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Alignment of the UMLS Semantic Network with BioTop

Methodology and Assessment

Ontology Alignment

- Linking two ontologies by detecting semantic correspondences between their representational units
- Types of correspondences:
  equivalence, subsumption, others
- Purpose of ontology alignment:
  - Creating interoperability between semantically annotated data
  - Enriching semantics
  - Cross-Validation of ontologies
- Requirements of ontology alignment:
  - comparable scope
  - comparable context
  - comparable semantic foundations

Outline

- Introduction
  - BioTop
  - UMLS SN
- Methodology
  - UMLS SN: formal redefinition
  - Interactive Mapping
- Assessment
  - Ontology Cross-Validation
  - NE co-occurrence validation
  - UMLS SN cluster consistency
- Conclusion

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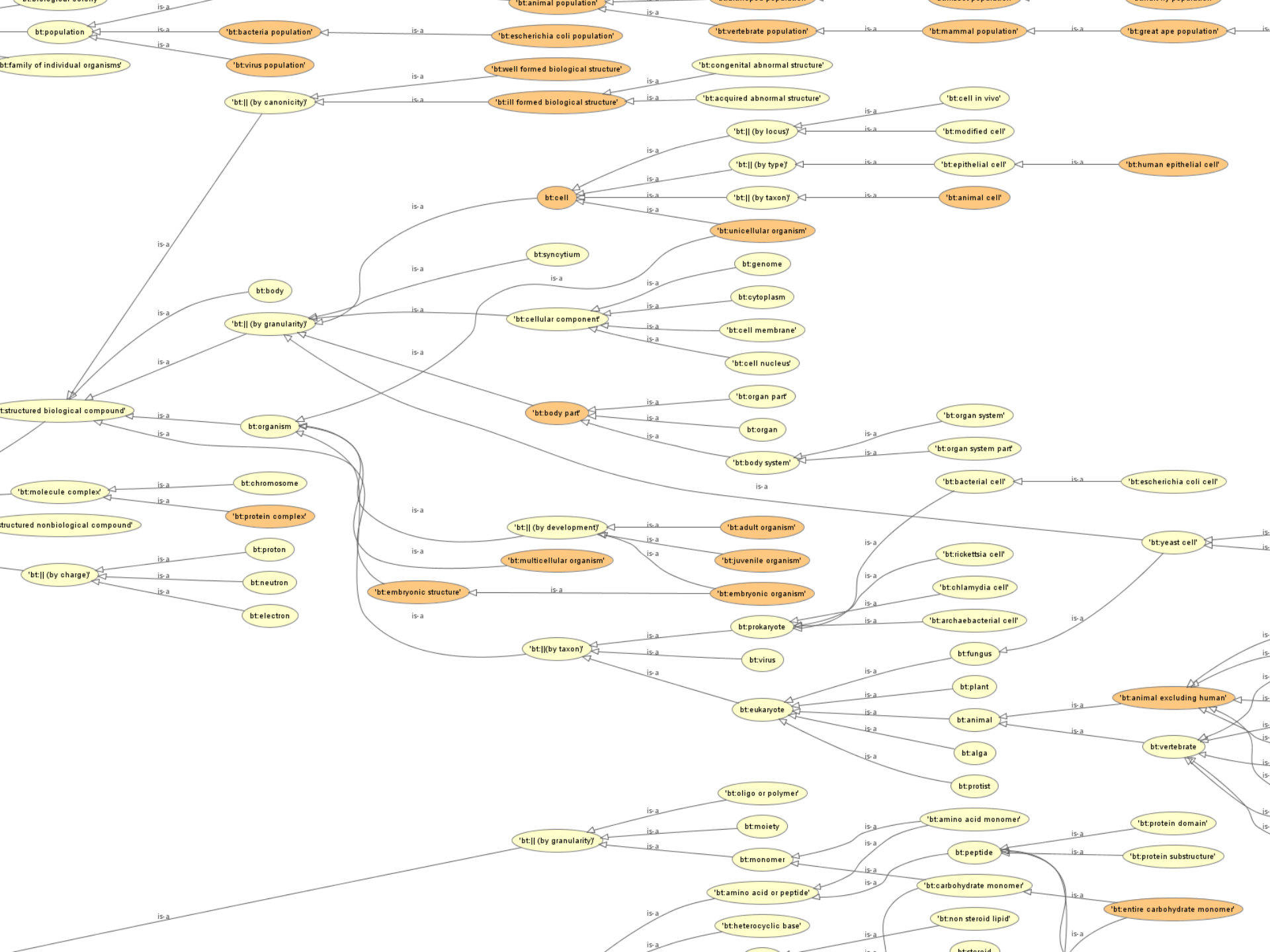
BioTop – a Life Science Upper Ontology

- Recent development (starting 2006, Freiburg & Jena)
- Goal: to provide formal definitions of upper-level types and relations for the biomedical domain
- Uses description logics (OWL-DL)
  - 339 classes, 60 relation types
  - 373 subclass axioms
  - 80 equivalent class axioms, 66 disjoint class axioms
- Compatible with BFO and DOLCE lite
- links to OBO ontologies
- downloadable from: http://purl.org/biotop

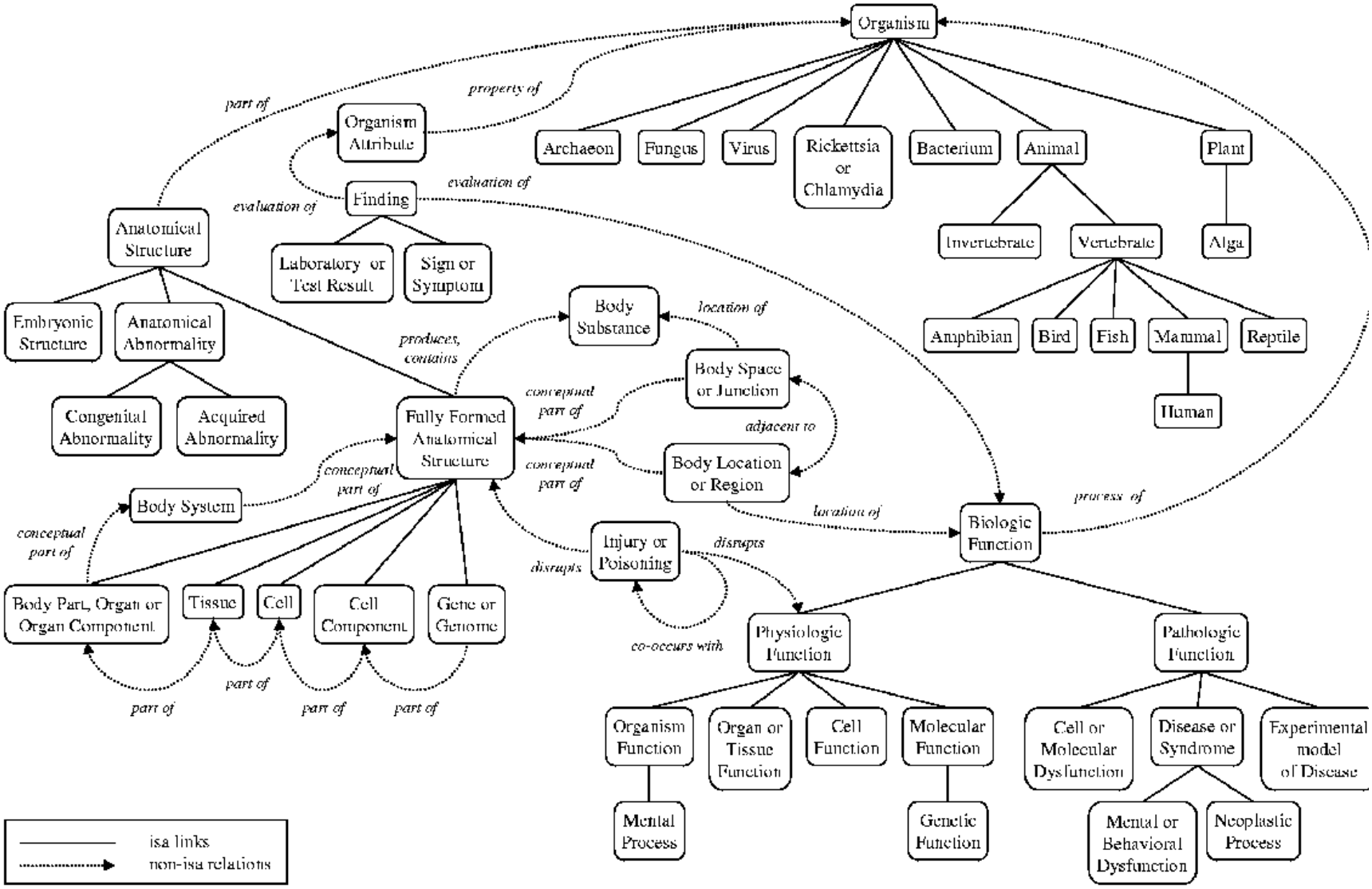

bt:population
'bt:bacteria population'
'bt:escherichia coli population'
'bt:virus population'
'bt:family of individual organisms'
'bt:animal population'
'bt:vertebrate population'
'bt:mammal population'
'bt:great ape population'
'bt:well formed biological structure'
'bt:congenital abnormal structure'
'bt:|| (by canonicity)'
'bt:ill formed biological structure'
'bt:acquired abnormal structure'
'bt:|| (by locus)'
'bt:cell in vivo'
'bt:modified cell'
'bt:|| (by type)'
'bt:epithelial cell'
'bt:human epithelial cell'
bt:cell
'bt:|| (by taxon)'
'bt:animal cell'
'bt:unicellular organism'
bt:syncytium
bt:genome
bt:cytoplasm
'bt:cellular component'
'bt:cell membrane'
'bt:cell nucleus'
bt:body
'bt:|| (by granularity)'
'bt:body part'
'bt:organ part'
bt:organ
'bt:body system'
'bt:organ system'
'bt:organ system part'
t:structured biological compound'
bt:organism
'bt:bacterial cell'
'bt:escherichia coli cell'
'bt:molecule complex'
bt:chromosome
'bt:protein complex'
structured nonbiological compound'
'bt:|| (by development)'
'bt:adult organism'
'bt:juvenile organism'
'bt:multicellular organism'
'bt:embryonic structure'
'bt:embryonic organism'
'bt:yeast cell'
'bt:rickettsia cell'
'bt:chlamydia cell'
'bt:archaebacterial cell'
bt:proton
'bt:|| (by charge)'
bt:neutron
bt:electron
'bt:prokaryote'
'bt:||(by taxon)'
bt:virus
bt:fungus
bt:plant
'bt:animal excluding human'
bt:eukaryote
bt:animal
bt:vertebrate
bt:alga
bt:protist
'bt:oligo or polymer'
'bt:|| (by granularity)'
bt:moiety
bt:monomer
'bt:amino acid monomer'
'bt:protein domain'
bt:peptide
'bt:protein substructure'
'bt:carbohydrate monomer'
'bt:amino acid or peptide'
'bt:entire carbohydrate monomer'
'bt:non steroid lipid'
'bt:heterocyclic base'
is-a

UMLS Semantic Network (SN)

- Upper-level semantic categorization framework for all (~1 M) concepts of the **UMLS Metathesaurus**
- Tree of 135 semantic types (e.g. *Tissue*, *Diagnostic_Procedure*)
- 53 associative relationships (e.g., *treats*, *location_of*)
- 612 relational assertions (triples), sanctioning the domain and range of relations {*Tissue*; *location_of*; *Diagnostic_Procedure*}
- mainly unchanged in the last 20 years

Unified Medical Language System (UMLS): Metathesaurus links over 100 biomedical vocabularies

UMLS Semantic Network (SN)



Comparison UMLS-SN - BioTop

	UMLS-SN	BioTop
Types / Classes	135	339
Relation Types	53	60 (object properties)
Axioms	612	509
Semantics	Implicit Frame-like Closed-world (?)	Explicit (description logics) Set-theoretic Open-world
Class subsumption ⊑	+	+
Relation subsumption ⊑	+	+
Domain / Range Restrictions	+	+
Relation Inheritance blocking	+	–
Full Definitions ≡	–	+
Disjoint Partitions	–	+
Negations ¬	–	+
Existential Restrictions ∃	–	+
Value Restrictions ∀	–	+

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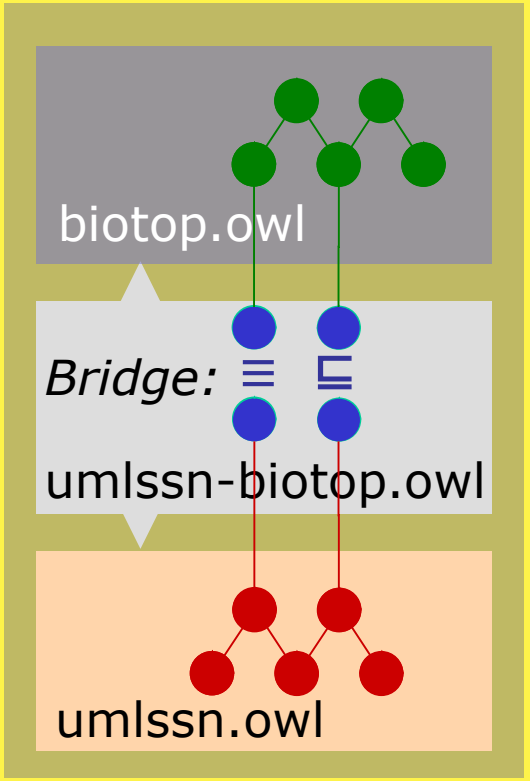
Methodology

1. Prerequisite: provide description logics semantics to the UMLS SN:

   umlssn.owl

2. Building a bridging ontology
   - Subsumption $\sqsubseteq$
   - Equivalence $\equiv$



Redefinition of UMLS SN semantics

Redefinition of UMLS SN semantics

- **Semantic Types**, e.g.: *Tissue*, *Diagnostic_Procedure*:
  - Types extend to classes of individuals
  - subsumption hierarchies = is-a hierarchies (every instance of a child is also an instance of each parent)
  - no explicit disjoint partitions
- **Semantic Relations**, e.g.: *treats*, *location_of*:
  - Reified as classes, **not** represented as OWL object properties
- **Triples**, e.g.: {*Tissue*; *location_of*; *Diagnostic_Procedure*}
  - domain and range restrictions = value restrictions on the roles *has-domain* and *has-range*

UMLS SN: Why SRs as classes …

and not OWL object properties? (I)

treats	Range	Disease	Person
Domain			
Drug		allowed	disallowed
Physician		disallowed	allowed

$$\mathit{TreatingPerson} \equiv \mathit{Action} \sqcap \exists\ \mathbf{has\_domain}.\mathit{Physician} \sqcap \exists\ \mathbf{has\_range}.\mathit{Person} \sqcap \forall\ \mathbf{has\_domain}.\ \mathit{Physician} \sqcap \forall\ \mathbf{has\_range}.\mathit{Person}$$

$$\mathit{TreatingDisease} \equiv \mathit{Action} \sqcap \exists\ \mathbf{has\_domain}.\mathit{Drug} \sqcap \exists\ \mathbf{has\_\ range}.\mathit{Disease} \sqcap \forall\ \mathbf{has\_domain}.\mathit{Drug} \sqcap \forall\ \mathbf{has\_\ range}.\ \mathit{Disease}$$

$$\mathit{Treating} \equiv \mathit{TreatingPerson} \sqcup \mathit{TreatingDisease}$$

UMLS SN: Why SRs as classes ..

and not OWL object properties? (II)

- Source Representation

Idea_or_Concept *conceptual_part_of* *Behavior*

"Defined not Inherited"

- Target Representation

$$Conceptual\_part\_of\_Domain\_Idea\_Or\_Concept\_Range\_\ Behavior\_Rest\_Class \sqsubseteq Conceptual\_part\_of \sqcap \forall\, has\_domain.\ Idea\_Or\_Concept\_Rest\_Class \sqcap \forall\, has\_range.\ Behavior\_Rest\_Class$$

$$Idea\_Or\_Concept\_Rest\_Class \equiv Idea\_Or\_Concept \sqcap \neg\, Temporal\_Concept \sqcap \neg\, Qualitative\_Concept \sqcap \neg\, Quantitative\_Concept \sqcap \neg\, Spatial\_Concept \sqcap \neg\, Functional\_Concept$$

$$Behavior\_Rest\_Class \equiv Behavior \sqcap \neg\, Individual\_Behavior \sqcap \neg\, Social\_Behavior$$

Representation of SRs and triples

- All triples including R are defined as subclasses of R

$$Affects\_Domain\_Cell\_Component\_Range\_Physiologic\_Function \sqsubseteq Affects \sqcap \forall has\_domain.\ Cell\_Component \sqcap \forall has\_range.\ Physiologic\_Function$$

- All parents are fully defined by the union of their children

$$Brings\_About \equiv Produces \sqcup Causes$$

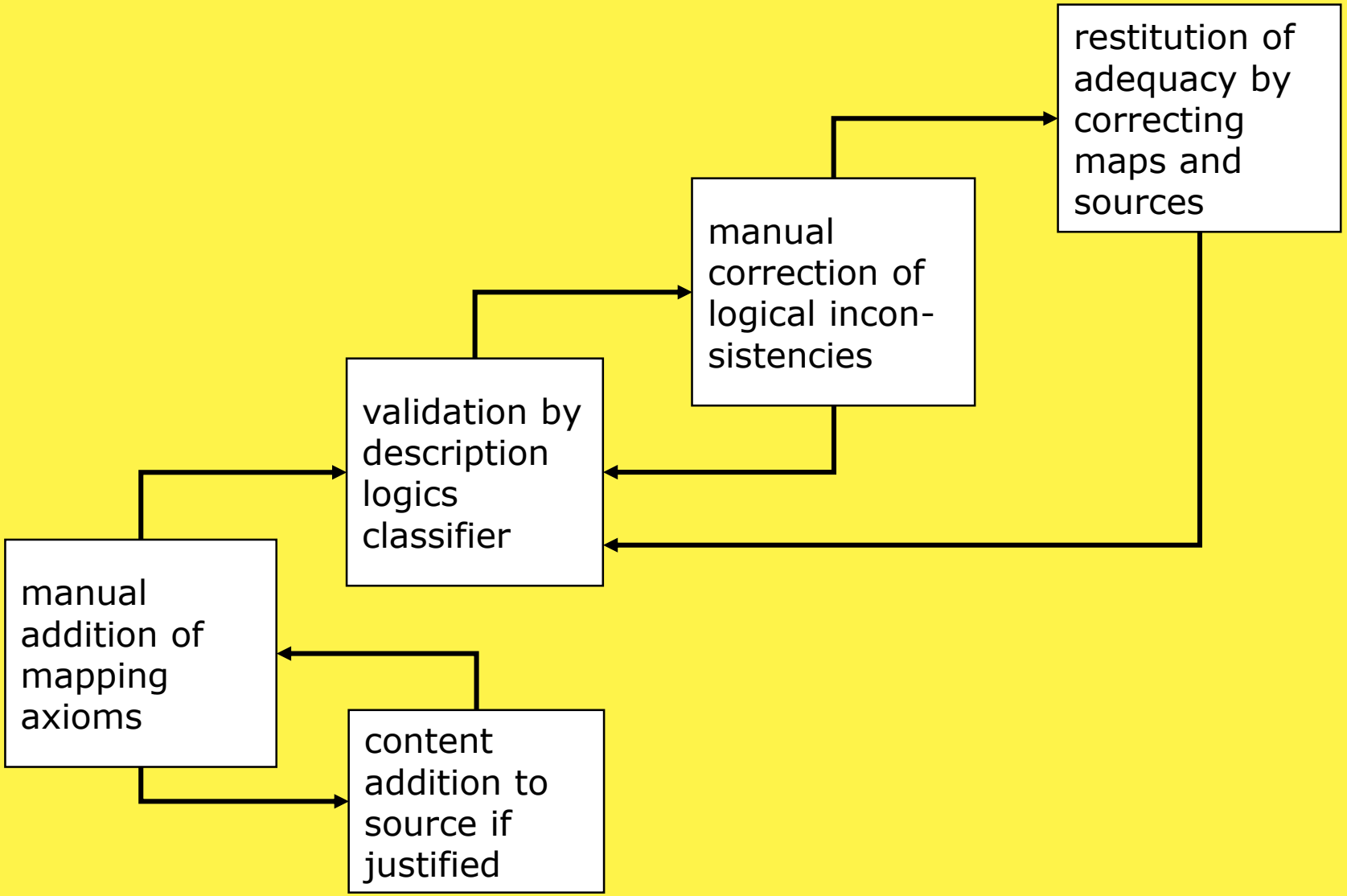
Mapping

Mapping

- Fully manually, using Protégé 4, consistency check with Fact++ and Pellet 1.5, supported by explanation plugin*
- Analyzing
  - UMLS SN hierarchies and free-text definitions
  - BioTop formal and free-text definitions
- Iterative check of
  - logic consistency (DL classifier)
  - domain adequacy (analysis of new entailments)

*(Horridge ISWC 2008)

Mapping workflow



Mapping of UMLS Types

- Direct Match (often after content addition to BioTop):

  sn:Plant ≡ bt:Plant

- Restriction mapping:

  sn:AnatomicalAbnormality ≡ bt:OrganismPart ⊓ ∃□ bt:bearerOf.bt:PathologicalCondition

- Union:

  sn:Gene_Or_Genome ≡ bt:Gene ⊔ bt:Genome.

- Out of scope

  sn:Daily_Or_Recreational_Activity ⊑ bt:Action ⊓ ∃□ bt:hasParticipant.bt:Human

- No mapping

  sn:Idea_or_concept

Mapping of UMLS Relations

- Mapping of domain and range

$$sn{:}hasDomain \equiv bt{:}hasAgent$$
$$sn{:}hasRange \equiv bt{:}hasPatient$$

- Mapping of (reified) SN relations

$$sn{:}Affects \equiv bt{:}Affecting$$

- Linkage of (reified) SN relations to BioTop relations by augmented restrictions:

$$sn{:}hasDomain \sqsubseteq \forall (bt{:}physicalPartOf \sqsubseteq \forall (ImmaterialPhysicalEntity \sqcup MaterialEntity)) \sqcap$$
$$sn{:}hasRange \sqsubseteq \forall (bt{:}hasPhysicalPart \sqsubseteq \forall (ImmaterialPhysicalEntity \sqcup MaterialEntity))$$

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Assessment: Cross-evaluation

- Formative evaluation of BioTop: Mapping and subsequent classification unveils hidden problems in BioTop:
  - Faulty disjointness axioms (e.g. *bt:Organic Chemical* was disjoint from *bt:Carbohydrate*)
  - ambiguities: Sequence as information entity vs. sequence as molecular structure
  - granularity mismatches:
    e.g. Chromosome as molecule

Assessment: NE co-occurrences

- Named Entity tagging, UMLS concept pairs identified in 15 M PubMed abstracts

Semantic Type 1: UMLS ID	NE 1	**Semantic Type 2**: UMLS ID	NE 2
Enzyme:C0916840	superoxide reductase	**Organic_Chemical**:C0001992	aldehyde
Finding:C0883391	free testosterone index	**Laboratory_Procedure**:C0020980	immunoassay
Food:C1145642	sorghum	**Invertebrate**:C0009276	beetles
Functional_Concept:C0332240	idiopathic	**Pharmacologic_Substance**:C0011685	desipramine
Functional_Concept:C1510670	feeds	**Intellectual_Product**:C0023683	life table
Gene_or_Genome:C0087142	v-Jun	**Mammal**:C0025920	C3H
Gene_or_Genome:C0600449	essential gene	**Hazardous_or_Poisonous_Substance**:C0000511	4-nitroquinolone-1-oxide
Geographic_Area:C0027978	New Zealand	**Idea_or_Concept**:C0018741	health resources
Hazardous_or_Poisonous_Substance:C0036248	stx	**Organic_Chemical**:C0000967	acetal

- Expert rating with sample of co-occurrences: which are semantically related?

Assessment: NE co-occurrences

		Expert judgment: should be related (52)	Expert judgment: Should not be related (93)
matching against SN triplets	SN: sanctioned	31	22
	SN: unsanctioned	21	71
Description logics classification	SN-BioTop: accepted	52	90
	SN-BioTop: rejected	0	3

- Using SN alone: very low agreement with expert rating
- Using SN+BioTop: very few rejections (only 3)
- Reasons:
  - false-positive rate: Expert rating done on NE (e.g. *Superoxide reductase unrelated with Aldehyde*), but system judgments at type level: *sn:Enzyme* related to *sn:Organic Chemical*
  - few rejections: DL's open world semantics

Assessment: finding incompatible semantic types

- Each UMLS concept is categorized by one or more UMLS SN types
- 397 different SN type combinations
- Using UMLS-SN BioTop Bridge: 133 combinations inconsistent, affecting 6116 UMLS concepts
- Main reason: hidden ambiguities, e.g.

$$sn{:}Manufactured\ Object \sqcap sn{:}HealthCareRelatedOrganization$$

(e.g. *Hospital* as building vs. organization).

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Conclusion

- Sucessful alignment between the (legacy) SN and the (novel) BioTop ontology
- Necessary: formal re-interpretation of SN
- Prospect: join large amount of data annotated by the SN with formal rigor of BioTop
- Strength: machine inference, consistency checking
- Challenge: Antagonize unwarranted effects of the open world semantics by making exhaustive use of disjoint partitions
- More use cases !

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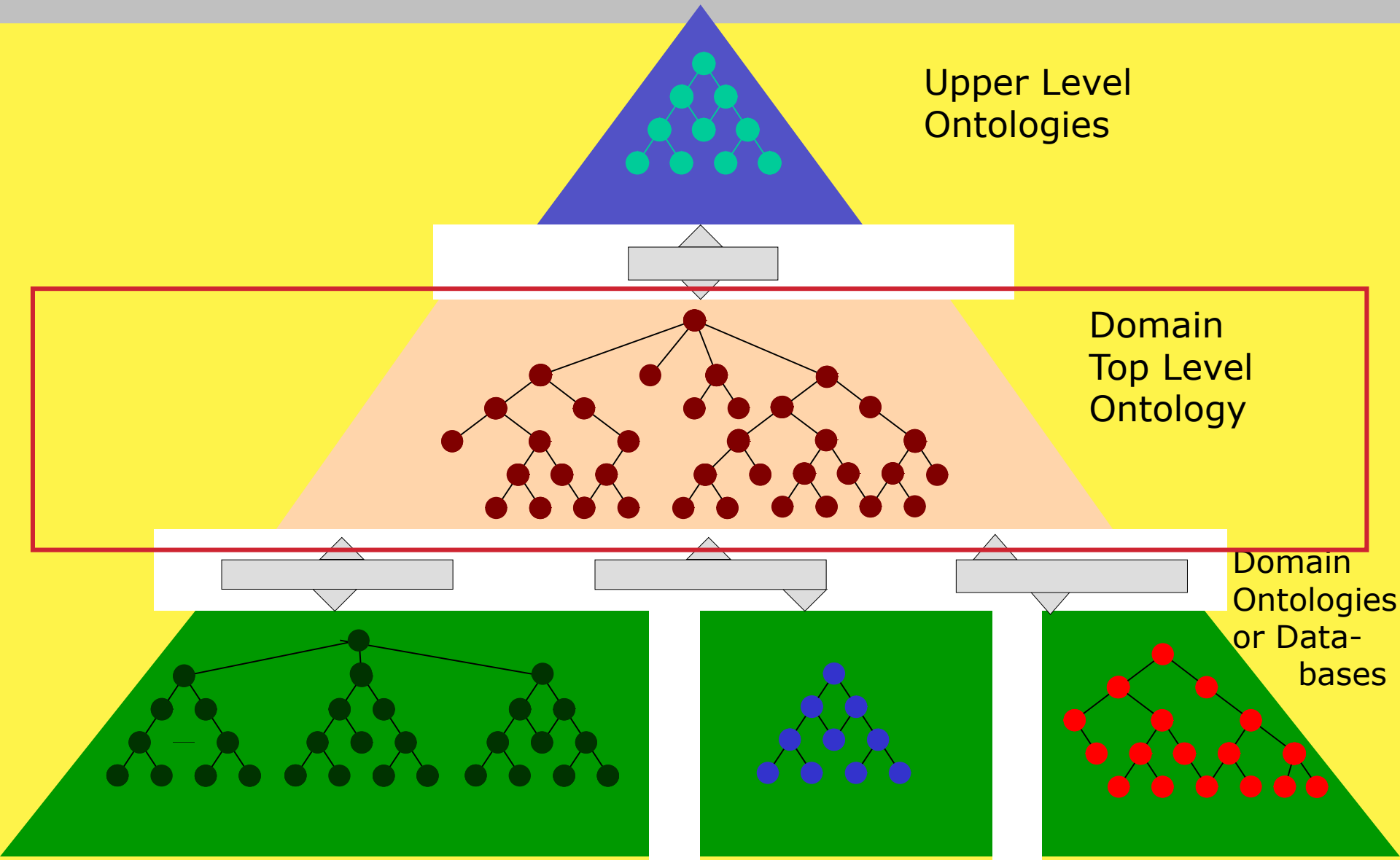
Ontology Stack



The Semantic Network of the UMLS