Basic Formal Ontology (BFO) And OBO Foundry Ontologies

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Outline

- Introduction to Ontology
- Ontology Application to Biomedical and Biological Fields
- Basic Formal Ontology (BFO)
- OBO Foundry Ontologies

INTRODUCTION TO ONTOLOGY

What is Ontology?

- A set of concepts within a domain and the relationships between those concepts
  - Controlled vocabulary
  - Relations (logical constraints among terms)
  - Machine interpretable and human understandable

- https://en.wikipedia.org/wiki/Ontology

Differences from other kind collections of terms

- Glossary (词汇表)
  - Alphabetical list of terms in a specific domain with definitions
  - No relations between the terms
- Terminology (术语)
  - A structured collection of concepts in a specific domain
  - Only has is-a relation
- Taxonomy (分类)
  - A branch of science of that deal with concept classification (e.g NCBITaxon)
  - Tree structure (parent-child relationship)
  - Similar to ontology, but on the technical side, ontologies imply a broader scope of information
- Thesaurus (词库)
  - A particular type of structured terms, where terms are grouped according to their similarity

The last three structured collection of concepts are similar to ontology, but ontologies contain more sophisticated relations. In addition, ontology contains 'universal' and 'particular' (class and instance) which are not applicable in the other 3 kinds of concept collections

Ontology Types Base on Scope

- Upper (top-level) ontology
  - Describing general knowledge that are the same across all knowledge domains
- Domain ontology
  - Describing a specific domain, such as organism, tissue, cell, cell line, etc.
  - Serve general purpose

  Both upper and domain ontology are reference ontologies
- Application ontology
  - describe knowledge for a particular application, can cross multiple domains

Further Readings

Tutorial and training materials:

http://ontology.buffalo.edu/smith/

ONTOLOGY APPLICATIONS IN BIOMEDICAL AND BIOLOGICAL FIELDS

Ontology Applications

- Data annotation
- Text mining (based on annotation)
- Build metadata standards (semantic framework)
- Linked data (semantic framework)
- Automation of science (reasoning, inference)

Data Annotation
Gene Ontology (GO)

- The Gene ontology has been developed to provide terms to consistently describe the gene and gene product attributes across species and databases
- Standardized annotation facilitate data integration cross various databases and enable the ability to query and retrieve genes or proteins based on their shared biology

Gene Ontology (GO)

COMMENTARY

Nature Genetics **25**, 25 - 29 (2000)
doi:10.1038/75556

Gene Ontology: tool for the unification of

Michael Ashburner[1, 5], Catherine A. Ball[3, 5], Judith A. Blake[4,
Heather Butler[1, 5], J. Michael Cherry[3, 5], Allan P. Davis[4, 5], Ka
Dwight[3, 5], Janan T. Eppig[4, 5], Midori A. Harris[3, 5], David P. Hi
Andrew Kasarskis[3, 5], Suzanna Lewis[2, 5], John C. Matese[3, 5],
Ringwald[4, 5], Gerald M. Rubin[2, 5] & Gavin Sherlock[3, 5]

1 FlyBase (http://www.flybase.bio.indiana.edu).

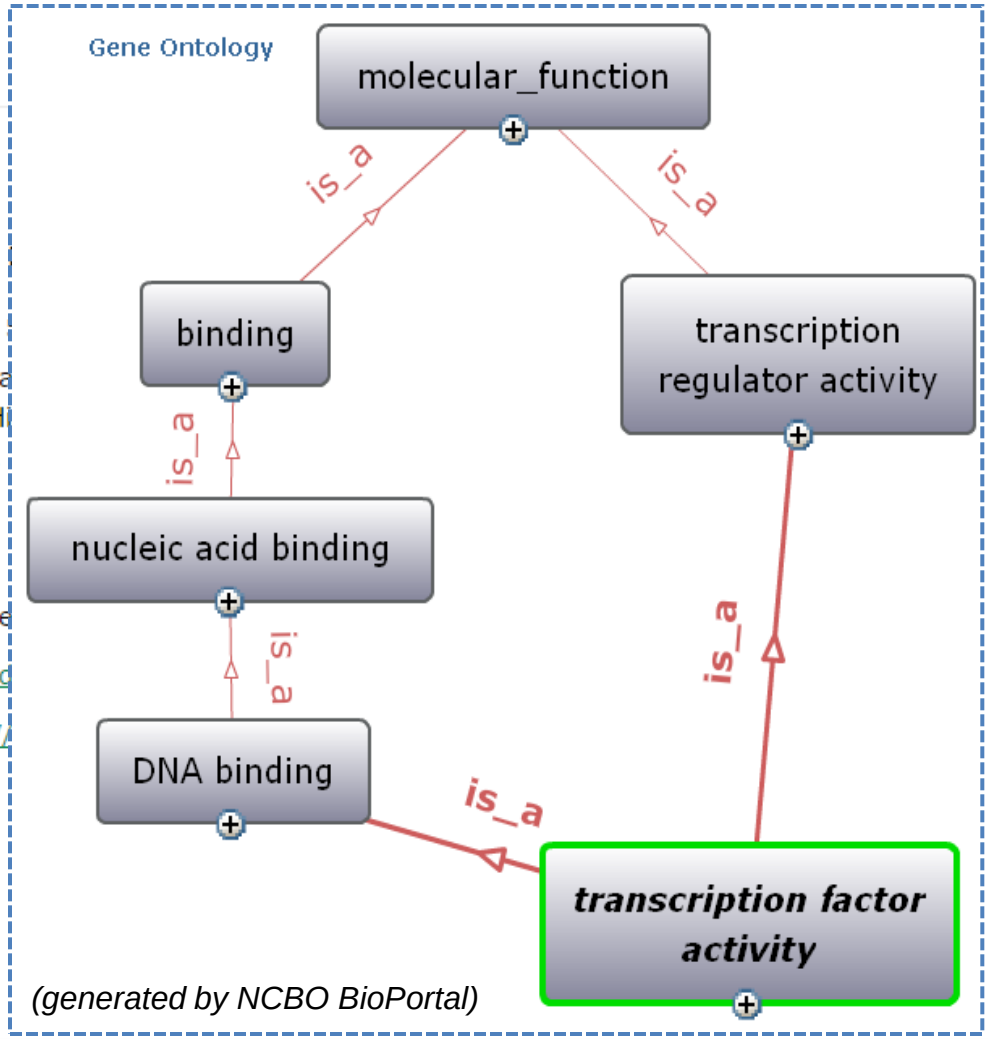
2 Berkeley Drosophila Genome Project (http://fruitfly.bdgp.berkele

3 Saccharomyces Genome Database (http://genome-www.stanforc

4 Mouse Genome Database and Gene Expression Database (http:/

5 The Gene Ontology Consortium

Citation over 16,000



(generated by NCBO BioPortal)

Text Mining

- Gene Ontology term enrichment analysis
  - interpreting functional characteristics of sets of genes based on Gene Ontology annotation

Identification of shared biological processes using GO terms

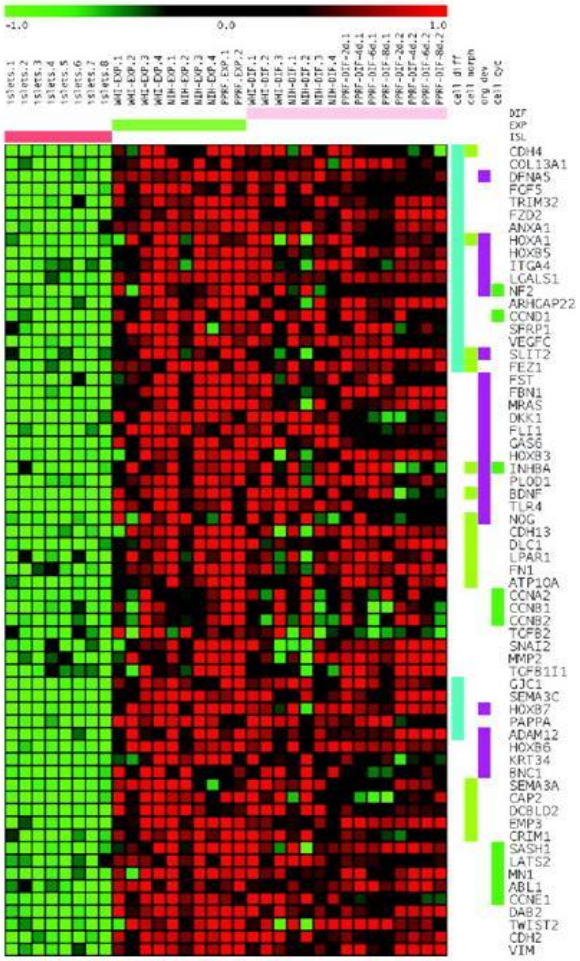


Table 3. *GO terms enriched for the list of active genes in expanded islets compared with functional islets*

Process	*P* Value
Anatomical structure morphogenesis	1.32E-12
Organ development	2.20E-12
Anatomical structure development	1.50E-10
⋮	⋮
Actin cytoskeleton organization	1.25E-06

P values were calculated by hypergeometric tests and indicate the probability of finding the term enriched by chance. GO, Gene Ontology.

(Meta-analysis of gene expression in human pancreatic islets after in vitro expansion. Kutlu B, *et al*. *Physiol Genomics. 2009 Sep 9; 39(1):72-81*)

Build Metadata Standards

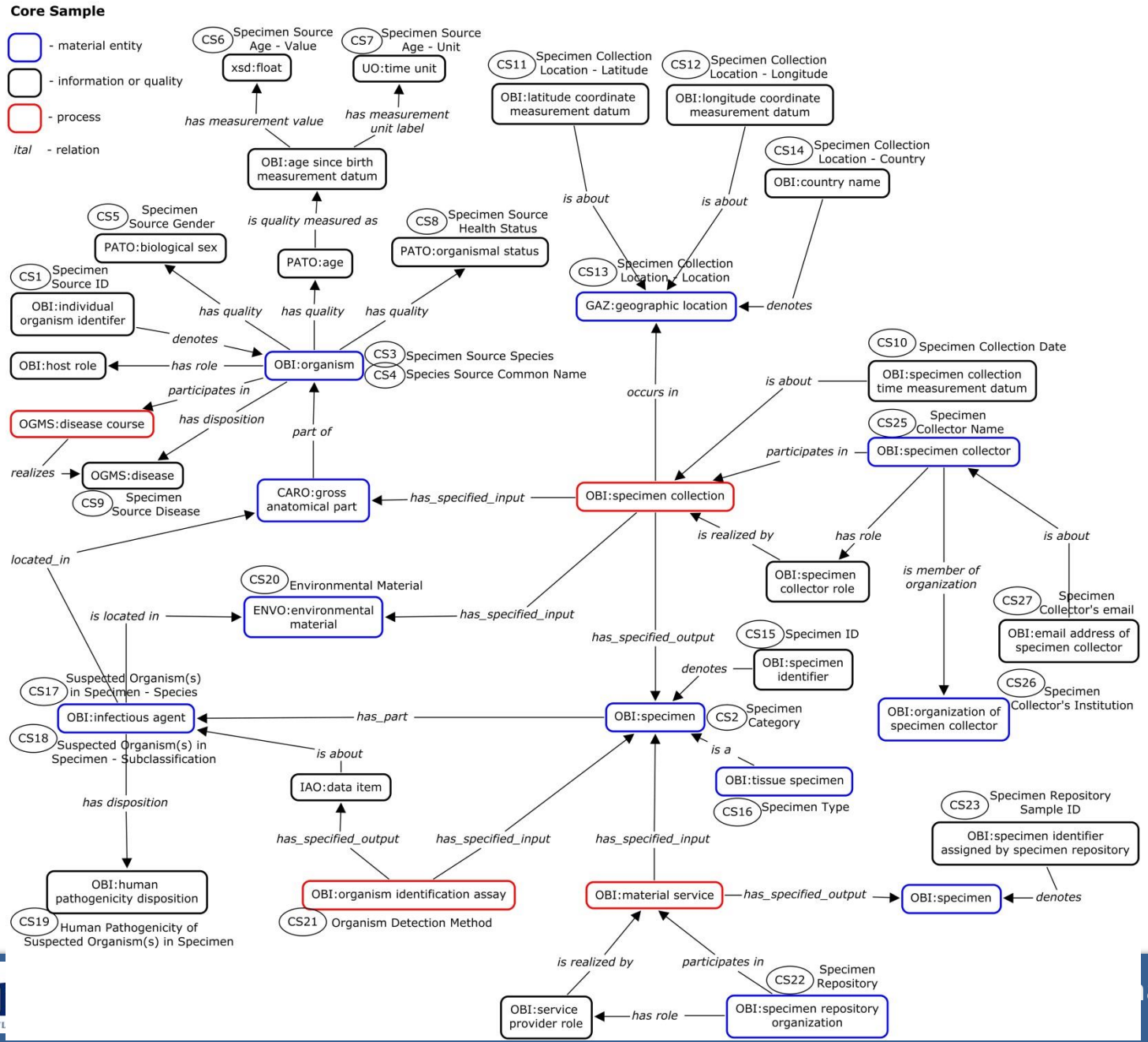
- Genome Sequencing Centers for Infectious Diseases (GSCIDs), the Bioinformatics Resource Centers (BRCs), and the U.S. National Institute of Allergy and Infectious Diseases (NIAID)
  - Project
  - Specimen
  - Sequencing
- http://www.niaid.nih.gov/labsandresources/resources/dmid/metadata/pages/default.aspx
- Dugan, Vivien G., et al. "Standardized Metadata for Human Pathogen/Vector Genomic Sequences." *PloS one* 9.6 (2014): e99979.

GSCID/BRC Project and Sample Application Standard v1.3 – Core Sample

Field ID	Field Name	Data Categories	OBO Foundry URL	BioSample Synonym	MIxS Synonym
CS1	Specimen Source ID	Host Characterization	http://purl.obolibrary.org/obo/OBI_0001141	host_subject_id	host_ subject_id
CS2	Specimen Category	Pathogen Detection	http://purl.obolibrary.org/obo/OBI_0100051	sample_category	
CS3	Specimen Source Species	Host Characterization	http://purl.obolibrary.org/obo/OBI_0100026	host*	host_taxid
CS4	Species Source Common Name	Host Characterization	http://purl.obolibrary.org/obo/OBI_0100026	Host_common_name	host_ common_ name
CS5	Specimen Source Gender	Host Characterization	http://purl.obolibrary.org/obo/PATO_0000047	host_sex	sex
CS6	Specimen Source Age - Value	Host Characterization	http://purl.obolibrary.org/obo/OBI_0001167	host_age	age
CS7	Specimen Source Age - Unit	Host Characterization	http://purl.obolibrary.org/obo/UO_0000003	host_age	
CS8	Specimen Source Health Status	Host Characterization	http://purl.obolibrary.org/obo/PATO_0001995	host_health_state	health_ disease stat
CS9	Specimen Source Disease	Host Characterization	http://purl.obolibrary.org/obo/OGMS_0000031	host_disease*	disease status
CS10	Specimen Collection Date	Specimen Isolation	http://purl.obolibrary.org/obo/OBI_0001619	collection_date*	collection date
CS11	Specimen Collection Location - Latitude	Specimen Isolation	http://purl.obolibrary.org/obo/OBI_0001620	lat_lon*	geographic location (latitude and longitude)
CS12	Specimen Collection Location - Longitude	Specimen Isolation	http://purl.obolibrary.org/obo/OBI_0001621	lat_lon*	geographic location (latitude and longitude)

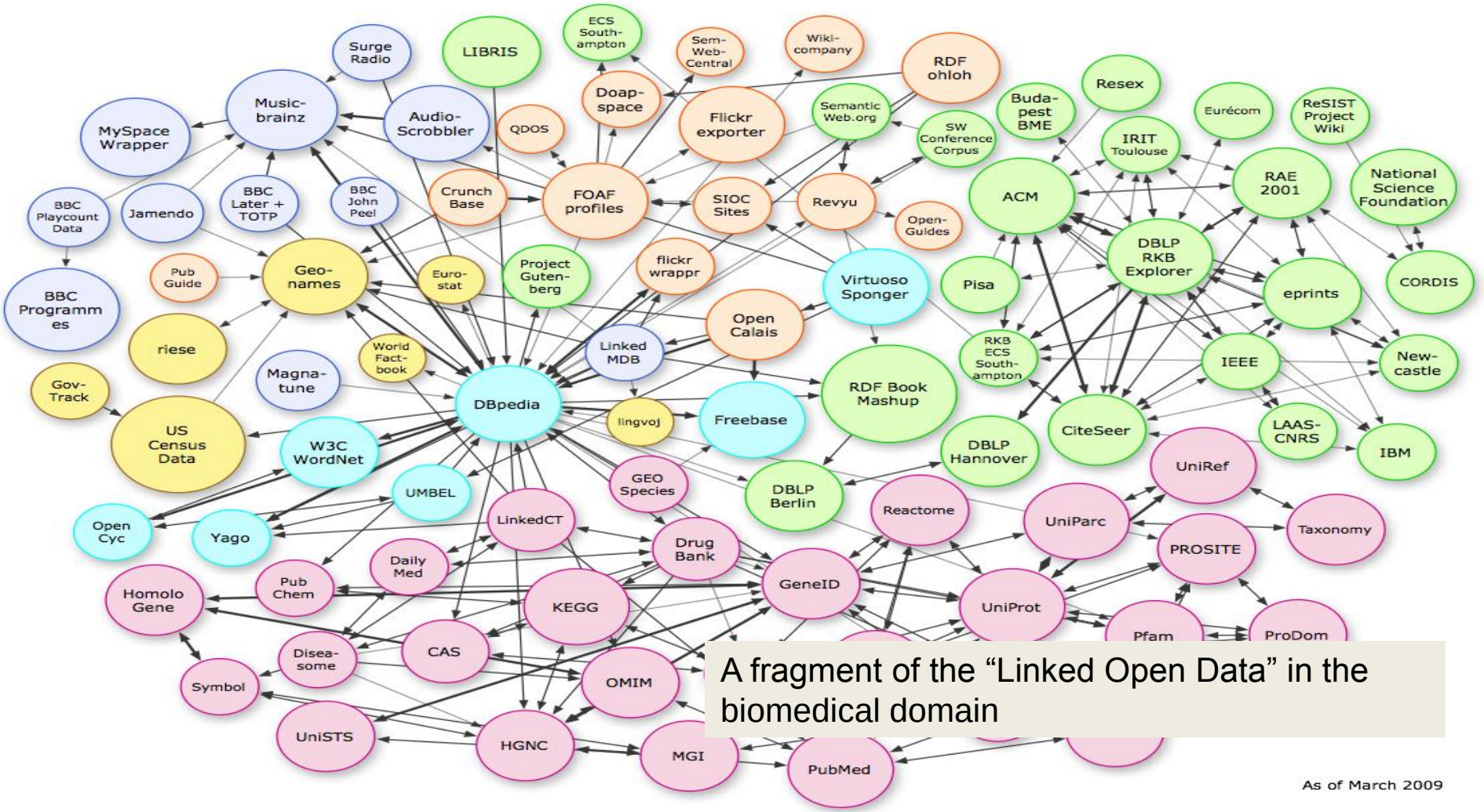
http://www.niaid.nih.gov/labsandresources/resources/dmid/metadata/pages/default.aspx

Semantic representation of sample and its associated attributes based on ontology



Linked Data

- Publishing structured data so that it can be interlinked and become more useful through semantic queries (e.g. SPARQL).

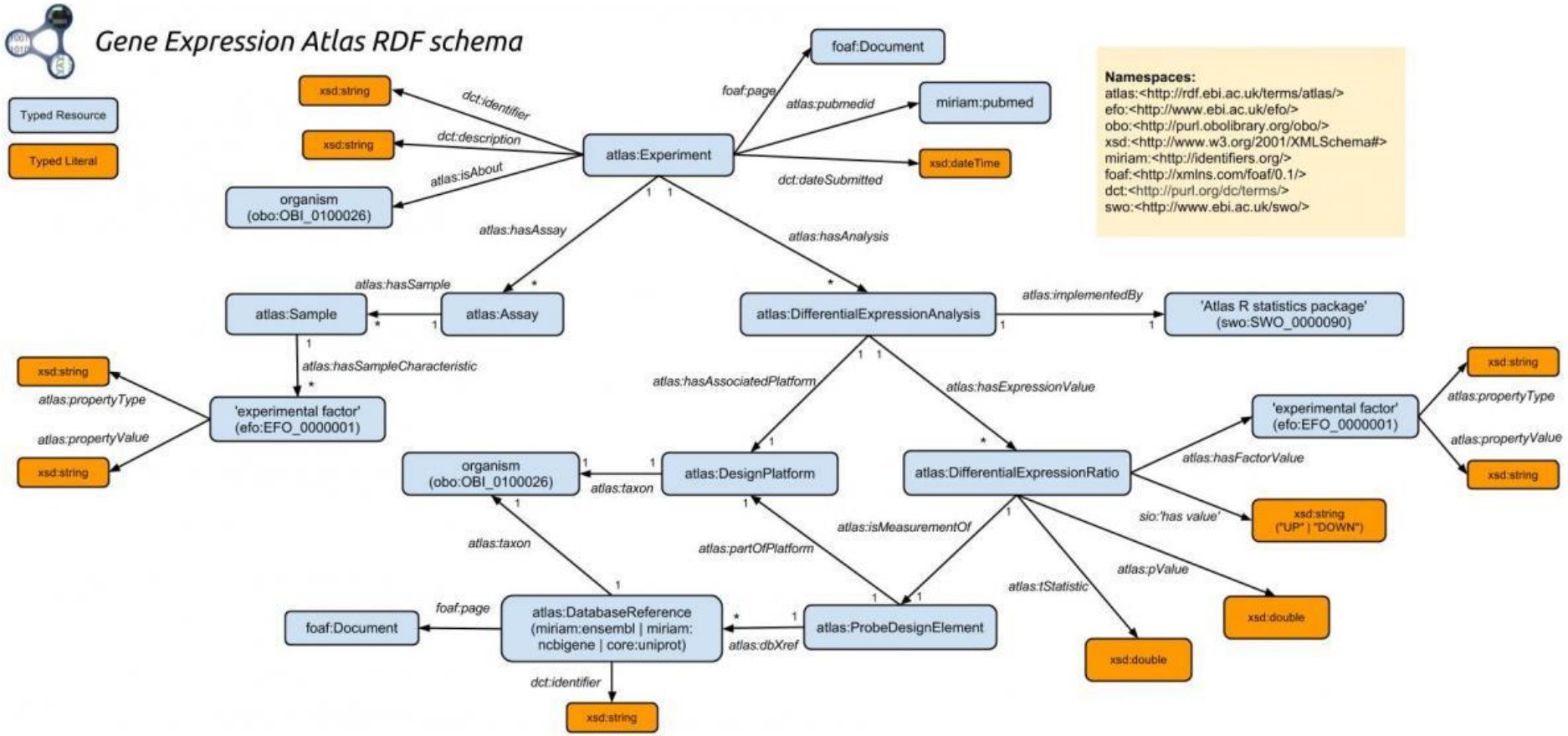


EBI RDF platform

- Resource description framework (RDF):
  - http://www.w3.org/TR/rdf-primer/
  - A technology for conceptual description or modeling of information
  - Data is represented by sets of subject-predicate-object statements ("triples") that form a directed graph
- Triplestore (RDF store):
  - database for the storage and retrieval of triples through semantic queries
  - triple is a data entity composed of subject-predict-object

The EBI RDF platform: linked open data for the life sciences. *Jupp S, et al*. Bioinformatics. 2014 May 1;30(9):1338-9.

Semantic Model



https://www.ebi.ac.uk/rdf/documentation/atlas

Automation Of Science

Robot Scientist (Adam)

TIME
IN PARTNERSHIP WITH CNN
SEARCH TIME.COM
Specials

The Top 10 Everything of 2009

TIME charts the highs and lows of the past year in 50 wide-ranging lists

Select a Section | Story | All Best and Worst Lists

Top 10 Scientific Discoveries

BACK NEXT

374 of 500 | View All

4. A Robot Performs Science

By EBEN HARRELL Tuesday, Dec. 08, 2009

By any standard, it was an elementary discovery — the identification of the role of about a dozen genes in a yeast cell. But what made this finding a major breakthrough was the unlikely form of the scientist: a robot. In April, "Adam," a machine designed at Aberystwyth University in Wales, became the first robotic system to make a novel scientific discovery with virtually no human

- Based on existing knowledge, the Robot Scientist made hypotheses, carried out the experiments to test the hypotheses, interpreted the results and then drew conclusions without human intervention

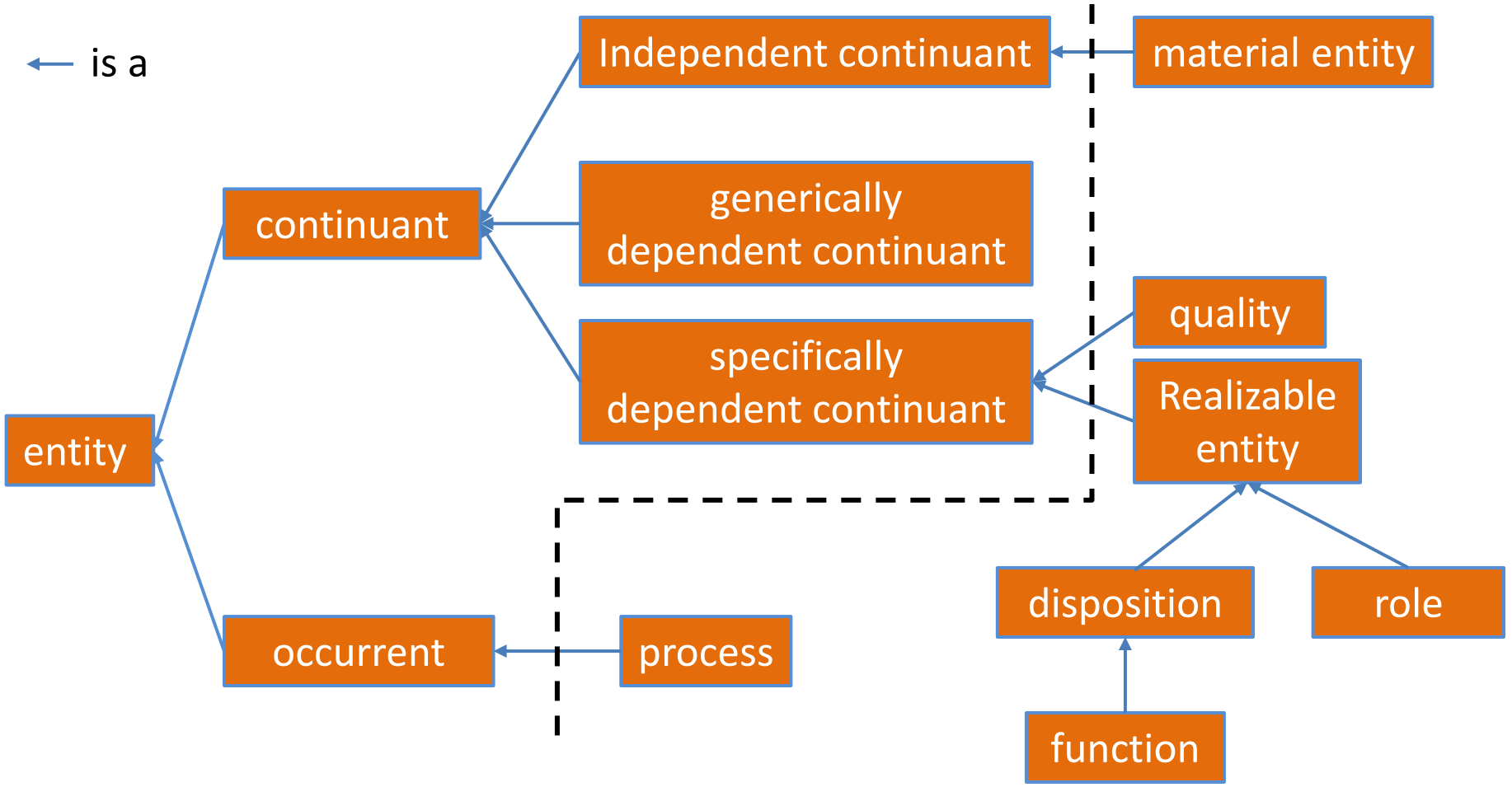
The automation of science. King RD, Rowland J, Oliver SG, Young M, Aubrey W, Byrne E, Liakata M, Markham M, Pir P, Soldatova LN, Sparkes A, Whelan KE, Clare A. *Science. 2009 Apr 3;324(5923):85-9.*

BASIC FORMAL ONTOLOGY (BFO)

Basic Formal Ontology (BFO)

- A simple, small top-level ontology to support information integration in scientific research
- An ontology represent reality
- BFO website
  - http://ifomis.uni-saarland.de/bfo/
- BFO development Github site
  - https://github.com/BFO-ontology/BFO
- BFO 2.0 specification
  - https://github.com/BFO-ontology/BFO/raw/master/docs/bfo2-reference/BFO2-Reference.pdf

Basic Formal Ontology



Continuants

- continue to exist through time, preserving their identity while undergoing different sorts of changes
- independent continuants – objects, material entity, ...
- dependent continuants – qualities, attributes, shapes, potentialities ...

(Barry Smith and Alan Ruttenberg)

Occurrents

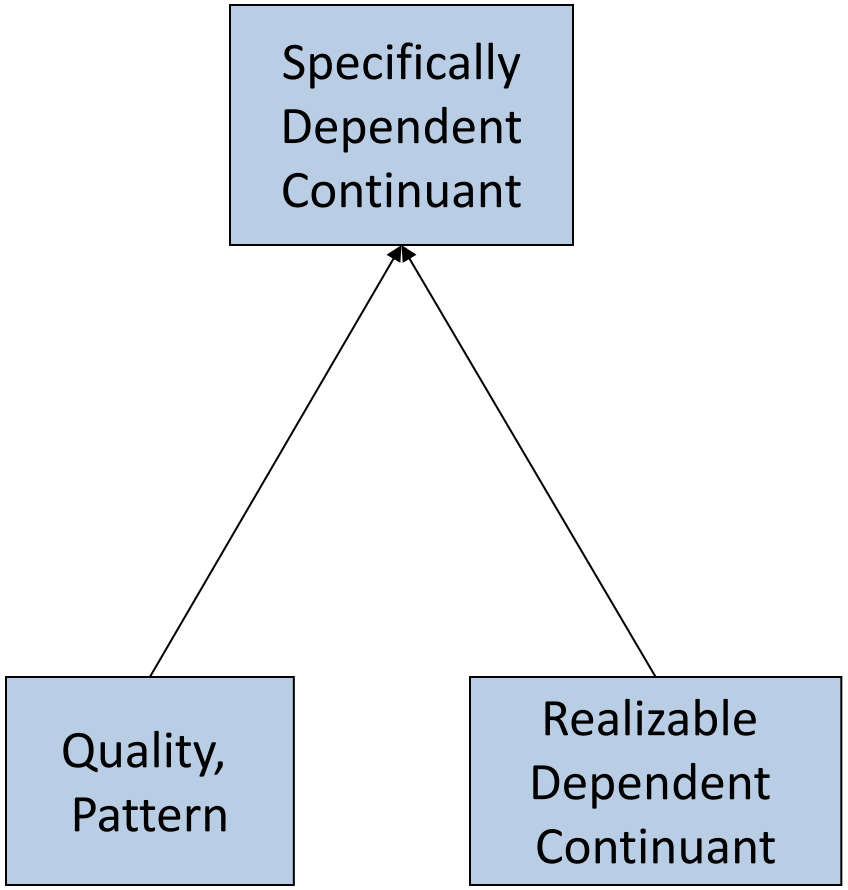
- processes, events, happenings
  - your life
  - this process of accelerated cell division

(Barry Smith and Alan Ruttenberg)

Independent Continuant

- Continue to exist through time independently
  - an atom
  - a molecule
  - an organism
  - a chair

Specifically Dependent Continuants



if the bearer ceases to exist, then its quality, function, role ceases to exist

the color of my skin

the function of my heart to pump blood

my weight

(Barry Smith and Alan Ruttenberg)

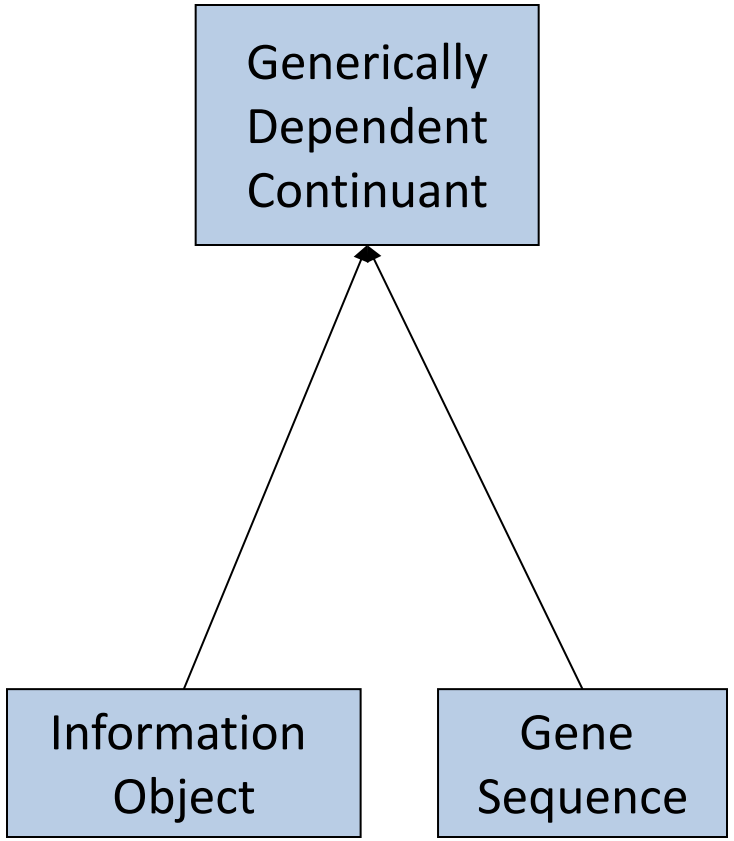
Generically Dependent Continuants

if one bearer ceases to exist,
then the entity can survive,
because there are other bearers

(copyability)

the pdf file on my laptop

the DNA (sequence) in this chromosome



(Barry Smith and Alan Ruttenberg)

Role (externally-grounded realizable entity)

role =def. a realizable entity

- which exists because the bearer is in some special physical, social, or institutional set of circumstances in which the bearer does not have to be, and
- is not such that, if it ceases to exist, then the physical make-up of the bearer is thereby changed.

(Barry Smith and Alan Ruttenberg)

Disposition (an internally-grounded realizable entity)

disposition =def.

a realizable entity which if it ceases to exist, then its bearer is physically changed, and

whose realization occurs when this bearer is in some special physical circumstances, in virtue of the bearer's physical make-up

(Barry Smith and Alan Ruttenberg)

Function (a disposition designed or selected for)

function =def.

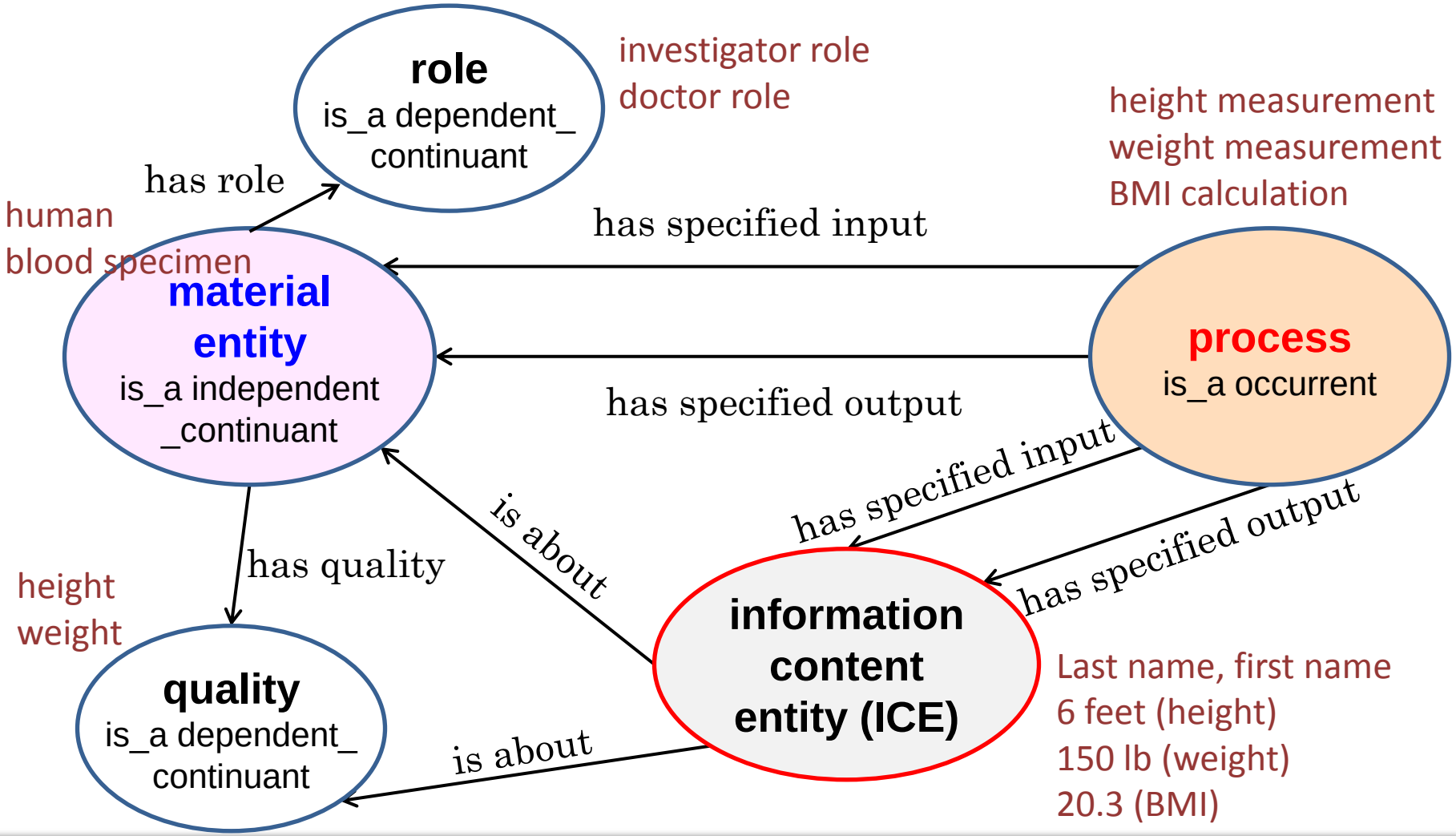
a disposition that

exists in virtue of the bearer's physical make-up, and

this physical make-up is something the bearer possesses because it came into being, either through evolution (in the case of natural biological entities) or through intentional design (in the case of artifacts), in order to realize processes of a certain kind.

(Barry Smith and Alan Ruttenberg)

Relations Between Main Entities



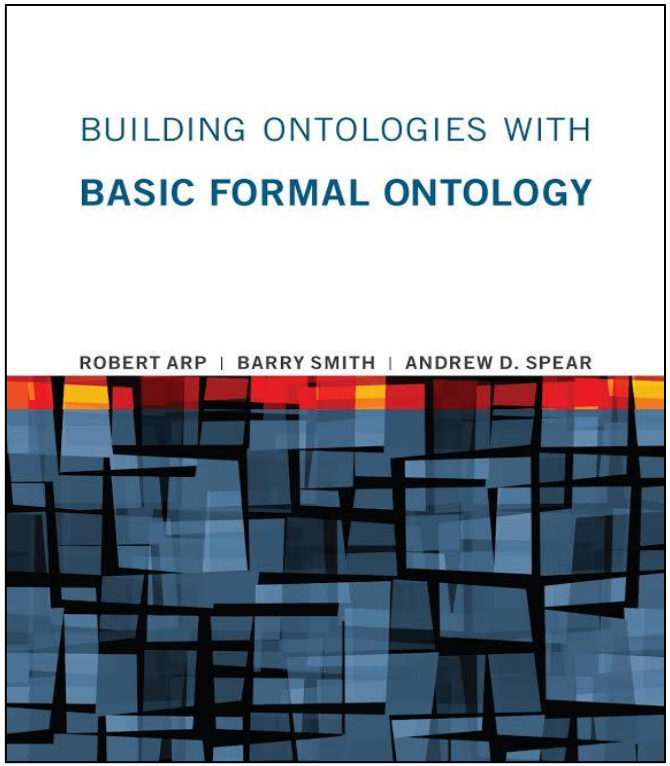
Users of BFO

- http://ifomis.uni-saarland.de/bfo/users
- Over 160 ontologies
  - GO Gene Ontology
  - CL Cell Ontology
  - SO Sequence Ontology
  - ChEBI Chemical Ontology
  - PATO Phenotype (Quality) Ontology
  - FMA Foundational Model of Anatomy Ontology
  - ChEBI Chemical Entities of Biological Interest
  - PRO Protein Ontology
- Over 50 Institutions, Groups and Projects
  - Air Force Research Laboratory, Rome, New York
  - Applied Physics Laboratory (APL), Johns Hopkins University
  - Berkeley Bioinformatics Open-Source Projects (BBOP)
  - Biomedical Knowledge Engineering Lab at Seoul National University (SNU BiKE)
  - Brain Operation Database (BODB)
  - MediCognos / Microsoft Healthvault

Further Readings

- BFO 2 tutorial
  - http://ncorwiki.buffalo.edu/index.php/Basic_Formal_Ontology_2.0
- Introduction of BFO 2 given by Dr. Barry Smith
  - https://www.youtube.com/watch?v=iTNQYyh88-Y
  - https://www.youtube.com/watch?v=IMCBON2me3Y

Building Ontology With BFO



This book addresses the important, 2000 year old challenge of how to soundly formalize the content and organization of scientific knowledge. As a user and teacher of ontological methods in medicine and engineering, I have for years warned my students that the design of domain ontologies is a black art with no theoretical foundations and few practical principles. Without progress on the problem, I argue, many fields ranging from informatics and computer science to AI and cognitive science will struggle to achieve their enormous potential, or to do so in a way that is convincing or safe. I now have a much more positive story for my students. Arp, Smith, and Spear have pulled together years of experience and lessons learned in diverse application domains into a treasure trove of guidance and good practice for the ontology builder. In the journey from black art to a truly scientific theory for ontology design, this book is an important milestone.

—John Fox, Department of Engineering Science, University of Oxford; Director, OpenClinical

Paperback | **$30.00 Short** | **£20.95** | ISBN: 9780262527811 | 248 pp. | 7 x 9 in | 32 b&w illus.| July 2015

eBook | **$21.00 Short** | ISBN: 9780262329576 | 248 pp. | 32 b&w illus.| August 2015

https://mitpress.mit.edu/index.php?q=books/building-ontologies-basic-formal-ontology

Acknowledgements

- Barry Smith
- Alan Ruttenberg
- All BFO developers and contributors

OBO FOUNDRY ONTOLOGIES

OBO Foundry Ontologies

Perspective

Nature Biotechnology **25**, 1251 - 1255 (2007)
Published online: 7 November 2007 | doi:10.1038/nbt1346

The OBO Foundry: coordinated evolution of ontologies to support biomedical data integration

Barry Smith[1], Michael Ashburner[2], Cornelius Rosse[3], Jonathan Bard[4], William Bug[5], Werner Ceusters[6], Louis J Goldberg[7], Karen Eilbeck[8], Amelia Ireland[9], Christopher J Mungall[10], The OBI Consortium[11], Neocles Leontis[12], Philippe Rocca-Serra[9], Alan Ruttenberg[13], Susanna-Assunta Sansone[9], Richard H Scheuermann[14], Nigam Shah[15], Patricia L Whetzel[16] & Suzanna Lewis[10]

The value of any kind of data is greatly enhanced when it exists in a form that allows it to be integrated with other data. One approach to integration is through the annotation of multiple bodies of data using common controlled vocabularies or 'ontologies'. Unfortunately, the very success of this approach has led to a proliferation of ontologies, which itself creates obstacles to integration. The Open Biomedical Ontologies (OBO) consortium is pursuing a strategy to overcome this problem. Existing OBO ontologies, including the Gene Ontology, are u coordinated reform, and new ontologies are being created o of an evolving set of shared principles governing ontology de The result is an expanding family of ontologies designed to b interoperable and logically well formed and to incorporate a representations of biological reality. We describe this OBO F initiative and provide guidelines for those who might wish to involved.

Common Upper Level Ontology, Basic Formal Ontology (BFO)
Common relations, Relation Ontology (RO)

Nature Biotechnology **25**, 1251 - 1255 (2007)
Published online: 7 November 2007 | doi:10.1038/nbt1346

The OBO Foundry: coordinated evolution of ontologies to support biomedical data integration

- Mission: Develop a family of interoperable ontologies that are both logically well-formed and scientifically accurate
- Approach: Participants voluntarily adhere (and contribute) to ontology development principles that facilitate the foundry mission
- Principles include (among others):
  - licensing that facilitates re-use
  - common machine readable syntax
  - standardized naming conventions
  - non-overlapping content and re-use
- Ontologies that want to participate in the Foundry are peer-reviewed for principle compliance

Nine OBO Member Ontologies

chebi **CHEBI**	Chemical Entities of Biological Interest	A structured classification of molecular entities of biological interest focusing on 'small' chemical compounds. Detail
doid **DOID**	Human Disease Ontology (CC BY)	An ontology for describing the classification of human diseases organized by etiology. Detail
go **GO**	Gene Ontology (CC BY)	An ontology for describing the function of genes and gene products Detail
obi **OBI**	Ontology for Biomedical Investigations (CC BY)	An integrated ontology for the description of life-science and clinical investigations Detail
pato **PATO**	Phenotypic quality (CC BY)	An ontology of phenotypic qualities (properties, attributes or characteristics) Detail
po **PO**	Plant Ontology (CC BY)	The Plant Ontology is a structured vocabulary and database resource that links plant anatomy, morphology and growth and development to plant genomics data. Detail
pr **PR**	PRotein Ontology (PRO) (CC BY)	An ontological representation of protein-related entities Detail
xao **XAO**	Xenopus anatomy and development (CC BY)	Anatomy and development of the African clawed frog (*Xenopus laevis*). Detail
zfa **ZFA**	Zebrafish anatomy and development (CC BY)	A structured controlled vocabulary of the anatomy and development of the Zebrafish Detail

ontologies have been reviewed by experts

Over Hundred Of Ontologies In OBO Library

aeo	Anatomical Entity Ontology	AEO is an ontology of anatomical structures that expands CARO, the Common Anatomy Reference Ontology Detail
aero	Adverse Event Reporting Ontology (cc) BY	The Adverse Event Reporting Ontology (AERO) is an ontology aimed at supporting clinicians at the time of data entry, increasing quality and accuracy of reported adverse events Detail
apo	Ascomycete phenotype ontology	A structured controlled vocabulary for the phenotypes of Ascomycete fungi Detail
bcgo	Beta Cell Genomics Ontology (cc) BY	An application ontology built for beta cell genomics studies. Detail
bco	Biological Collections Ontology	An ontology to support the interoperability of biodiversity data, including data on museum collections, environmental/metagenomic samples, and ecological surveys. Detail
bfo	Basic Formal Ontology (cc) BY	The upper level ontology upon which OBO Foundry ontologies are built. Detail
bspo	Biological Spatial Ontology (cc) BY	An ontology for respresenting spatial concepts, anatomical axes, gradients, regions, planes, sides, and surfaces Detail
bto	BRENDA tissue / enzyme source BRENDA license	A structured controlled vocabulary for the source of an enzyme comprising tissues, cell lines, cell types and cell cultures. Detail
caro	Common Anatomy Reference Ontology	An upper level ontology to facilitate interoperability between existing anatomy ontologies for different species

OBO Foundry Principles

Common sense principles
- open – licensing that enables re-use
- format – OWL / OBO
- uris - identifiers
- versioning – deal with it
- documented – tell others how to use it
- locus of authority – contact person
- users – have more than 1

Metadata principles
- textual definitions
- naming conventions

Foundry specific principles
- delineated content
- relations
- collaboration
- maintenance

Since 2014: Review of Review process
→ Ongoing process to clarify the wording of the principles and criteria to be used to evaluate ontologies for compliance

Notify us of problems via issue tracker https://github.com/OBOFoundry/OBOFoundry.github.io/issues

http://www.obofoundry.org/principles/fp-000-summary.html

Open

- Recommended License: Creative Commons 3.0 BY License

Common Format

- OBO Format
- OWL (RDF/XML)

URIs

- Prefix:
  - Need register to OBO Foundry
- Numeric Local ID

- ID Policy
  - http://www.obofoundry.org/id-policy.html

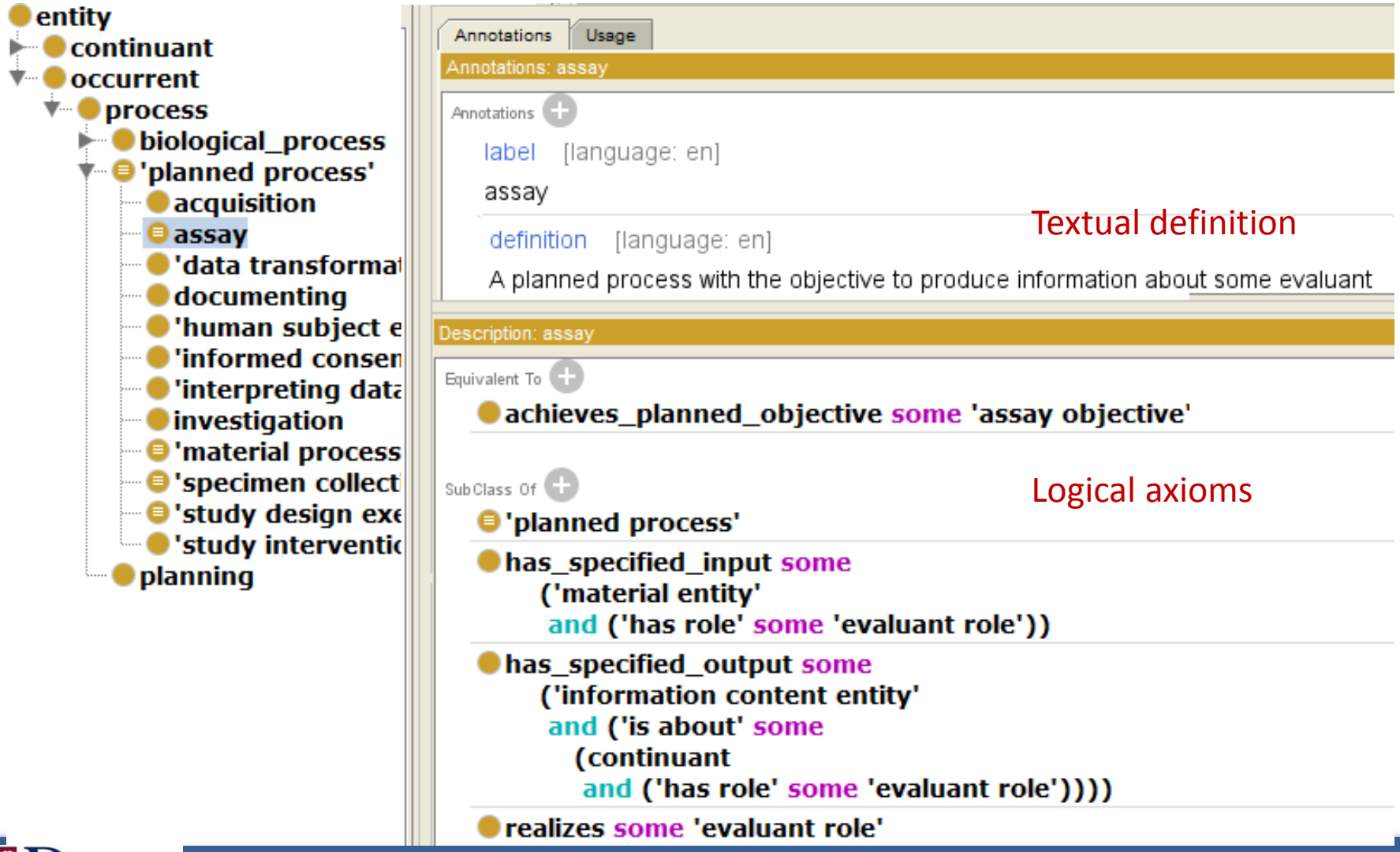
Versioning

- Successive releases given unique version numbers
  - Unique PURL created for each historic release
    http://purl.obolibrary.org/obo/obi/2015-12-07/obi.owl
  - Main PURL for latest stable release
    http://purl.obolibrary.org/obo/obi.owl
- Commonly used version control repositories
  - Github
  - Sourceforge

Textual Definitions

- Each term need to have textual definition
- Concise
- Aristotelian form

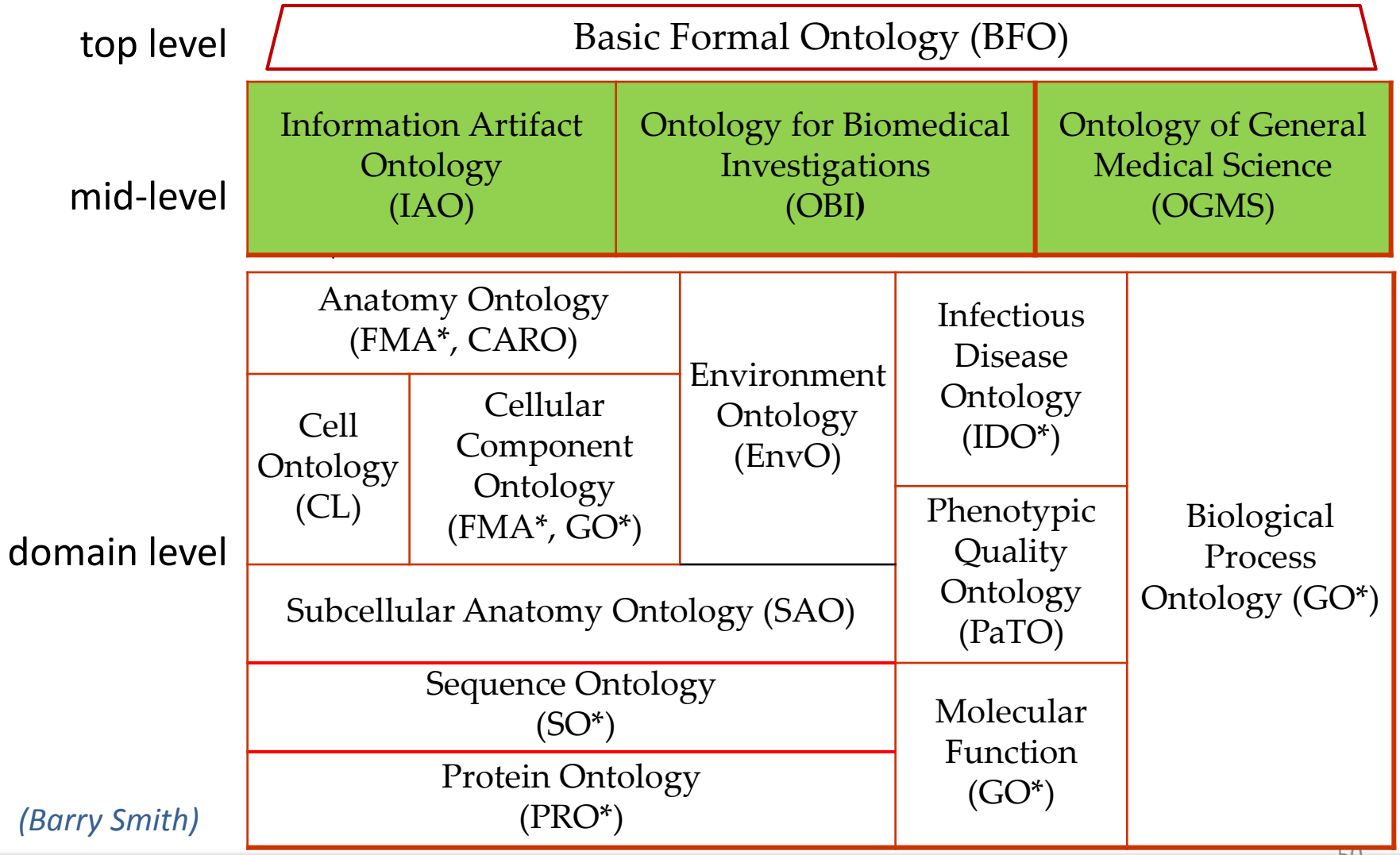
Example: Assay



Relations

- Relations Ontology
  - collection of relations intended primarily for standardization across ontologies in the OBO Foundry and wider OBO library
  - http://www.obofoundry.org/ontology/ro.html
- Core relations
  - Minimal subset intended to work with BFO-classes
  - http://purl.obolibrary.org/obo/ro/core.owl

How is the OBO Foundry organized?



(Barry Smith)

Each OBO Foundry Ontology Covers A Specific Biological and Clinical Area

- Gene Ontology (GO): biological process, molecular function, cell components
- Protein Ontology (PR): protein (cross species)
- Cell Line Ontology (CLO): cell line
- Cell Type (CL) : cell type
- Uber Anatomy Ontology (UBERON): cross-species anatomy
- Phenotypic Quality (PATO): quality
- Ontology for Biomedical Investigations (OBI): all aspects of an experiments

Scope and Scale of OBO Ontologies

<table>
<tr><th>RELATION TO TIME
GRANULARITY</th><th colspan="3">CONTINUANT</th><th colspan="2">CONTINUANT</th><th>OCCURRENT</th></tr>
<tr><td></td><td colspan="3">INDEPENDENT</td><td colspan="2">DEPENDENT</td><td></td></tr>
<tr><td>ORGAN AND ORGANISM</td><td>Organism (NCBI Taxonomy)</td><td colspan="2">Anatomical Entity (FMA, CARO)
XAO | ZFA</td><td>Organ Function (FMP, CPRO)</td><td rowspan="2">Phenotypic Quality (PaTO)</td><td rowspan="3">Biological Process (GO)</td></tr>
<tr><td>CELL AND CELLULAR COMPONENT</td><td>Cell (CL)</td><td colspan="2">Cellular Component (FMA, GO)</td><td>Cellular Function (GO)</td></tr>
<tr><td>MOLECULE</td><td colspan="3">Molecule (SO, RnaO)
ChEBI | PRO</td><td colspan="2">Molecular Function (GO)</td><td>Molecular Process (GO)</td></tr>
</table>

Communicate With OBO Foundry

- Issue trackers
  - https://github.com/OBOFoundry/OBOFoundry.github.io/issues
- Mailing list (OBO discuss list)
  - https://lists.sourceforge.net/lists/listinfo/obo-discuss

Communicate With OBO Foundry Ontology Term Requests and Bug Reports

- Find the right home for your term
- Overview of Ontology
  - Issue tracker
  - Mailing list
  - Homepage
  - ……

Links can be found on the OBO Foundry ontology website

http://www.obofoundry.org/ontology/obi.html

Ontology for Biomedical Investigations

An integrated ontology for the description of life-science and clinical investigations

OntoBee | AberOWL | OLS | BioPortal

Ontology repository

The Ontology for Biomedical Investigations (OBI) project is developing an integrated ontology for the descri
life-science and clinical investigations.

- Browse OBI on Ontobee
- Download OBI: http://purl.obolibrary.org/obo/obi.owl
- OBI homepage
- OBI mailing list

Mailing list, contact developers

For issues and new term request

- To cite a journal article for OBI please use the following: Brinkman et al, J Biomed Semantics, 2010
- To refer to the most current information on the OBI project, please use the following: The OBI Consortium http://purl.obolibrary.org/obo/obi
- To use OBI, remember the licensing terms: OBI is released under CC-by 3.0 Unported License

ID Space	obi
PURL	http://purl.obolibrary.org/obo/obi.owl
License	CC-BY
Homepage	http://obi-ontology.org
Contact	Bjoern Peters
Trackers	http://purl.obofoundry.org/obo/obi/tracker
Domain	experiments

View | Edit | PURL

Edit the metadata for this pa
fork and pull request!) Place

Products

obi.owl	OBI
obi/obi_core.owl	OBI Core

Browse OBO Foundry Ontologies On Web

- Bioportal Website

  http://bioportal.bioontology.org/

  – All biological and clinical related ontologies and terminologies

- Ontobee Website

  http://www.ontobee.org

  – OBO Foundry ontologies

- Ontology Lookup Service

  http://www.ebi.ac.uk/ols/beta/ontologies

- AberOWL Repository

  http://aber-owl.net/ontology/

Register Ontology Under OBO Foundry

- Announce your ontology on the OBO Discuss list
  - https://lists.sourceforge.net/lists/listinfo/obo-discuss
- Request a PURL and an entry in the registry
  - http://www.obofoundry.org/docs/Policy_for_OBO_namespace_and_associated_PURL_requests.html

Tutorials

- OBO Tutorial/Workshop at ICBO conferences
  - http://ncorwiki.buffalo.edu/index.php/2013_ICBO_OBO_tutorial
  - http://ncorwiki.buffalo.edu/index.php/2014_ICBO_OBO_Tutorial
  - http://ncorwiki.buffalo.edu/index.php/2014_ICBO_OBO_Workshop
  - http://icbo2015.fc.ul.pt/workshops.html
  - Material: https://github.com/jamesaoverton/obo-tutorial

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