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Homolonto: alignment of anatomical ontologies
More and more anatomical ontologies...

ZFIN
Zebrfish

FlyBase
Drosophila

Xenbase
Xenopus

eVOC
Human

emap edinburgh mouse atlas project
Human - Mouse
... and an ongoing effort to link them

- **Xenbase**
- **ZFIN**
- **CARO**
  Common Anatomy Reference Ontology
- **UBERON**
  Multi-species Anatomy Ontology
- **Teleost Anatomical Ontology**
- **MIAA**
  Minimum Information about anatomy
Evolutionary approach => appropriate comparison criterion: **Homology**

Strict Homology: two anatomical structures within different organisms which originated from a structure of their common ancestral organism.
Some problems:

- different but similar terms for the same organ
  human ontology: "intersubcardinal venous anastomosis"
  mouse ontology: "inter-subcardinal venous anastomosis"
Homology relationships between anatomies

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  "ganglion" defined only from its hierarchy

- different relationships between homologous terms
  
  human ontology: "optic vesicle" part_of "eye"
  zebrafish ontology: "optic vesicle" part_of "immature eye"
Homolonto

-Software to generate homology relationships
-Pairwise alignments of species-specific anatomical ontologies
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Classification of elementary matching approaches, Euzenat and Shvaiko
Homolonto

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Homolonto

O_2 \rightarrow Statistics \rightarrow User input \rightarrow Word matching \rightarrow P \rightarrow Structure matching \rightarrow P' \rightarrow H \rightarrow Weighting

O_1 \rightarrow \text{Iterate} \rightarrow User input \rightarrow A
Test case: Xenopus-zebrafish ontologies

anatomical structure - anatomical structure

opercular artery - external carotid artery

validated
invalidated

Score

Iteration

naris - nostril

neural tube - neurocoel
pronephric tubule - nephrostome
anterior presumptive neural plate - neuroectoderm inner layer
Test case: Xenopus-zebrafish ontologies

213 first pairs: 80% validated - contains 91% of homologs validated
Generating a multi-species ontology

-Homolonto: generates pairwise relationships between ontologies

ZFA:0000008 brain

EHDDAA:2629 brain

XAO:0000010 brain
Generating a multi-species ontology

-Homolonto: generates pairwise relationships between ontologies

ZFA:0000008 brain  
XAO:0000010 brain

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-Merging pairwise alignments: generates groups of homologs

HOG:0000157 brain

ZFA:0000008  
XAO:0000010

EHDDAA:2629
Generating a multi-species ontology

- Homolonto: generates pairwise relationships between ontologies

\[ \text{ZFA:0000008 brain} \leftrightarrow \text{EHDDAA:2629 brain} \]
\[ \text{XAO:0000010 brain} \]

- Merging pairwise alignments: generates groups of homologs

\[ \text{HOG:0000157 brain} \]

\[ \begin{align*}
\text{ZFA:0000008} \\
\text{XAO:0000010} \\
\text{EHDDAA:2629}
\end{align*} \]

=> List of Homologous Organs Groups (HOGs)
Generating a multi-species ontology

-HOGs need to be structured as an ontology to allow reasoning
-At a minimum, relationships amongst them have to be designed

![Diagram showing relationships between HOGs]

HOG:0000157 brain

part_of

HOG:0000383 forebrain

part_of

HOG:0000070 hindbrain

=>Algorithm to infer relationships between HOGs
Inferring relationships amongst HOGs

Retrieve all paths

HOGs composition statistics

Removing redundancies

Reconciliation between ontologies

Removing cyclic relationships

User input

HOG ontology

User input
Results

Use of Homolonto, followed by a curation process:
- 4 species: human, mouse, zebrafish, Xenopus
- 6 ontologies: ZFA, EHDDAA, EV, EMAPA, MA, XAO

HOG ontology in OBO:
- 1241 HOGs, 311 with description, 400 with synonyms
- 1595 relations, 367 part_of, 12 is_a

External Mapping file:
- involving 5314 anatomical structures
- all manually reviewed, providing evidence codes and references
Conclusion

The HOG ontology has been successfully implemented into Bgee

Application examples:

- Decrypthon: searching for genes involved in muscle dysfunctions
- CRESCENDO: nuclear receptors function throughout development

- Tissue expression complementarity after duplication
Perspective

Cross-species mapping: need for a representation formalism:

- Mapping of species-specific structures to a common ontology?

- What about mappings not based on homology (e.g. analogy)?
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SIB

CRESCEndo