications of the ACM*. 45, No. 2.
GÓMEZ-PÉREZ, A. 2004. Ontology Evaluation. *Handbook on Ontologies.* 251-274.
GRENON, P., SMITH, B., AND GOLGBERG, L. 2004. Biodynamic Ontology: Applying BFO in the Biomedical Domain. *From D. M. Pisanelli ed., Ontologies in Medicine, Amsterdam: IOS Press,* 20-38
GRUNINGER, M. AND FOX, M.S. 1995. Methodology for the Design and Evaluation of Ontologies. *In: Proceedings of the Workshop on Basic Ontological Issues in Knowledge Sharing*, IJCAI-95, Montreal.
HARTMANN, J., SPYNS, P., GIBOIN, A., MAYNARD, D., CUEL, R., SUÁREZ-FIGUEROA, M. C. SURE, Y. 2005. Methods for ontology evaluation. EU-IST Network of Excellence NoE IST-2004-507482 KWEB.
KALFOGLOU, Y. & SCHORLMER, M. 2003. Ontology Mapping: The State Of The Art. *The Knowledge Engineering Review*, 181: 1–31.
KALFOGLOU, Y. & SCHORLMER, M. 2006. Issues with evaluating and using publicly available ontologies. In *Proceedings 4th International EON Workshop, Evaluating Ontologies for the Web*, Edinburgh, Scotland.
KEET, C,M. 2006. A Taxonomy of types of granularity. *IEEE International Conference on Granular Computing GrC.*
KISHORE, R., SHARMAN, R., AND. RAMESH, R. 2004. Computational Ontologies and Information Systems: I. Foundations. Communications *of the Association for Information Systems* , Volume14, pp.158-183.
KOHLER, J., PHILIPI, S. & LANGE, M. 2003. SEMEDA: Ontology based semantic integration of biological databases. *Bioinformatics*, 19, 2420 -2427.
KUMAR, A., LINAYIP, Y., SMITH, B. & GRENON, P. 2006. Bridging the gap between medical and bioinformatics: An ontological case study in colon carcinoma. *Computers in Biology and Medicine* 36, 694–711
LAMBRIX, P. & TAN, H. 2006. Sambo. A system for aligning and merging biomedical ontologies *Web Semantics: Science, Services and Agents on the World Wide Web*, 4 196 - 206
MAIGA, G. & WILLIAMS, D. 2008. A Flexible Approach for User Evaluation of Biomedical Ontologies. International Journal of Computing and ICT Research. ISSN 1996-1065. Volume 2 2 Dec. 2008, 62-74; Available: http://www.ijcir.org/volume2-number2/index.php
NOY F. &. MUSEN, M.A. 2002. Evaluating Ontology-Mapping Tools: Requirements and Experience. *Available: http: //seer.nj.nec.com.* Accessed 6 may 2006.
PINTO, H. S., & MARTINS, J. P. 2000. Reusing Ontologies. In *Proceedings of AAAI 2000 Spring Symposium Series, Workshop on Bringing Knowledge to Business Processes,* AAAI Press.
REY-PEREZ, D., MAOJO, V., GARCIA-RESAL, M., ALONSO-CALVO, R., BILLHARDT, H., MARTIN-SÁNCHEZ, F., & SOUSA, A. 2006. ONTOFUSION: Ontology-based integration of genomic and clinical databases. *Computers in Biology and Medicine*, 36, 712-730.
ROSSE, C., KUMAR, A. JOSE LV MEJINO JR, DANIEL L COOK, LANDON T DETWILERN AND B. SMITH, 2005."A Strategy for Improving and Integrating Biomedical Ontologies", *Proceedings of AMIA Symposium 2005, Washington DC, 639–643.*
SMITH, B., CEUSTERS, W., KLAGGES, B., KÖHLER, J. KUMAR, A.,LOMAX, J., MUNGALL, C., NEUHAUS, F., RECTOR, AL., ROSSE, C., 2005. Relations in Biomedical Ontologies. *Genome Biology.*
SIOUTOS, N., CORONADO, S., HABER, M., HARTEL, F., SHAIU, W., & WRIGHT, W. C. 2006. NCI thesaurus: A semantic model integrating cancer-related clinical and molecular information. *Journal of Biomedical Informatics.*

TARTIR,S., AND ARPINAR B. 2005. OntoQA: Metric-Based Ontology Quality Analysis. in IEEE Workshop on Knowledge Acquisition from Distributed, Autonomous, Semantically Heterogeneous Data and Knowledge Sources.

USHOLD, M. & M. GRUNINGER. 1996. Ontologies: Principles, methods and applications, in *The Knowledge Engineering Review*, 112, 93–55.

VRANDECIC., D, AND SURE, Y. 2007. How to Design Better Ontology Metrics.

YUGYUNG, L., SUPEKAR, K. & GELLER, J. 2006 Ontology Integration: Experience with medical Terminologies. *Computers in Biology and Medicine*, 36, 893 - 919.

ZHANG, H., CHENG, G., AND QU YUZHONG.2007. Ontology summarization based on rdf sentence graph. *In lproceedings of the 16th international conference on World Wide Web.* Banff, Alberta, Canada.

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