Virtual Fly Brain: An ontology-linked schema of the *Drosophila* Brain

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Abstract

Drosophila neuro-anatomical data is scattered across a large, diverse literature dating back over 75 years and a growing number of community databases. Lack of a standardized nomenclature for neuro-anatomy makes comparison and searching this growing data-set extremely arduous.

A recent standardization effort [1] has produced a segmented, 3D model of the Drosophila brain annotated with a controlled vocabulary. We are formalizing these developments to produce a web-based ontology-linked atlas in which gross brain anatomy is defined, in part, by labelled volumes in a standard reference brain.

We have developed new relations that allow us to use this well-defined gross anatomy as a substrate to define neuronal types according to where they fasciculate and innervate as well as to record the neurotransmitters they release, their lineage and functions. The resulting ontology will provide a vocabulary for annotation and a means for integrative queries of neurobiological data.

The ontology and associated images, queries and annotations will be integrated into the Virtual Fly Brain website with the aim of providing a system that neuro-biologists can use for browsing and structured queries of neuro-anatomy and related data without any need for ontology expertise.

[1] http://jfly.iam.u-tokyo.ac.jp/temp/janelia

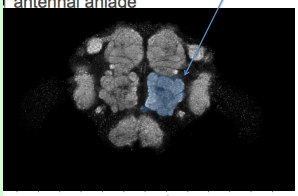
Virtual Fly Brain website mockup

Search as you type

Browse-able image stack
– volume defining chosen term highlighted
– terms can be chosen by clicking image
– slider moves image through Z-series

Term Name: (Include obselete terms)

antennal
antennal disc
antennal lobe
antennal nerve
antennal anlage



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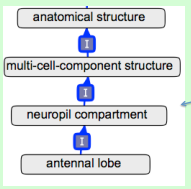
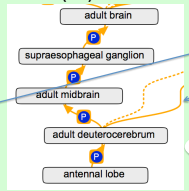
id: FBbt:00003924
name: antennal lobe
def: "A paired neuropil compartment of the deutocerebrum lying in front of the protocerebral neuropil compartments. The two antennal lobes are connected by the antennal commisure and receive odorant receptor neuron axons from the antennal nerve and antenno-subesophageal tract. Each lobe is also connected to the antenno-cerebral tracts and the broad root and is divided into about 50 glomeruli." [Stocker et al., 1990, Cell Tissue Res. 262(1): 9--34]
is_a neuropil compartment
part_of: adult deutocerebrum
connected_to: antennal nerve
connected_to: antenno-subesophageal tract
connected_to: broad root
connected_to: inner antenno-cerebral tract
connected_to: outer antenno-cerebral tract
connected_to: antennal commisure

We thank Arnim Jenett for kindly allowing us to use his labeled image stack.

What is (the) antennal lobe?



What is (the) antennal lobe part of?



Clickable graphs for context and browsing

Users enter query elements via search-as-you-type

Template queries:
• Find neurons that innervate (the) [antennal lobe] and innervate (the) [lateral horn]
• …

drives OWL-DL query via FaCT++ reasoner

Query (class expression)

neuron and innervates some ('antennal lobe' or part_of some 'antennal lobe') and innervates some ('lateral horn' or part_of some 'lateral horn')

Execute | Add to ontology

Query results

Descendant classes (4)
'DA1 vPN'
'DL1 adPN'
'VA1lm lPN'

Super classes
Ancestor classes
Equivalent classes
Subclasses

Statements integrated by reasoner to find 'DL1 adPN'.

Note, the definition of innervates means that this query works despite using a more general relationships than those used to record innervation by 'DL1 adPN'.

Annotation finder
•Find genes expressed in these structures
•Find GAL4 drivers expressed in these structures
•Find alleles causing phenotypes in these structures

Mines FlyBase data for annotations using the terms found by queries

Classifying neurons requires new relations.

NAME: **fasciculates_with** **DOMAIN**: neuron **RANGE**: neuron projection bundle
DESCRIPTION: Relation between a neuron and the neuron projection it fasciculates with.
DEFINITION: x **fasciculates_with** y iff: for some 'neuron projection' (np), np **part_of*** x AND np **overlap*** y AND np **aligned_with**** y
NOTE: This fits well with the PATO textual definition of fasciculated: "A structural quality inhering in a bearer by virtue of the bearer's forming a bundle of aligned anatomical fibers, as of muscle or nerve."

NAME: **synapsed_to** **DOMAIN**: neuron OR (**part_of** some neuron) **RANGE**: unrestricted
DEFINITION: n1 **synapses_with** n2 iff: for some synapse (s), some presynaptic membrane (pre), some postsynaptic membrane (post): pre **part_of** s AND post **part_of** s AND pre **part_of** n1 AND post **part_of** n2

NAME: **synapsed_by** **DOMAIN**: unrestricted **RANGE**: neuron OR (**part_of** some neuron)
DEFINITION: n1 **synapsed_by** n2 iff: for some synapse (s), some presynaptic membrane (pre), some postsynaptic membrane (post): pre **part_of** s AND post **part_of** s AND pre **part_of** n2 AND post **part_of** n1

NAME: **dendrite_innervates** **DOMAIN**: neuron **RANGE**: unrestricted (?)
DESCRIPTION: Relation between a neuron and the structure in which its dendrite receives synapses.
DEFINITION: x **dendrite_innervates** y iff: for some dendrite (d), d **part_of** x AND x **synapsed_by** y

NAME: **axon_innervates** **DOMAIN**: neuron **RANGE**: unrestricted
DESCRIPTION: Relation between an axon and the structure it synapses to
DEFINITION: x **axon_innervates** y: iff: for some axon (a), a **part_of** x AND x **synapsed_to** y

NAME: **innervates**
DEFINITION: dendrite_innervates OR **axon_innervates**
NOTE: Defining a general innervates relation allows recording and querying of innervation when direction is unknown.

NAME: **releases_neurotransmitter** **DOMAIN**: neuron **RANGE**: chemical entity
DESCRIPTION: Relation between a neuron and the neurotransmitter it releases.
DEFINITION: x **releases_neurotransmitter** y iff: for some 'neurotransmitter secretion' (ns), x **has_function_in*** ns AND ns **has_participant*** y

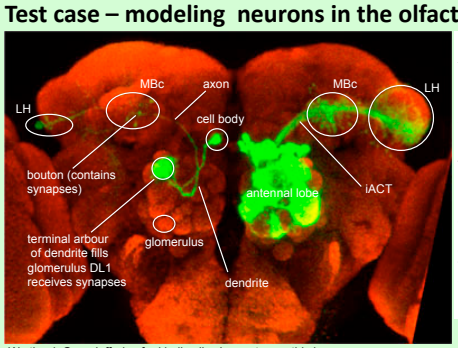
CONVENTIONS: **instance_level_relations_in_bold_with_undercores;** types are underlined; instances are lower case strings of letters and numbers. An instance of some specific type is referred to by the idiom: some type (instance). Types referred to come from GO:biological_process, GO:cellular_component, CHEBI or the Drosophila anatomy ontology. iff = if and only if.
* Indicates relations already in ro.obo or ro_proposed.obo
** PATO relational quality

New relations allow 'necessary and sufficient' definitions for many neuronal classes, for example:

name: cholinergic neuron
EquivalentTo: neuron and **releases_neurotransmitter** some acetylcholine

name: olfactory receptor neuron
EquivalentTo: neuron and **has_function_in** some detection of chemical stimulus involved in sensory perception of smell (GO)

Test case – modeling neurons in the olfactory system



We thank Greg Jefferies for kindly allowing us to use this image.

Antennal lobe projection neurons: fruit fly brain with labelled **antennal lobe projection neurons** (green). On the **left,** a single neuron, **DL1 adPN** has been labeled, on the **right** a clonally related group of **30 cells derived from** a single neural stem cell **neuroblast adPN**. Each of the labeled neurons has a dendrite that innervates a single antennal glomerulus and an axon that passes through the inner antenno-cerebral tract (**iACT**) to innervate the mushroom body calyx (**MBc**) and the lateral horn (**LH**).

name: antennal glomerulus DL1
is_a: gomerulus
SubClassOf: **part_of** some antennal lobe

name: DL1 adPN
def: "Antennal lobe projection neuron from the ad PN neuroblast lineage with a dendrite that innervates antennal glomerulus DA1 and an axon that fasciculates in the inner antenno-cerebral tract (iACT) and innervates the mushroom body calyx (MBc) and lateral horn (LH)." [FlyBase:FBrf0141667]
is_a: antennal lobe projection neuron
SubClassOf: **fasciculates_with** some inner antenno-cerebral tract (iACT)
SubClassOf: **develops_from** some adPN neuroblast
SubClassOf: **dendrite_innervates**: some antennal glomerulus DL1
SubClassOf: **axon_innervates** some mushroom body calyx (MBc)

name: ORN ab1A
def: "A cholinergic olfactory neuron whose sensory dendrite terminates in an ab1 basiconic sensillum and whose axon fasciculatr the antennal nerve that innervates antennal glomerulus DA1." [FlyBase:FBrf0187305]
is_a: neuron
SubClassOf: **fasciculates_with** some antennal nerve
SubClassOf: **axon_innervates** some antennal glomerulus DL1
SubClassOf: **part_of** some basiconic sensillum ab1 (?)
SubClassOf: **releases_neurotransmitter** some acetylcholine (CHEBI)
SubClassOf: **has_function_in** some detection of chemical stimulus involved in sensory perception of smell (GO)
is_a (inferred): olfactory receptor neuron
is_a (inferred): cholinergic neuron

Classifications inferred by reasoner

Unresolved issue:
What is the relationship between a sensory dendrite and the sense organ it is stimulated in? Biologists commonly use innervates for this, but our definition of innervates requires synapses. The above example uses **part_of**, but this may not be suitable.