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FUNCARO: A Functional Extension to CARO

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Abstract. Biological structures are commonly classified by functional as well as structural criteria. Here, I propose an upper ontology for functionally defined systems and other functionally defined anatomical structures such as sense organs and glands.

Keywords: function, gene ontology, biological process, anatomy, CARO

1 Introduction

"Structure without function is a corpse; function without structure is a ghost" [1]

Biological structures are commonly classified by functional as well as structural criteria. Some commonly used anatomical terms cannot be defined at all without referring to function: sense organ, gland, endocrine system.

For anatomy ontologies to be interoperable, we need to provide standard ways of classifying anatomical structures according to function. In order to make anatomy ontologies that combine structural and functional classification maintainable, these standards need to be suitable for use in auto-classification by reasoners [2].

The biological process sub-ontology of the gene ontology [3] has a wealth of definitions and classifications for biological processes. With a suitable bridging relation, these can be used to record function.

I propose a draft standard upper ontology, FUNCARO (FUNctional CARO), that combines terms from CARO [4] and the GO biological process ontology to provide a standard framework for functional classification of anatomical structures. I conclude with a discussion of some of the limitations of the approach.

2 Methods

Formal definitions are all given in OWL 2 DL [5], Manchester syntax [6]. **Object properties** are in bold, annotation properties are underlined, *Manchester syntax* itself is italicized.

Given the dominance of OBO 1.2 format in the bio-ontology world, I outline solutions for both OBO and OWL. Throughout this paper I use a nested class expression in OWL of the form "A **has_function** *some* (**realized_by** *only* P)" to define the functions of anatomical structures. ro.owl [8] defines a suitable relation for use in OBO ontologies: '**has_function_in**' is defined as an expansion [7] to '**has_function** *some* (**realized_by** *only* Y?).

IDs[1] for ontology terms mentioned:

multicellular organismal process; GO:0032501

detection of stimulus involved in sensory perception; GO:0050906

detection of chemical stimulus involved in sensory perception; GO:0050907

detection of chemical stimulus involved in sensory perception of taste; GO:0050912

secretion; GO:0046903

endocrine hormone secretion; GO:0060986

cortisol secretion; GO:0043400

immune response; GO:0006955

multicellular anatomical structure; CARO: 0010000

A draft version of FUNCARO, funcaro.owl, along with required imported files (funcaro_GO_helper_terms.owl and caro_2.owl, which in turn imports terms from PATO_helper.owl) can be found here: https://arthropod-anatomy-ontology.googlecode.com/svn/trunk/ontologies/trunk/

[1] IDs are in OBO format, for URI, replace ':' by _ and prepend "http://purl.obolibrary.org/obo/".

3 Results

3.1 Sense Organs

The gene ontology (GO) class 'detection of stimulus involved in sensory perception' has 30 subclasses that are fantastically useful for classifying sense organs and sensory neurons. These have been used to define over 1000 classes in the Drosophila anatomy ontology [9]. Unfortunately, CARO does not have a suitable term for organ that can be used as a general genus for classes of sensory organ. We need a term that can refer to small clusters of cells that form most of the sensory organs of arthropods [10] as well as the more complicated sense organs of vertebrates. One possibility is:

label: organ
definition: "A multicellular anatomical structure that is largely delimited by a morphological boundary."
SubClassOf: 'multicellular anatomical structure'

But this clearly applies to developing anatomical structures that nobody would refer to as organs. The term "organ" has strong connotations of function. For example, Henderson's dictionary of biological terms has the definition: "any part or structure of an organism adapted for a special function or functions" [12]. We reflect this functional criterion for class membership by adding a further clause to the definition and adding a functional restriction:

label: organ
definition: "A multicellular anatomical structure that is largely delimited by a morphological boundary and has parts that collectively function in some physiological process."
SubClassOf: 'multicellular anatomical structure'
SubClassOf: **has_function** *some* (**realized_by** *only* 'multicellular organismal process')

With organ defined, we can now use the GO 'detection of sensory stimulus' terms to define and auto-classify 31 sense organ terms. For example:

'sense organ' *EquivalentTo*: organ *that* **has_function** (**realized_by** *only* 'detection of stimulus involved in sensory perception')

'chemosensory organ' *EquivalentTo*: organ *that* **has_function** (**realized_by** *only* 'detection of chemical stimulus involved in sensory perception')

'gustatory organ' *EquivalentTo*: organ *that* **has_function** (**realized_by** *only* 'detection of chemical stimulus involved in sensory perception of taste')

'detection of chemical stimulus involved in sensory perception of taste' *SubClassOf* 'detection of chemical stimulus involved in sensory perception' *SubClassOf* 'detection of stimulus involved in sensory perception'

∴ 'gustatory organ' *SubClassOf* 'chemosensory organ' *SubClassOf* 'sense organ'

GO also defines sensory perception classes that these 'detection of stimulus' classes are part of. If these more general terms are used to define the functions of neurons and neural circuits involved, then we can use reasoning to define perceptual systems.

3.2 Functionally Defined Systems

For functionally defined systems such as the respiratory system, the endocrine system, or the immune system we need to automate population of a partonomy, rather than classification under the system term.

It is useful to define a genus term for functional systems:

label: 'functional system'
definition: "A material anatomical entity defined by the common function of its component parts. These parts may or may not be connected to form a single structure."
SubClassOf: 'material anatomical entity'
SubClassOf: **has_function** *some* (**realized_by** *only* 'multicellular organismal process')

Individual functional systems are subclasses of this. For example:

label: endocrine system
EquivalentTo: '**functional system**' *that* **has_function** *some* (**realized_by** *only* 'endocrine hormone secretion'

A term for components of this system populates the partonomy:

label: endocrine system component
EquivalentTo: 'anatomical structure' *that* **has_function** *some* (**realized_by** *only* 'endocrine hormone secretion'
SubClassOf: **part_of** *some* 'endocrine system'

Or, if implementing entirely in OWL, we can replace this with a general class axiom:

'anatomical structure' *that* **has_function** *some* (**realized_by** *only* 'endocrine hormone secretion' *SubClassOf*: **part_of** *some* 'endocrine system

With these in place, if we define:

'adrenal gland' *SubClassOf*: **has_function** *some* (**realized_by** *only* 'cortisol secretion')

'cortisol secretion' *SubClassOf* 'endocrine hormone secretion'

∴ 'adrenal gland' **part_of** *some* 'endocrine system'

3.3 Glands

Glands are another type of structure that it is only possible to define functionally. We can define glands as types of organ that function in secretion. For example:

gland *EquivalentTo*: organ *that* **has_function** *some* (**realized_by** *only* secretion)

'endocrine gland' *EquivalentTo*: organ *that* **has_function** *some* (**realized_by** *only* 'endocrine hormone secretion')

'adrenal gland' *SubClassOf*: **has_function** *some* (**realized_by** *only* 'cortisol secretion')

'cortisol secretion' *SubClassOf* 'endocrine hormone secretion' *SubClassOf* 'secretion'

∴ 'adrenal gland *SubClassOf* 'endocrine gland' *SubClassOf* gland

4 Discussion

4.1 Definition of Organ

The definition of organ here is an improvement on existing purely structural definitions (for example, see the FMA) in that it much better reflects actual usage of the term across species. However, there is still room for improvement, particularly in adding restrictions on the types of boundary that organs can have and in narrowing down the kinds of functions which are required for an anatomical structure to be an organ.

4.2 Potential Problems with Using GO

One of the major challenges to this approach is coordination with the Gene Ontology to make sure that suitable terms are available. In some cases, there is some circularity with Gene Ontology term definitions that we need to resolve. For example, the term 'immune response', which one might expect to be ideal for defining an immune system and its components, references the immune system:

label: immune response
definition: "Any immune system process that functions in the calibrated response of an organism to a potential internal or invasive threat."

The general term 'gland' may also be problematic. GO defines excretion as a subtype of secretion. So by our definition, an excretory organ is a gland. This is certainly not what biologists would expect. One possible way around this is to define glands as sites of both synthesis and secretion, but this is also likely to have exceptions.

4.3 Conclusions

The GO biological process ontology contains a wealth of terms that can be used as functional differentia for defining anatomical classes. Even without additional work, many of these can be used successfully to classify large numbers of anatomical classes. In this paper I have demonstrated the utility if GO terms for functional classification, expanding on an approach that has already been very widely used in the Drosophila anatomy ontology to classify sense organs and sensory neurons [9].

In collecting examples of functional classification in an upper ontology constructed using CARO, FUNCARO provides design patterns for anatomy ontology editors to follow in their work, and so encourages much-needed harmonization of approaches across multiple anatomy ontologies.

In some cases, successful functional classification using GO will require collaboration with GO editors to better define terms. The Gene Ontology editors are very responsive to requests for correction or review of term definitions and their relationships via their tracker [11]. Collaboration with anatomists could also be of benefit to GO – improving and clarifying the terms they have and adding missing terms.

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