



Introduction to ontologies in the life sciences

Dagmar Waltemath dagmar.waltemath@uni-rostock.de

In the last fifty years the development of **new technologies**, the increasing interconnectedness amongst people in all parts of the globe and the continuous increase in the size of scientific, economic and consumer groups, has lead to a veritable explosion in the amount of data that is produced, used and in need of management world-wide. This is especially true in areas such as the biological sciences, medical research and medical practice. In these disciplines thousands of scientists, doctors and clinicians are contributing daily to a massive body of biomedical knowledge and information. Now, like never before in history, the amount of information that is available and being added to daily by the results of new scientific experiments, research and clinical trials constitutes a veritable ocean of extraordinary depth and breadth.

(Quotation: Ontology for the Twenty First Century: An Introduction with Recommendations by Andrew D. Spear)







Background

1999-2006	Diploma Thesis on "A Schema matching architecture for the bioinformatics domain" (DiplInf., University of Rostock, University of Linköping)
2009-2011	Doctorate in Database and Information Systems on "Annotation-based storage and retrieval of models and simulation descriptions in computational biology" (DrIng., University of Rostock)
2011	Post-doctoral training, Computational Neuroscience, (Norwegian University of Life Science, Ås/Norway)
Since 2012	Junior Research Group Leader "Model and Simulation Management for Systems Biology" (University of Rostock)



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Outline

- What is an ontology?
- Why are ontologies so popular in biomedical research?
- Example ontologies in the life sciences & neuroscience
- Guidelines for Good Ontology Design (L. Jansen, J. Röhl)
- OWL
- Reasoning, mapping, alignment ...
- Methods & Tools for ontology development: Protégé
- Practical: Modeling with Protégé (L. Schwabe)











Managing the sea of information

The problem then, in a nutshell, is to chart the ever-growing sea of information in such a way that its various **parts**, portions and depths can be **efficiently** accessed, used, **navigated** and **reasoned** about by human individuals.

(Quotation: Ontology for the Twenty First Century: An Introduction with Recommendations by Andrew D. Spear)



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The solution

Use computers !

- Computers reliably store huge amount of information
- they are able to efficiently, reliably and automatically retrieve and reason about the information that they store
- information stored in a computerized format can be made instantly accessible to individuals in all parts of the globe via the internet.







Obstacle to that solution

Use computers !

- Scientists speak different languages, use different terminologies, and results are presented in different formats
- Computers... speak different languages, use different terminologies, and results are stored in different formats
- Data is not interoperable

"Data silo problem" (Barry Smith)









Obstacle to that solution

Use computers !

"Just making data digital doesn't make it ready for integration" (Larson, Martone, 2009)

- How to reason with data when you find it?
- How to understand the significance of data you collected earlier?
- How to integrate with other people's data?









So?

Use computers and ontologies!

"Define common ontologies!"



Image: http://tomgruber.org/bio/bio.htm

What is an "Ontology"?

(Quotation: The role of common ontology in achieving sharable, reusable knowledge bases by T. Gruber, 1991)

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Introduction

So?

Use computers and ontologies!

"Define common ontologies!"

vocabularies of representational **terms** – classes, relations, functions, object constants – with agreed-upon **definitions**, in the form of human readable text and machine-enforceable, declarative **constraints** on their **well-formed** use.



Image: http://tomgruber.org/bio/bio.htm

Definitions may include restrictions on **domains** and **ranges**, placement in subsumption **hierarchies**, class-wide facts **inherited** to instances, and other **axioms**.

(Quotation: The role of common ontology in achieving sharable, reusable knowledge bases by T. Gruber, 1991)









Origins and history

First fields of application

Philosophy: Science of Being (Aristotle, Metaphysics, IV, 1)

- What characterizes being?
- Eventually, what is being?

Artificial intelligence: existing concepts and relationships for agents

- · Concentrates on what exists
- Definitions associate the names of entities in the universe of discourse (e.g., classes, relations, functions, or other objects) with human-readable text describing what the names are meant to denote, and formal axioms that constrain the interpretation and well-formed use of these terms









Origins and history

Information Science

Ontologies are information artefacts that attempt to give precise formulations of the properties and relations of certain types of entities (Hofweber, 2012).



ONTOLOGIES

Better computational descriptions of science

Simon White believes that information can be better shared if everyone makes use of ontologies

Scientific Computing World: July/August 2005







Origins and history

Computer Science

An ontology is an engineering artifact.

- Constituted by a specific vocabulary used to describe a certain reality, plus a set of explicit assumptions regarding the intended meaning of the vocabulary
- Thus, an ontology describes a formal specification of a certain domain:
 - Shared understanding of a domain of interest
 - Formal and machine manipulable model of a domain of interest
- Definition (Gruber, 1992): "An ontology is a specification of a conceptualization.
 - Conceptualization: couching of knowledge about the world in terms of entities
 - Specification: concrete representation of this conceptualization









(Source: A training course in eight lectures by Barry Smith; Figure: bioportal.bioontology.org)







Biomedical ontology

- Biomedical ontology is concerned with the principled definition of biological classes and the relations among them.
- Often associated to the idea of open data (Barry Smith)
- A prerequesite to data reuse and data linking

• Note: biomedical ontologies in practise are more than lists of terms (taxonomies), but do not necessarily meet the requirements of formal organization ("ontology gradient")





What is an ontology?

Defining "ontology in bio-medical research"

Standardisation

- Standards provide
 - Common structure and terminology
 - Reducing data redundancy
- Standards allow
 - Use of common tools and techniques
 - Common training
 - Single validation

the computational modeling in biology network

'Ontology' = good standards in terminology (Barry Smith, 2008)









Terminology

Structure of controlled vocabularies



Ontology – Ambiguity, Synonym, Hierarchy, CUSTOM Associations

(Source: Building controlled vocabularies for metadata harmonization by Zaharee, 2013)









(Source: A training course in eight lectures by Barry Smith, following Leo Obrst)







Controlled vocabulary

- prescribed list of terms or headings each one having an assigned meaning (Currier et al., 2005);
- a list of terms (e.g. words, phrases) that is used to tag (label) information in a consistent way.

afferent neuron

A neuron which conveys sensory information centrally from the periphery



A neuron which sends impulses peripherally to activate muscles or secretory cells.

(Terms taken from the CL: purl.bioontology.org/ontology/CL)









Taxonomy

• Hierarchical classification of defined groups of things on the basis of shared characteristics











Ontology adds Relations

- Terms in an ontology are hierarchically structured, with the most general term on top and the most specific term at the bottom
- Terms are put into qualified relation with each other
- Example: Neuron definitions in the Cell Type ontology <u>http://purl.bioontology.org/ontology/CL</u>

















Requirements

...terminology, definitions, etc. that are entered into biomedical information databases should be **interoperable** between databases, internally coherent and **well-defined**, and **accurate** to the facts of reality as reflected in the current (and developing) state of **knowledge** possessed in the biomedical sciences

(Quotation: Ontology for the Twenty First Century: An Introduction with Recommendations by Andrew D. Spear)









Good ontologies

Formal

 The meaning of terms in an ontology is unambiguously defined to avoid misunderstanding and stated using mathematical axioms and definitions that enable automated reasoning.

Explicit

 make domain assumptions explicit for reasoning and support human understanding of a domain.

Adequate

 to the domain to be represented and thus have to reflect current scientific knowledge available about the domain to be modeled.

(Definition: GoodOD, http://www.iph.uni-rostock.de/GoodOD-Guideline.1299.0.html)







afferent neuron

Defining "ontology in bio-medical research"

Ontology information is interpretable

- By humans
- By computers Reasoning



(Visualization: Bioportal http://bioportal.bioontology.org/ontologies/46604?p=terms&conceptid=CL%3A0000527&jump_to_nav=true#visualization)









Ontologies as starting points



(Figure adapted from A Practical Introduction to Ontologies & OWL by Alan Rector http://www.co-de.org/resources/tutorials/intro/slides/Introduction.ppt)







Ontologies in bio-medical research







Reasons to use ontologies in biology

- Biology and medicine are two disciplines that rely on previously obtained knowledge
- Biology is a data rich discipline and this data needs to be made comparable, i.e. it must be integrated
- Biology has always dealt with categorization and structuring of systems, e.g. tree of life, where living organisms are classified into Kingdom, Phylum, and Class





Reasons to use ontologies in biology

- Community reference system (comparison of results to other project results worldwide)
- Common access to information
- Explicit relationships and underlying logic allow for automated reasoning to related entities
- Explicit bridging relationships between different ontologies for exploring underlying mechanisms







Applications

Use Cases: Representation of encyclopedic knowledge

- structure and make explicit encyclopedic biomedical knowledge in a form that is accessible to both researchers and machines
- "reference ontologies", e.g. FMA specifies canonical knowledge for a domain, using a comprehensive set of entities and a large set of relationships









Applications

Use Cases: Data Annotation

Annotation: A comment attached to a particular section of an object

- Annotation with ontologies is typically performed after (high throughput) data is acquired, often by dedicated annotators or curators
- Annotators: Process textual metadata to automatically tag text with as many ontology terms as possible, ie. combination of text mining and ontology
- E.g.: NCBO Annotator <u>http://bioportal.bioontology.org/annotator</u>

Use of Gene Ontology Annotation to 📧 understand the peroxisome proteome in humans

Prudence Mutowo-Meullenet[®], Rachael P. Huntley, Emily C. Dimmer, Yasmin Alam-Faruque, Tony Sawford, Maria Jesus Martin, Claire O'Donovan and Rolf Apweiler

(Source: http://www.slideshare.net/drnigam/how-bio-ontologies-enable-open-science-presentation; Larson, Martone, 2009)







Applications

Use Cases: Data Exploration

DOPAMINE BIOSYNTHETIC PATHWAY (PW:0000802)







Applications

Use Cases: Data Query

- E.g., search for "tumors in mouse brain"
- by allowing grouping of annotations

brain	20
hindbrain	15
rhombomere	10

Query brain without ontology20Query brain with ontology45

(Source: A training course in eight lectures by Barry Smith, 2008)







Applications

Use Cases: Data Search of heterogeneous data

- e.g., search for "the process of creating glucose": 'glucose synthesis', 'glucose biosynthesis', 'glucose formation', 'glucose anabolism', 'gluconeogenesis'
- An ontology can provide one class/identifier with several alternative names for the same concept (synonymy), abbreviations and acronyms gluconeogenesis

	Term information 🕴 Term neighborhood 🖡 External references 🖡 1220 gene product associations 🕈		
Term Information			
Accession	GO:0006094		
Ontology	Biological Process		
Synonyms	exact: glucose biosynthesis exact: glucose biosynthetic process		
Definition	The formation of glucose from noncarbohydrate precursors, such as pyruvate, amino acids and glycerol. Source: MetaCyc:GLUCONEO-PWY		
Comment	None		
Subset	Prokaryotic GO subset		
Community	Add usage comments for this term on the GONUTS wiki.		

(Source: Biomedical ontologies: a functional perspective by .Rubin et al., 2008; Figure: Gene Ontology)







Applications

Use Cases: Data exchange among applications

Ontologies can specify how data is to be exchanged with resources

- Ontologies as explicit specification of terms used to express the biomedical information
- Relationships among data types in databases
- E.g., MGED Ontology for standardized description of microarray experiments (MO)



(Source: The MGED Ontology: a resource for semantics-based description of microarray experiments by Whetzel et al., 2003)





Applications

Use Cases: Reasoning with data

- Use ontologies to infer knowledge they contain
- Integrate current knowledge about a system from different data repositories
- Allow researchers to pose and test hypotheses (for consistence with the knowledge base)







Applications

Use Cases: Model Management

• Annotation based search, retrieval and comparison

4 Curated Models returned.

Name	BioModels ID	Rank
Golomb2006_SomaticBurs	BIOMD000000118	1. (<u>0.0015</u>)
Golomb2006_SomaticBursting_n	BIOMD000000119	2. (<u>0.0015</u>)
Locke2008_Circadian_Cl	BIOMD000000185	3. (<u>0.0011</u>)
Keizer1996_Ryanodine_receptor_	BIOMD000000060	4. (<u>9.1442</u>)

(Source: demo search in BioModels Database,

http://www.ebi.ac.uk/biomodels-main/



(Source: **Retrieval, alignment, and clustering of computational models based on semantic annotations** by Schulz et al., 2011)







Applications

Use Cases: Model Management

• Annotation-based difference detection and visualisation



(Source: Difference detection in Budhat, http://budhat.sems.uni-rostock.de/)



(Source: Arcadia. http://arcadiapathways.sourceforge.net/)

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Applications

Use Cases: Semantic similarity in text mining









Applications









Applications











Created on Many Ever (http://many-ever









(Source: LinkedOpen Data Cloud 2011, by Richard Cyganiak and Anja Jentzsch. http://lod-cloud.net/)





Applications

Bio2RDF – Integrating resources

What is Linked Open Data (LOD) and why is it good for you?

Ask Europeana: http://vimeo.com/36752317

Or Tim Berners-Lee directly:

http://www.ted.com/talks/tim_berners_lee_the_year_open_data_went_worldwide.html







Applications

How do you use ontologies in your daily work?





Components of an ontology

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"An ontology is a specification of a conceptualization." (Gruber, 1992)

simulation experiment management system

Class

- set of entities or 'things' within a domain; e.g.: <u>eukaryotic cells</u> (are kinds of cells that have a nucleus)
- Classes represent the canonical description of an entity

Relation

describes the interactions between classes or a classes properties; e.g. Eukaryotic Cell isSubclass of Cell

(Source: Ontology-based knowledge representation for bioinformatics by Stevens et al., 2000)













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Components of an ontology

More information in the afternoon talk

"An ontology is a specification of a conceptualization." (Gruber, 1992)

Property

captures further knowledge about the relationships between classes; e.g. <u>Eucaryotic_Cell_hasPart_Nucleus</u>

Axiom

constrains values for classes; e.g. *nucleic acids <u>shorter than</u> 20 residues are oligonucleotides*

Instance

- 'things' represented by a concept; e.g.: <u>human cytochrome C</u> is an instance of the concept Protein
- Instances represent the individual example of a class

(Source: Ontology-based knowledge representation for bioinformatics by Stevens et al., 2000)









More information in the afternoon talk



Adapted from: A training course in eight lectures by Barry Smith (2008)









Operations on ontologies

Merge

- Creation of a new ontology by linking existing ones
- Requirement: New ontology must contain all knowledge from the original ones

Mapping

- Expressing how the concepts in one ontology can be translated into another one
- Note: one-to-one mappings are typically not possible

Alignment

mapping ontologies in both directions (with modification of original ontologies)









Operations on ontologies

Refinement

- mapping from ontology A to ontology B so that every concept of A has equivalent in B Unification
- Two-way refinement

Integration

 looking for the same parts of two different ontologies A and B while developing new ontology C that allows to translate between ontologies A and B

Inheritance

 ontology A inherits everything from ontology B (classes, relations, axioms); no inconsistency introduced by additional knowledge contained in ontology (Modularity) (Source: http://www.obitko.com/tutorials/ontologies-semantic-web/operations-on-ontologies.html)







Components of an ontology

"An ontology is a specification of a conceptualization." (Gruber, 1992)

The components of an ontology need to be described, stored and exchanged in a formal manner.







Data exchange standards for ontologies

Languages for explicit specification

- In order to manage and perform computations on the different relationships between entities, ontologies are usually encoded into a language that allows a machine to manage and utilize the information.
- Notion of an ontology is independent of the language in which it is encoded







Technicalities

More information in

the afternoon talk

and tomorrow

Data exchange standards for ontologies

Languages for explicit specification

- Graphical
 - Semantic networks
 - topic maps
 - UML
- Logic-based
 - Description logics
 - Rules
 - First order logic
 - Conceptual graphs

Every gardener likes the sun. (Ax) gardener(x) => likes(x,Sun) You can fool some of the people all of the ti (Ex)(At) (person(x) \uparrow time(t)) \Rightarrow can-fool You can fool all of the people some of the ti (Ax)(Et) (person(x) \uparrow time(t) => can-fool() All purple mushrooms are poisonous. $(Ax) (mushroom(x) ^ purple(x)) \Rightarrow poison$ No purple mushroom is poisonous. \sim (Ex) purple(x) ^ mushroom(x) ^ poisono $(Ax) (mushroom(x) \land purple(x)) => \sim poisonous(x)$ There are exactly two purple mushrooms. $(Ex)(Ey) mushroom(x) ^ purple(x) ^ mushroom(y) ^ purple(y) ^ ~(x=y)$ 1Z) Class: Nuclear/VembraneReceptorGeneProduct EquivalentTo: GeneProduct that has_molecular_function some ReceptorActivity

(Sources: http://www.cs.man.ac.uk/%7Ehorrocks/Teaching/cs646/Slides/ontologies.ppt; Exploring Gene Ontology Annotations with OWL by Jupp et al., 2011)

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Data exchange standards for ontologies

Web Ontology Language (OWL)

- W3C standard with a large and growing ecosystem of developers
- Description Logics
- Using OWL in Protégé you can:
 - Query your ontology
 - E.g., for sophisticated queries on your website
 - Quickly find mistakes
 - Automate classification
- "Manchester syntax" for more intuitive ontology modeling
- Note: Round tripping from OBO to OWL allows to develop in OBO while taking advantage of OWL and Protégé for reasoning

(Sources: http://www.cs.man.ac.uk/%7Ehorrocks/Teaching/cs646/Slides/ontologies.ppt; Exploring Gene Ontology Annotations with OWL by Jupp et al., 2011)

More information in tomorrow's talk











Data exchange standards for ontologies

More information in tomorrow's talk

Open Biomedical Ontologies (OBO) format

- controlled vocabularies for shared use across different biological and medical domains
- subset of the concepts in the OWL description logic language, with several extensions for meta-data modeling
- text file format for OBO ontologies
- Goals:
 - Human readability
 - Ease of parsing
 - Extensibility
 - Minimal redundancy





Summary Part 1

"An ontology may take a variety of forms, but necessarily it will include a vocabulary of terms, and some specification of their meaning. This includes definitions and an indication of how concepts are inter-related which collectively impose a structure on the domain and constrain the possible interpretations of terms."

(Quotation: The enterprise ontology by Uschold et al., 1998)







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