Machine learning with biomedical ontologies

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Learning Outcomes

- Introduce Ontologies and the description logic
- Discuss unsupervised machine learning methods that can “embed” from one structure to another
- Introduce different methods that use ontologies in machine learning models
- Introduce mOWL, a software library for machine learning with ontologies
- Incorporate mOWL in Biomedical data analysis using different approaches

Preliminaries: What are Ontologies?

- “ An ontology is a **logical theory** designed in order to capture the **intended models** corresponding to a certain conceptualization and to **exclude the unintended** ones” … Guarino 2009

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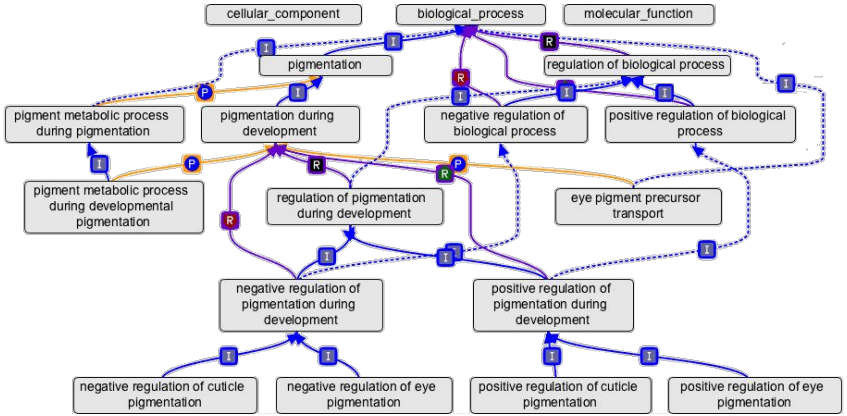
GENEONTOLOGY



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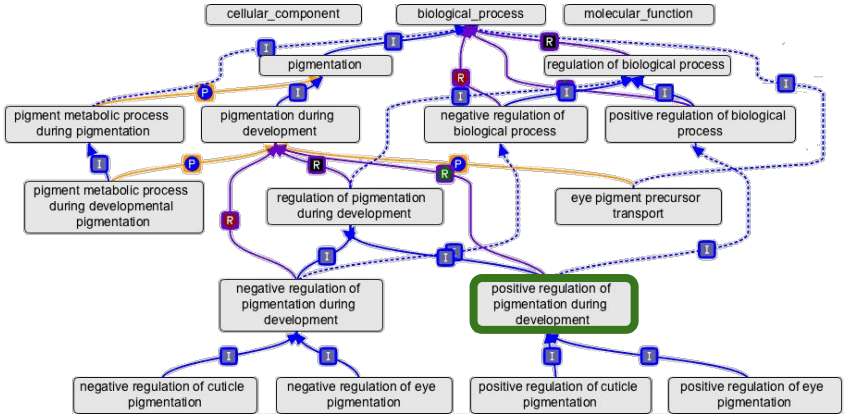

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$$positiveregulationofdevelopmentalpigmentation \equiv biologicalprocess \sqcap \exists positivelyregulates.developmentalpigmentation$$

$$positiveregulationofdevelopmentalpigmentation \sqsubseteq \exists positivelyregulates.developmentalpigmentation$$

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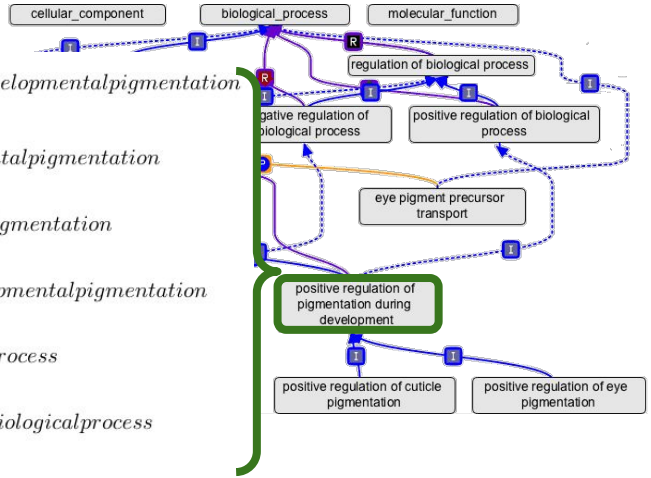
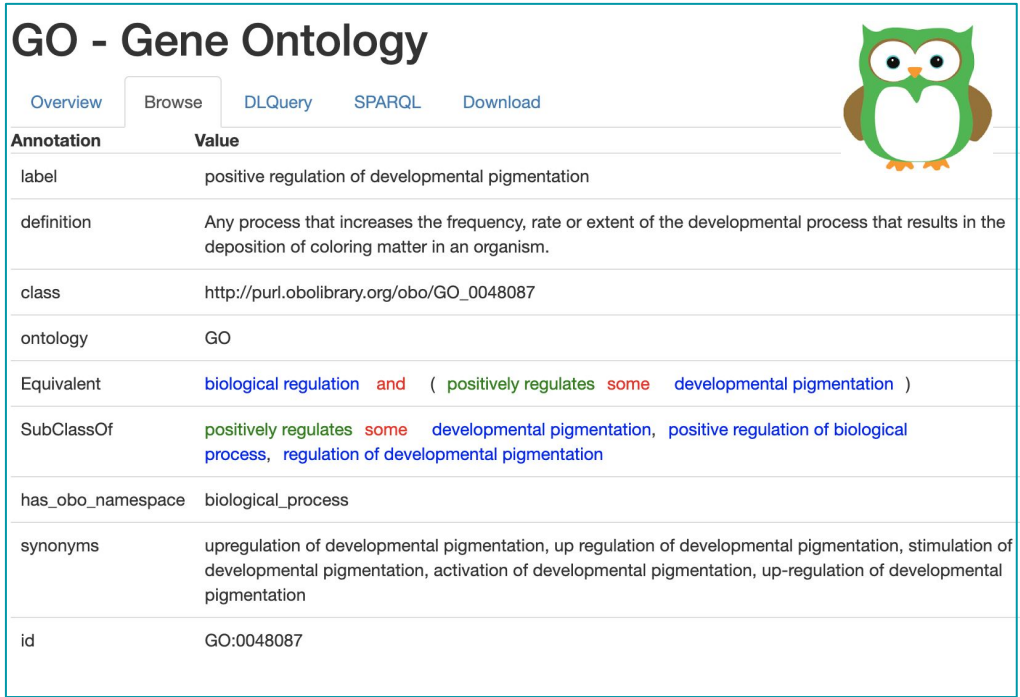


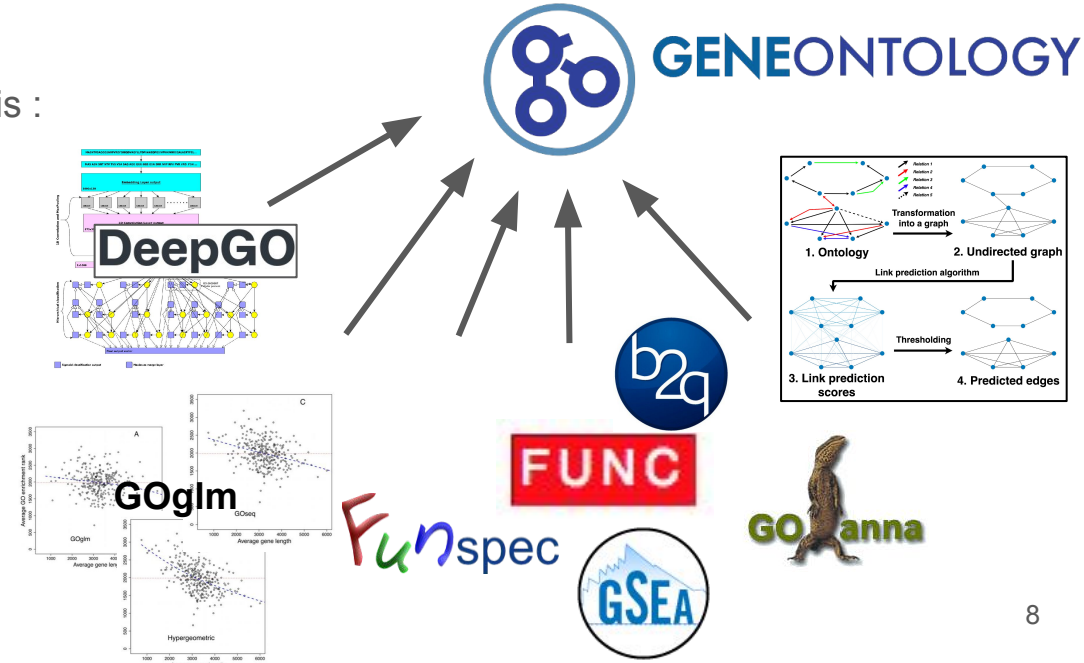
Preliminaries: What are Ontologies?

- " An ontology is a **logical theory** designed in order to capture the **intended models** corresponding to a certain conceptualization and to **exclude the unintended** ones" … Guarino 2009
- Classes and relations
- Standard identifiers
- Axioms and formal definitions
- Metadata:
  - Labels, Synonyms
  - database cross references
  - ….



Introduction

- Examples of ontologies application in biomedical domain:
  - Annotation and data integration
  - Ontologies as vocabularies
  - Statistical and predictive data analysis :
    - Enrichment analysis
    - Semantic similarity
  - Regression analysis
  - Relation prediction
  - Classification
    - Supervised
    - Unsupervised

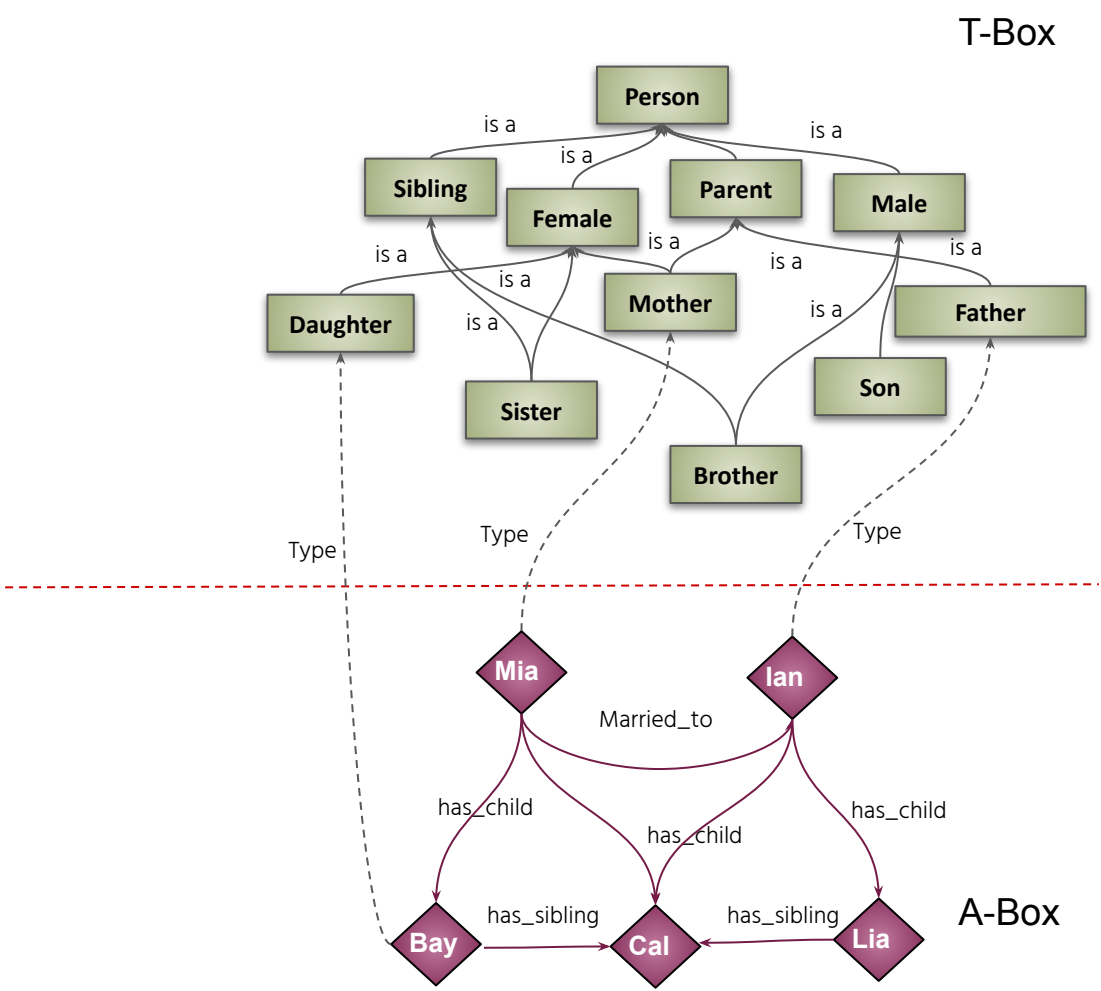


Preliminaries: ontologies

- Ontology consist of :

  O={C,R,I,⊢}

- T-Box
  - Set of terminological
- A-Box
  - Set of assertions



Preliminaries: ontologies

- Description Logic (DL) is used to formally and explicitly represent ontologies

Name	DL syntax	Semantics
Top concept	$\top$	$\Delta^{\mathcal{I}}$
Bottom concept	$\bot$	$\emptyset$
Concept	C	$C^{\mathcal{I}} \subseteq \Delta^{\mathcal{I}}$
Concept disjunction	$C_1 \sqcap C_2$	$C_1^{\mathcal{I}} \cap C_2^{\mathcal{I}}$
Concept conjunction	$C_1 \sqcup C_2$	$C_1^{\mathcal{I}} \cup C_2^{\mathcal{I}}$
Concept negation	$\neg C$	$\Delta^{\mathcal{I}} \backslash C^{\mathcal{I}}$
Universal restriction	$\forall R.C$	$\{x \in \Delta^{\mathcal{I}} \mid \forall y \in \Delta^{\mathcal{I}}((x,y) \in R^{\mathcal{I}} \wedge y \in C^{\mathcal{I}})\}$
Existential restriction	$\exists R.C$	$\{x \in \Delta^{\mathcal{I}} \mid \exists y \in \Delta^{\mathcal{I}}((x,y) \in R^{\mathcal{I}} \rightarrow y \in C^{\mathcal{I}})\}$
Subclass of	$C_1 \sqsubseteq C_2$	$C_1^{\mathcal{I}} \subseteq C_2^{\mathcal{I}}$
Subproperty of	$R_1 \sqsubseteq R_2$	$R_1^{\mathcal{I}} \subseteq R_2^{\mathcal{I}}$
Equivalent class	$C_1 \equiv C_2$	$C_1^{\mathcal{I}} = C_2^{\mathcal{I}}$
Equivalent property	$R_1 \equiv R_2$	$R_1^{\mathcal{I}} = R_2^{\mathcal{I}}$

Concepts , Roles

Person $\sqsubseteq \top$
Female $\sqcap$ ***Male*** $\sqsubseteq \bot$
Female $\sqcup$ ***Male*** $\sqsubseteq \top$
Female $\equiv \neg$ ***Male***
Parent $\equiv \exists$ ***has_child***. ***Person***
Son $\sqsubseteq$ ***Male*** $\sqcap \exists$ ***child_of***. ***Person***
Mother $\sqsubseteq$ ***Female*** $\sqcap$ ***Parent***
Sibling $\sqsubseteq \exists$ ***has_sibling***. ***Person***
has_brother $\sqsubseteq$ ***has_sibling***

Preliminaries: ontologies

- Description Logic (DL) is used to formally and explicitly represent ontologies

DL Syntax	Manchester Syntax
$C \sqcap D$	C and D
$C \sqcup D$	C or D
$\neg C$	not C
$\exists R.C$	R some C
$\forall R.C$	R only C
$(\geq nR.C)$	R min n C
$(\leq nR.C)$	R max n C
$(= nR.C)$	R exactly n C
$\{a\} \sqcup \{b\} \sqcup \ldots$	{a b ...}

Classes , Relations

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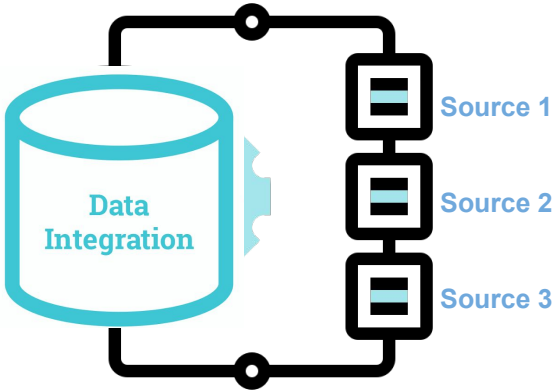
How Ontologies are used in Databases

- Annotations and data integration
  - Ontologies play a crucial role in facilitating data integration across databases due to their usage of standard identifiers for classes and relations



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How Ontologies are used in Databases

- Annotations and data integration

GAF fields

The annotation flat file format is comprised of 17 tab-delimited fields.

Column	Content	Required?	Cardinality	Example	
1	DB	required	1	UniProtKB	
2	DB Object ID	required	1	P12345	
3	DB Object Symbol	required	1	PHO3	
4	Qualifier	required	1 or 2	NOTlinvolved_in	
5	GO ID	required	1	GO:0003993	
6	DB:Reference (IDB:Reference)	required	1 or greater	PMID:2676709	
7	Evidence Code	required	1	IMP	
8	With (or) From	optional	0 or greater	GO:0000346	
9	Aspect	required	1	F	
10	DB Object Name	optional	0 or 1	Toll-like receptor 4	
11	DB Object Synonym (ISynonym)	optional	0 or greater	hToll	Tollbooth
12	DB Object Type	required	1	protein	
13	Taxon(Itaxon)	required	1 or 2	taxon:9606	
14	Date	required	1	20090118	
15	Assigned By	required	1	SGD	
16	Annotation Extension	optional	0 or greater	part_of(CL:0000576)	
17	Gene Product Form ID	optional	0 or 1	UniProtKB:P12345-2	

How Ontologies are used in Databases

- Annotations and data integration

1. UniProtKB
2. A0A024RBG1
3. NUDT4B
4. enables
5. GO:0003723
6. GO_REF:0000043
7. IEA
8. UniProtKB-KW:KW-0694
9. F
10. Diphosphoinositol polyphosphate phosphohydrolase
11. NUDT4B
12. NUDT4B
13. Protein
14. taxon:9606 20221109
15. UniProt
16.
17.

1. MGI
2. MGI:1913300
3. 0610009B22Rik
4. enables
5. GO:0001222
6. MGI:MGI:4834177|GO_REF:0000096
7. ISO
8. UniProtKB:P0DI82
9. F
10. RIKEN cDNA 0610009B22 gene
11.
12. protein_coding_gene
13. taxon:10090
14. 20210709
15. MGI
16.
17.

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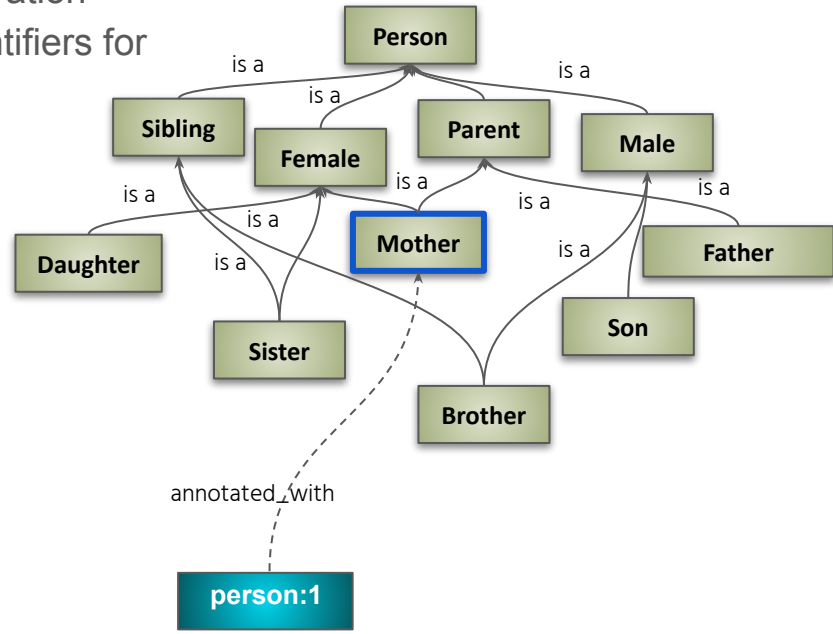

- True path rule:
  - Annotation for a class is passed to its ancestors

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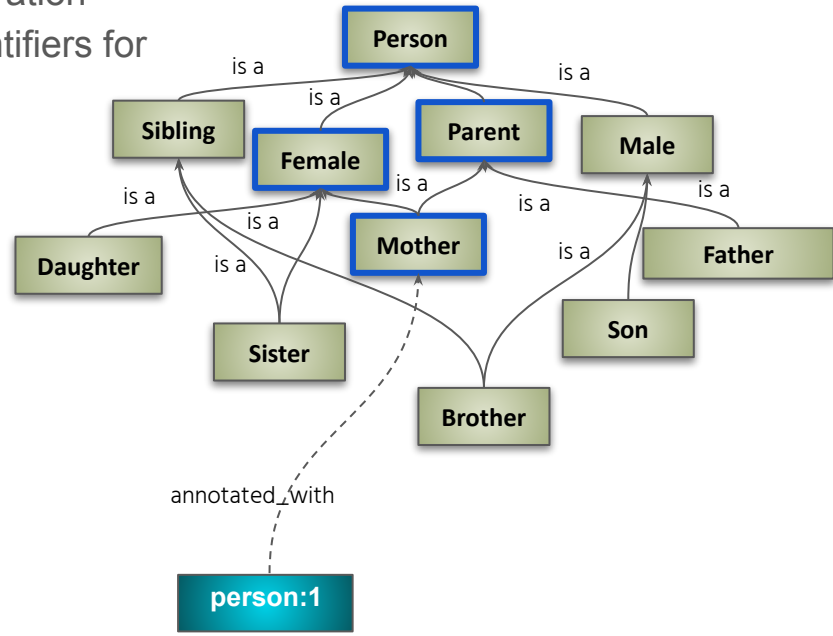

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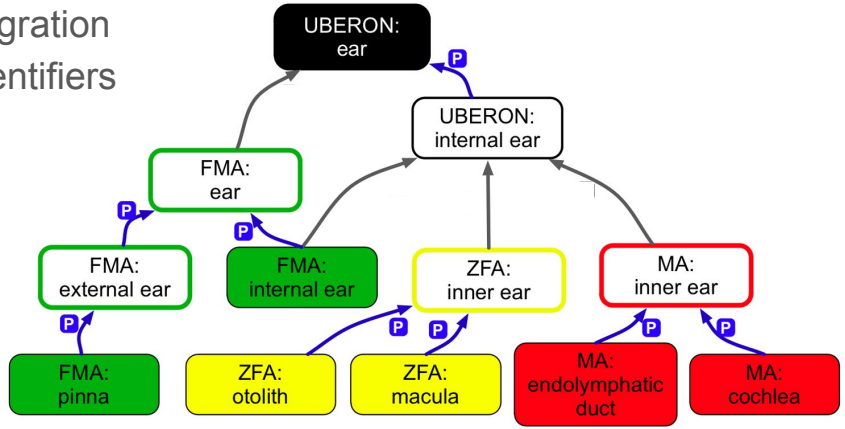

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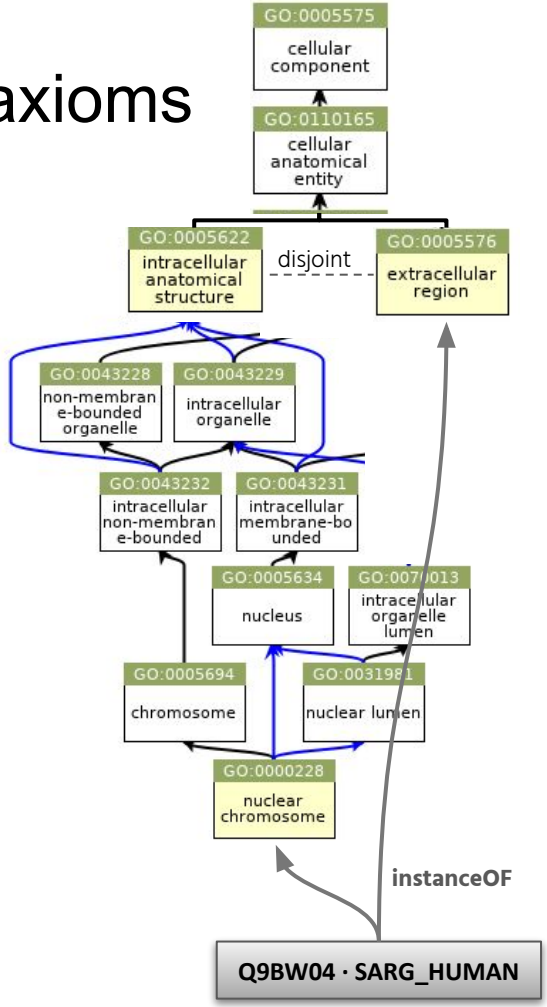
[1]Washington, N. L., Haendel, et al. (2009). Linking human diseases to animal models using ontology-based phenotype annotation. *PLoS biology*, 7(11), e1000247.

Transforming GO annotations to ontology axioms

- Problem when annotations are added as instances of GO classes



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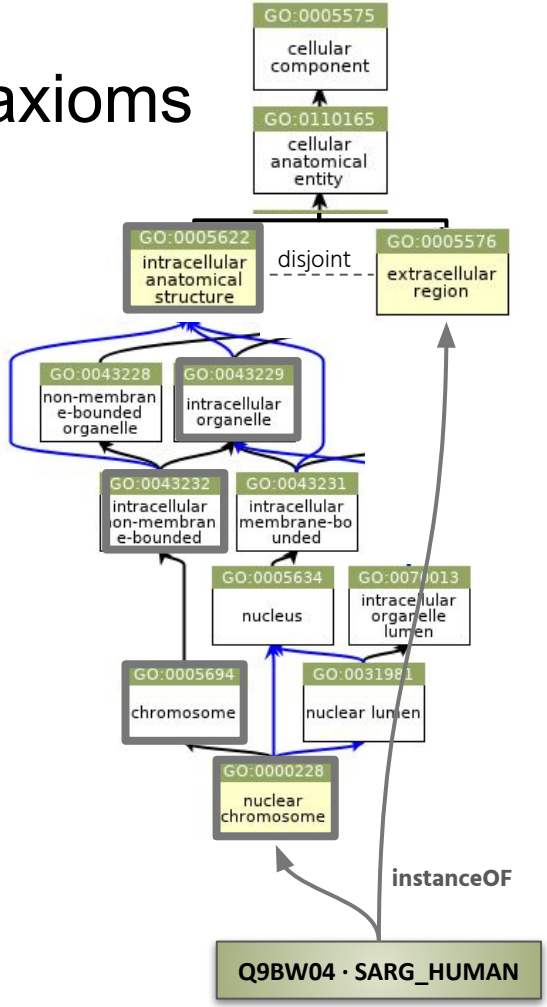

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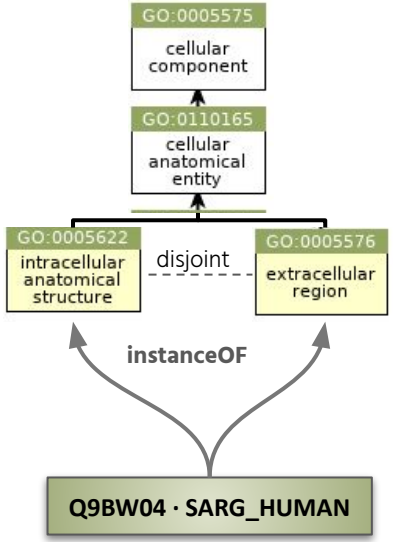
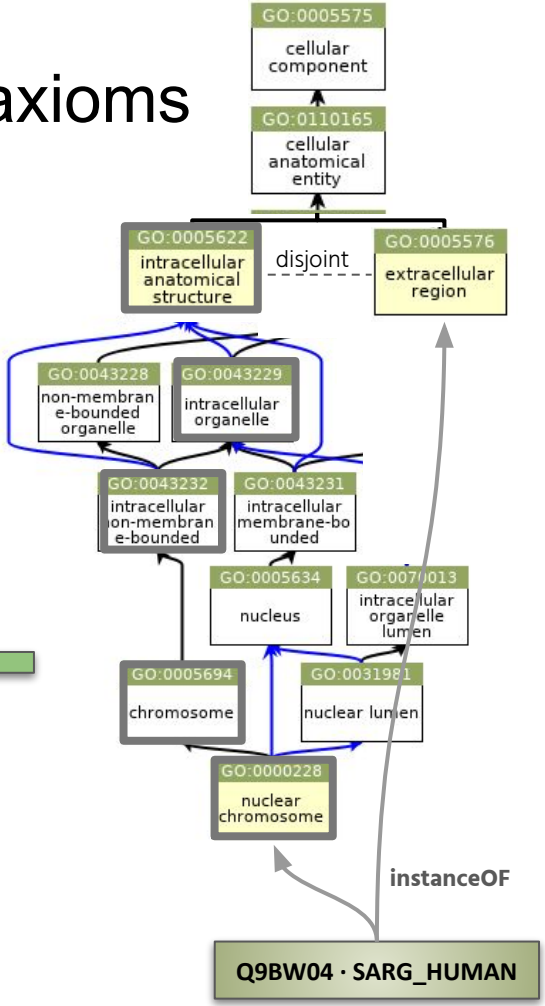




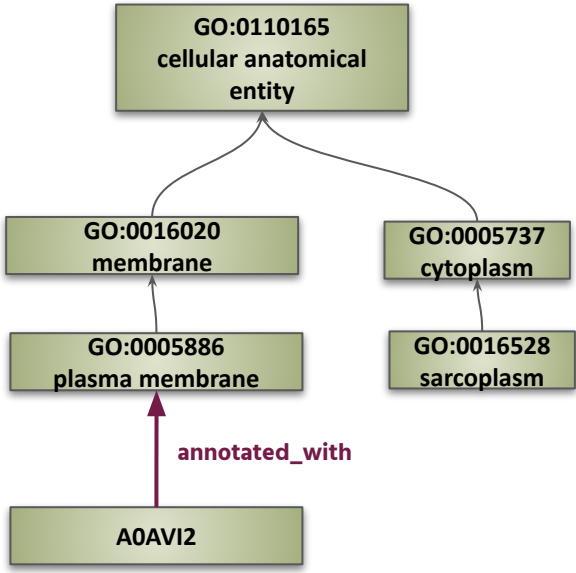
Transforming GO annotations to ontology axioms

- Annotations to T-Box

  The annotated entity **C** is added as a class to the ontology

  The annotation is added a relation R as follows

  $$\mathbf{C} \sqsubseteq \exists R.\ \mathbf{D}$$



Example:

Annotating protein **A0AVI2** To Gene Ontology

- $\mathbf{A0AVI2} \sqsubseteq \exists\ annotated\_with.\ \mathbf{Plasma\ membrane}$

T-Box

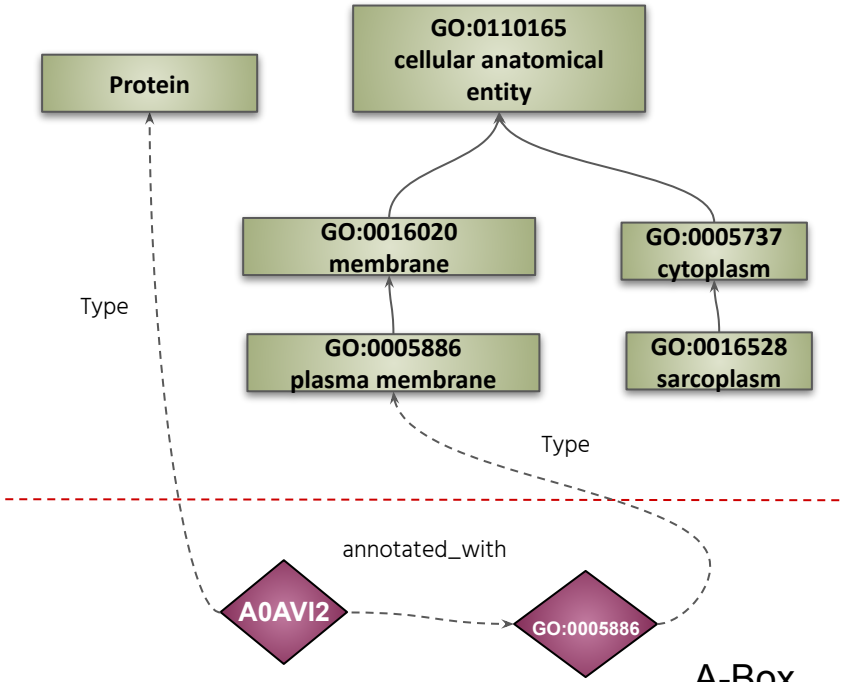
Transforming GO annotations to ontology axioms

Example:

Annotating protein **A0AVI2** To Gene Ontology

- Annotations to T-Box
  - ***A0AVI2*** $\sqsubseteq \exists$ *annotated_with.* ***GO:0005886***

- Annotations to A-Box
  - Protein(***A0AVI2***)
  - annotated_with(***A0AVI2, GO:0005886***)



Following this

- Ontologies and text mining → utilizing class labels and descriptions
- Graph based embedding → utilizing axioms and class labels and descriptions
- Syntactic embedding → utilizing axioms and class labels and descriptions
- Semantic embedding → utilizing axioms