A Visual Web Query System for NeuronBank Ontology

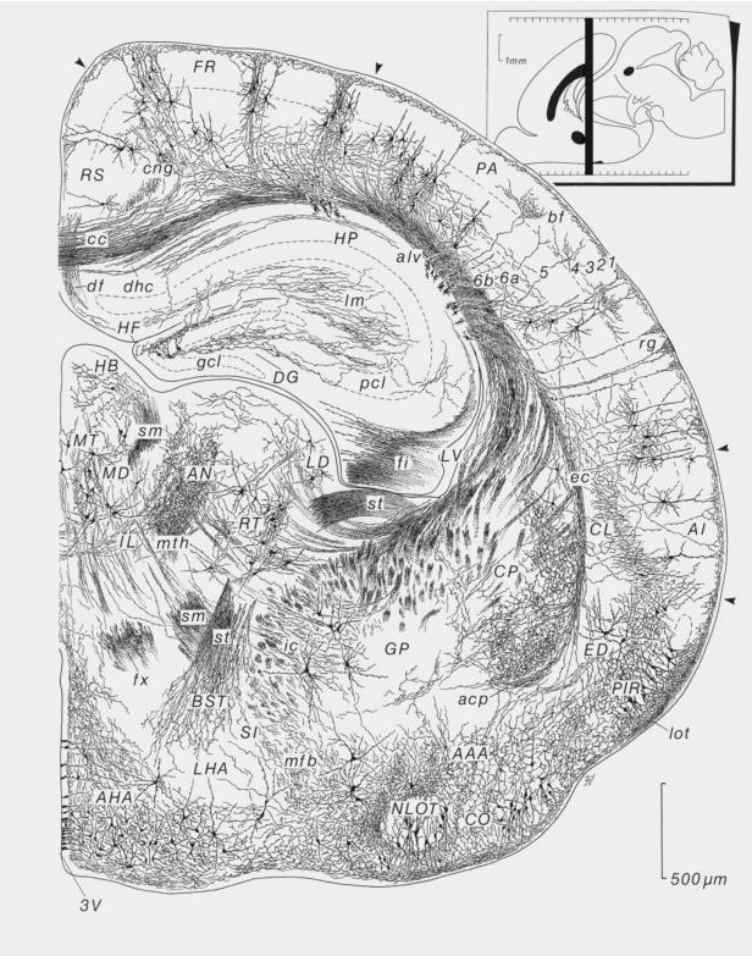
Weiling Li, Rajshekhar Sunderraman, and Paul Katz

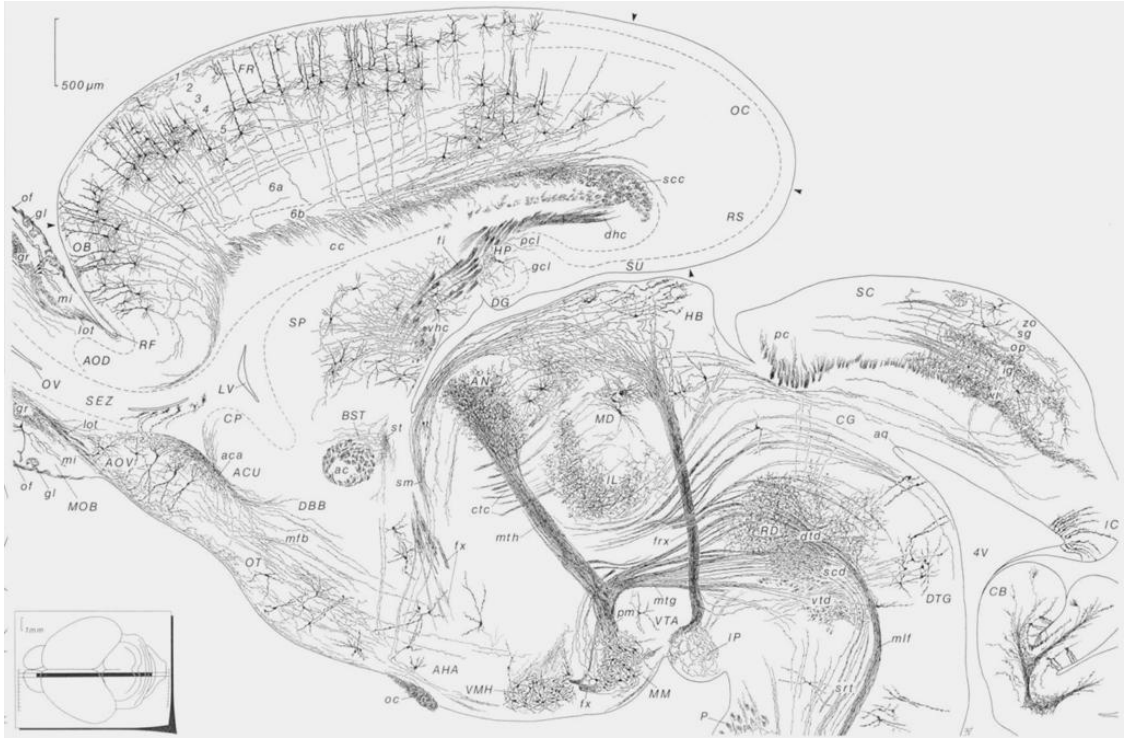
Georgia State University, Atlanta, GA

Outline

- Introduction
- Query sub-system overview
- Comparison with other visual query systems
- Conclusion

Understanding the brain requires understanding its circuitry

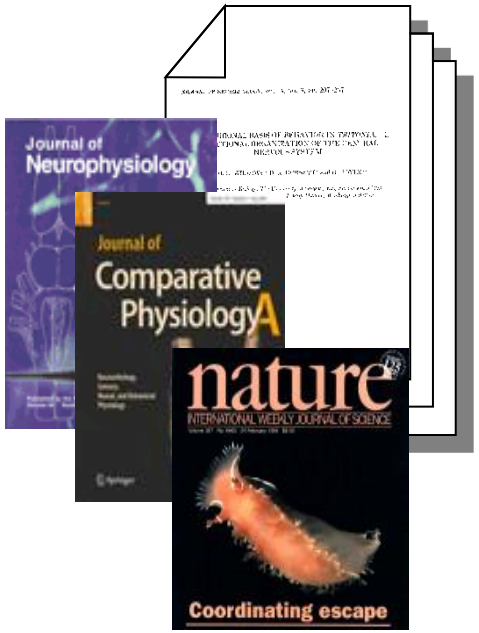




http://www.cajal.csic.es/V

Problem: We are using publications as a method to catalog neurons and neural circuits

- Information is distributed and fragmented.
- No means to efficiently search this knowledge.
- No means to publish incremental knowledge without a functional story.



Our Approach

- Traditional databases are not a good fit for the problem of storing information about neural circuitry
- Changes in representation would cause the database schema to change
- *Ontology:* A formal representation of a set of concepts within a domain and the relationships between those concepts
- We created a ontology for each species built upon the premise that some concepts are common across species.

NeuronBank.org: A Neuromics Tool

- NeuronBank is to neurons.
  - A place to publish knowledge about neurons and neural connectivity
  - A tool to search, analyze, and share knowledge of neurons and neural circuitry.
  - An ontology-based knowledge base system

NeuronBank.org: A Neuromics Tool

NeuronBank | Central

Guest | Login | New Account

Home

Search

- Branch Listing
- About
- Using NeuronBank
- News
- Resources
- Contact
- Home

Welcome to NeuronBank™ - Cataloging the "Neurome"

This is the homepage for the NeuronBank project, an effort to develop an online reference source and informatics tool for exploring our vast knowledge of identified neurons and the circuits they form. NeuronBank will organize information about identified neuron location, physiology, morphology, and connectivity, and help researchers to browse through known circuits, conduct comparative work between species, and classify new cell types. You can learn more about the rationale and design of the project here.

To get started with NeuronBank - Go to Branch Listing and choose a branch to explore or go to Using NeuronBank to get specific instructions or visit the Help, where you can also see a list of known bugs? NeuronBank also has its own Wiki for extended information about any entry. Registered users can contribute to this wiki.

The NeuronBank project is being developed as a collaborative effort across the Biology and Computer Science Departments at Georgia State University. The project team is led by Paul S. Katz, Sushil Prasad, Raj Sunderraman, and Ying Zhu.

The project is funded by grant from the Human Brain Project (NIH, NIMH R21 MH076753). The project was initiated with a seed grant from the GSU Brains and Behavior program. Additional funding was provided by NSF, NIH/NINDS, and the Center for Behavioral Neuroscience.

Join the list serve for users and developers to get updates about NeuronBank and to participate in discussions about its development. http://mailbox.gsu.edu/mailman/listinfo/neuronbank

Note - this application is compatible with **Firefox** and **Internet Explorer**. There are problems with Safari

NeuronBank.org: A Neuromics Tool

NeuronBank | Central

Guest | Login | New Account

Branch Listing

Search

- Branch Listing
- About
- Using NeuronBank
- News
- Resources
- Contact
- Home

Branch Listing

Branch	Prefix	Neurons	Permissions
Tritonia	Tri	43	Guest
SandBox	Sbx	26	Guest
Melibe	Mel	2	Guest

Instructions

- Click on the name of a branch to begin searching that branch.
- Each branch represents knowledge about neurons and synaptic connections of a species.
- Cross branch searches can be initiated from within any branch.
- The Prefix column is the three letters that precede all accession IDs for that branch.
- The number of neurons currently represented in each branch is shown.
- The last column shows your permissions for each branch. If you are not logged in, then your permissions are set to Guest.

NeuronBank.org: A Neuromics Tool

NeuronBank | *Tritonia*

Login | NewAccount

Central > Branch List > Tritonia > **Branch Home**

Find: On Tritonia Go

Branch Home

Browse Neurons

Search

Anatomical Search

This is the Home page for the *Tritonia* branch of NeuronBank. It contains information about the nervous system of *Tritonia diomedea* (Order: Nudibranchia, Subclass: Opisthobranchia, Class: Gastropoda, Phylum: Mullusca)

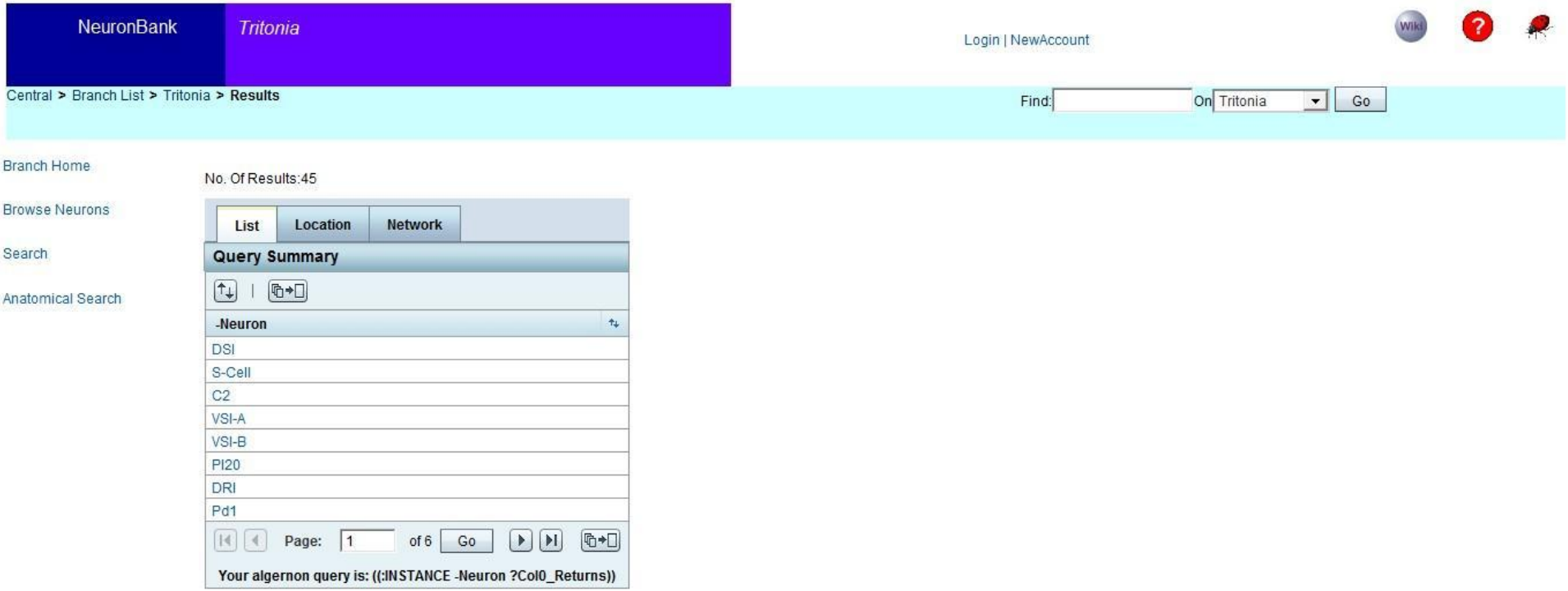
For more information about Tritonia, go to http://www.scholarpedia.org/article/Tritonia

The NeuronBank Wiki contains additional information about *Tritonia* neurons and connections including definitions for the ontology.

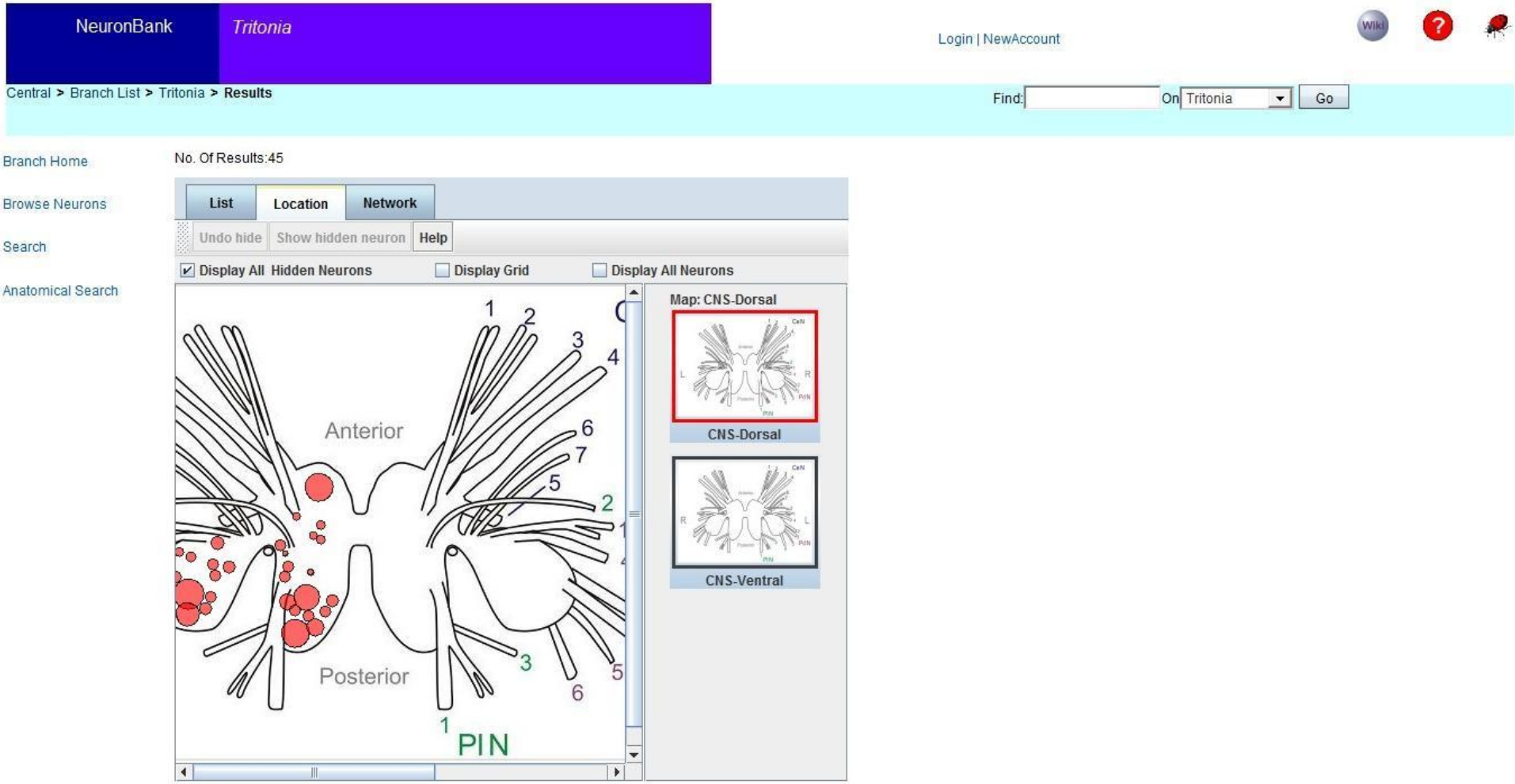
A simple URL for this page is http://www.neuronbank.org/branch/Tritonia

This knowledgebase is still under development. The project is funded by grant from the Human Brain Project (NIH, NIMH R21 MH076753). Previous support was from: NIH/NINDS, NSF, the GSU Brains and Behavior program, the Center for Behavioral Neuroscience, and a GSU RPE award. Join the Discussion Group for users to get updates about NeuronBank and to participate in discussions about its development

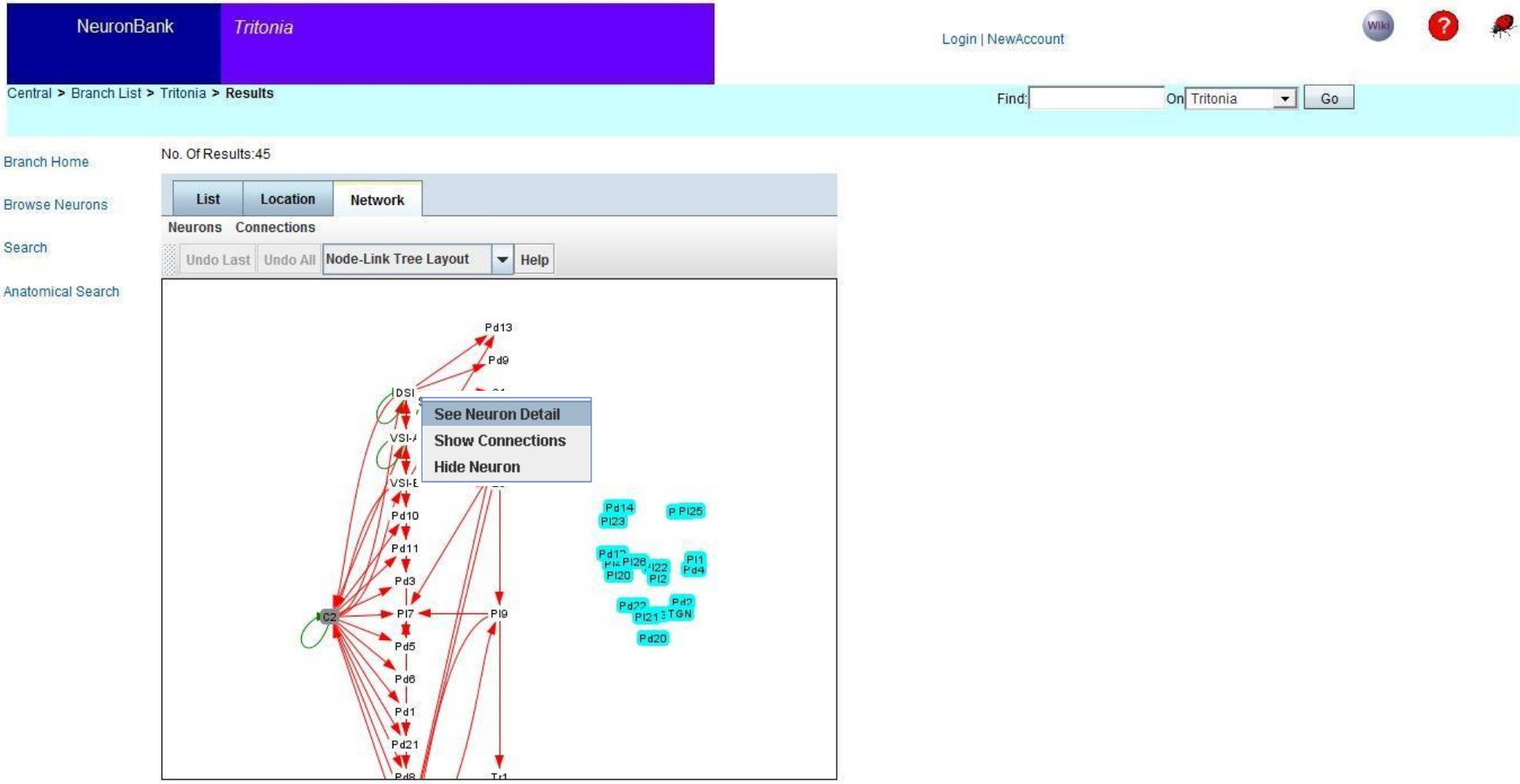
NeuronBank.org: A Neuromics Tool



NeuronBank.org: A Neuromics Tool



NeuronBank.org: A Neuromics Tool



NeuronBank.org: A Neuromics Tool

NeuronBank | *Tritonia*

Login | NewAccount

Central > Branch List > Tritonia > Results > **Detail**

Find: On Tritonia Go

Branch Home

Browse Neurons

Search

Anatomical Search

Back Forward

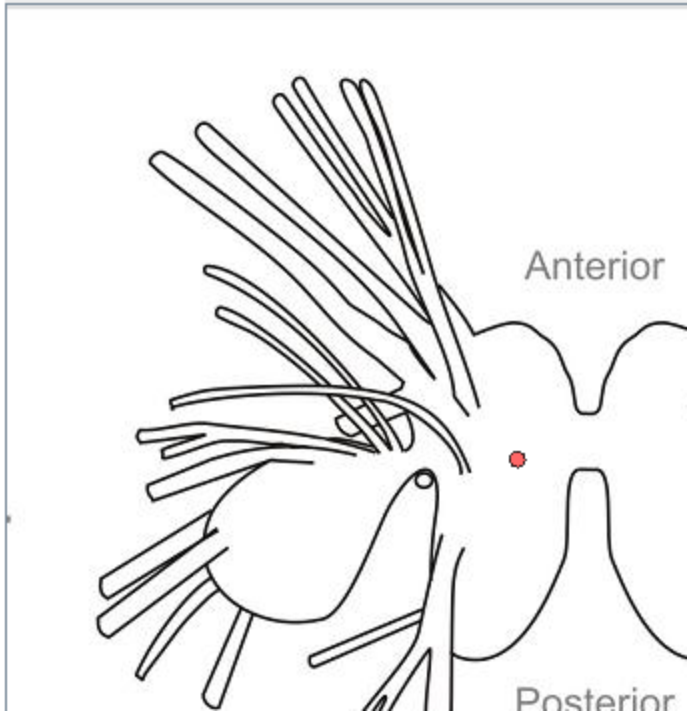
-Neuron - DSI

Property	Value
:CREATOR	Robert Calin-Jageman
:MODIFIER	pkatz
:MODIFICATION-TIMESTAMP	Jan 17, 2009
:CREATION-TIMESTAMP	May 21, 2006
-AccessionID	Tri0001043
:NAME	DSI
-Alias	Dorsal Swim Interneuron, Swim Interneuron, SI, DSI-A, DSI-B, DSI-C
-Cell_Count	3
-Soma_Coloration	Clear
-Swim_Phase	Dorsal
-Soma_Laterality	Bilateral
-Neuron_Type	Interneuron
-Behavior	Swimming
-Molecule	5HT
-Nerve_Projection	PdN5 [Annotations: 1]
-Activity_Resting	Irregular
-Soma_diameter	75+/-25 microns [Annotations: 2]

Location:

Undo hide | Show hidden neuron | **Help**

☑ **Display All Hidden Neurons** ☐ **Display Grid**



DSI

(Redirected from Tri0001043)

DSI is a Neuron in Tritonia.

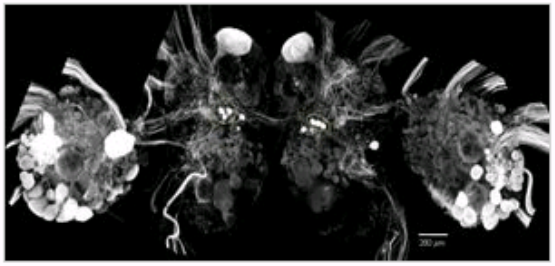
Contents [hide]

1 Basic information
2 Identification
3 Homology
4 References

Basic information

[edit]

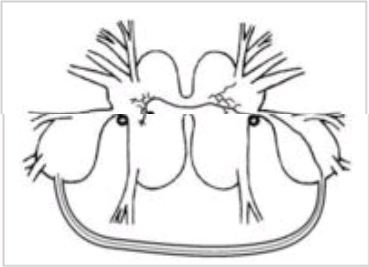
- **NeuronBank AccessionID** Tri0001043
- **Names and Aliases**- Dorsal Swim Interneuron, DSI, DSI-A, DSI-B,C, or just swim interneuron.
- **Species:** *Tritonia diomedea*
- **Neurotransmitter:** Serotonin



Serotonin immunohistochemistry shows the locations of the DSIs (circled).

There are three DSIs in each hemisphere of the cerebropleural ganglion. All three are serotonin-immunoreactive. They have axons that project contralaterally to the pedal ganglion. The DSIs play an important role in the swim central pattern generator. They have both synaptic and neuromodulatory actions on other neurons in the CPG. The DSIs also accelerate ciliary crawling by synapsing onto efferent neurons in the contralateral pedal ganglion.

The DSIs are members of the swim central pattern generator. They fire rhythmic bursts of action potentials during the swim motor pattern.



A drawing of a DSI with dendritic fields in the cerebral ganglia, projecting to the contralateral Pedal ganglion. Its axon projects out one of the Pedal connectives. Based on Getting et al.(1980)

Identification

Anatomy:

- Serotonergic Neuron in CeSP cluster with contralateral projecting axon.
- Generally the most lateral three neurons in the cluster are DSIs.
- In the dissection microscope, with some reflected illumination, the DSIs appear somewhat translucent with a small pigment spot.
- Cell fills show the DSIs exiting Pedal Nerve 5, which is the smaller of the two Pedal-Pedal connectives. But, electrophysiological data suggests that at least one DSI is present in Pedal Nerve

Homology

The DSIs are homologous to the CeSP-A neurons in other Nudibranchs. They are also homologous to neurons in a similar position across all gastropods. Here are the names of identified homologues in other species:

- Pleurobranchaea californica: As1-3
- Hermissenda crassicornis: CPT

References

[edit]

1. Fickbohm DJ, Lynn-Bullock CP, Spitzer N, Caldwell HK, Katz PS (2001) Localization and quantification of 5-hydroxytryptophan and serotonin in the central nervous systems of Tritonia and Aplysia. J Comp Neurol 437:91-105.
2. Getting PA (1977) Neuronal organization of escape swimming in Tritonia. J Comp Physiol A 121:325-342.
3. Getting PA (1981) Mechanisms of pattern generation underlying swimming in Tritonia. I. Neuronal network formed by monosynaptic connections. J Neurophysiol 46:65-79.
4. Getting PA, Lennard PR, Hume RI (1980) Central pattern generator mediating swimming in Tritonia. I. Identification and synaptic interactions. J Neurophysiol 44:151-164.
5. Hume RI, Getting PA (1982) Motor organization of Tritonia swimming. II. Synaptic drive to flexion neurons from premotor interneurons. J Neurophysiol 47:75-90.
6. Katz PS, Fickbohm DJ, Lynn-Bullock CP (2001) Evidence that the swim central pattern generator of Tritonia arose from a non-rhythmic neuromodulatory arousal system: Implications for the evolution of specialized behavior. Am Zool 41:962-975.
7. Katz PS, Frost WN (1995a) Intrinsic neuromodulation in the Tritonia swim CPG: Serotonin mediates both neuromodulation and neurotransmission by the dorsal swim interneurons. J Neurophysiol 74:2281-2294.
8. Katz PS, Frost WN (1995b) Intrinsic neuromodulation in the Tritonia swim CPG: The serotonergic dorsal swim interneurons act presynaptically to enhance transmitter release from interneuron C2. J Neurosci 15:6035-6045.
9. Katz PS, Getting PA, Frost WN (1994) Dynamic neuromodulation of synaptic strength intrinsic to a central pattern generator circuit. Nature 367:729-731. Tri0002301
10. McClellan AD, Brown GD, Getting PA (1994) Modulation of swimming in Tritonia: Excitatory and inhibitory effects of serotonin. J Comp Physiol A 174:257-266.
11. Newcomb JM, Fickbohm DJ, Katz PS (2006) Comparative mapping of serotonin-immunoreactive neurons in the central nervous systems of nudibranch molluscs. J Comp Neurol 499:485-505.
12. Newcomb JM, Katz PS (2007) Homologues of serotonergic central pattern generator neurons in related nudibranch molluscs with

Done

NeuronBank.org: A Neuromics Tool

NeuronBank | *Tritonia*

Login | NewAccount

Central > Branch List > Tritonia > **Browse/Search**

Find: On Tritonia Go

Branch Home

Browse Neurons

Search

Anatomical Search

--------Article | -Neuron | -----Modulation | Has Relationship With ...

Find -Article With Attributes ... | Find -Neuron With Attributes ... | Find -Modulation With Attributes ...

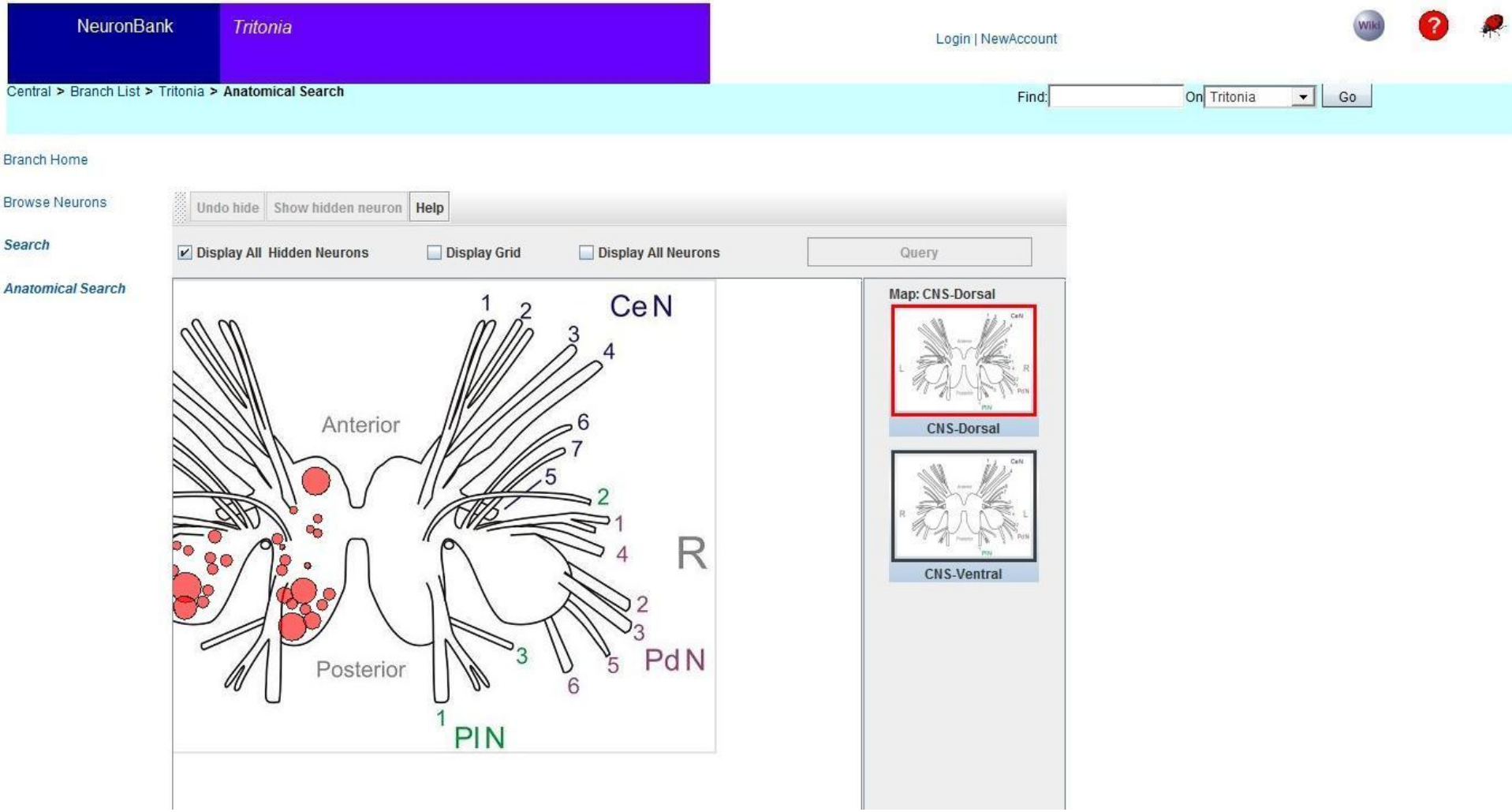
Select attributes ...	:CREATION-TIMESTAMP	Select attributes ...
-Contributor	-AccessionID	:DIRECT-TYPE
-Year	:NAME	:CREATOR
:NAME	-Alias	:MODIFIER
:DIRECT-TYPE	-Neuron_Part	:MODIFICATION-TIMESTAMP
:CREATOR	-V_Rest	:CREATION-TIMESTAMP
:MODIFIER	-Cell_Count	-AccessionID
:MODIFICATION-TIMESTAMP	-Soma_diameter	-Molecule
:CREATION-TIMESTAMP	-Activity_Resting	-Laterality
-AccessionID	-Behavior	
-Volume	-Nerve_Projection	
-Abstract	-Neuron_Type	

Add | Reset | Submit | Submit to All Branches

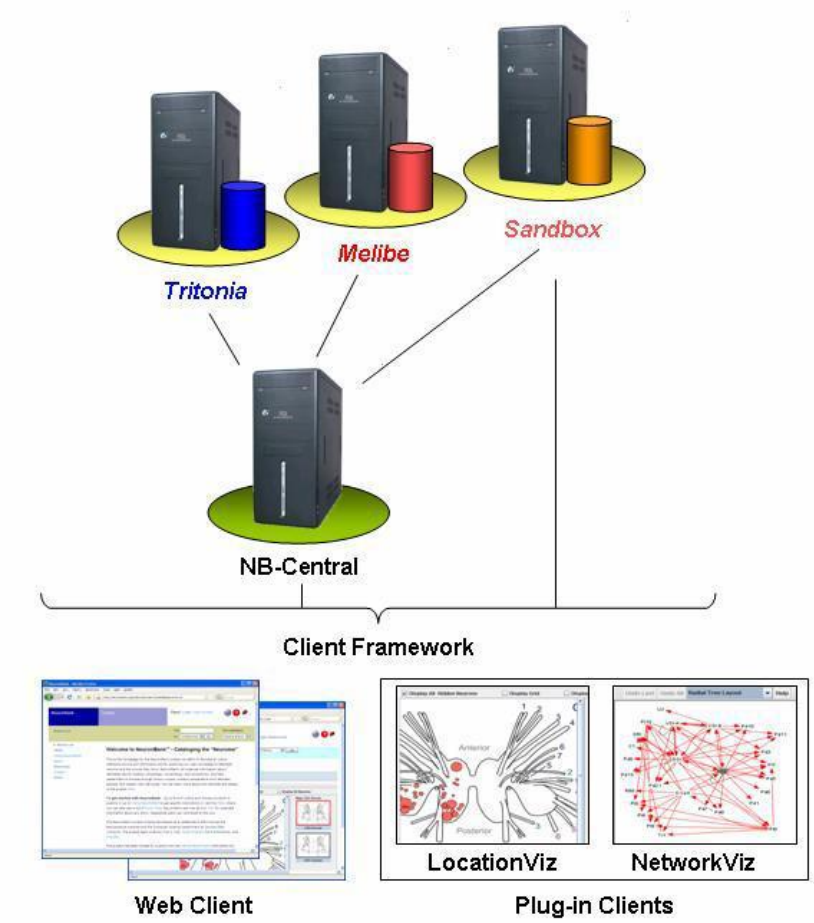
Query Criteria:

Class Name	Attribute	Operator	Value	Definitional	Remove
-Annotates.-Neuron	-Neuron_Type	is	Interneuron	☐	R

NeuronBank.org: A Neuromics Tool



Architeture of NeuronBank



BranchKB

- Extensible Data Backend
- Webservices
  - Ontology Broadcast
  - Algernon QL
  - Data I/O
- Branch Admin

NB-Central

- Universal Authentication
- Species Server Directory
- Cross-species search
- Ontology Database
- User profiles / searches
- Central Admin

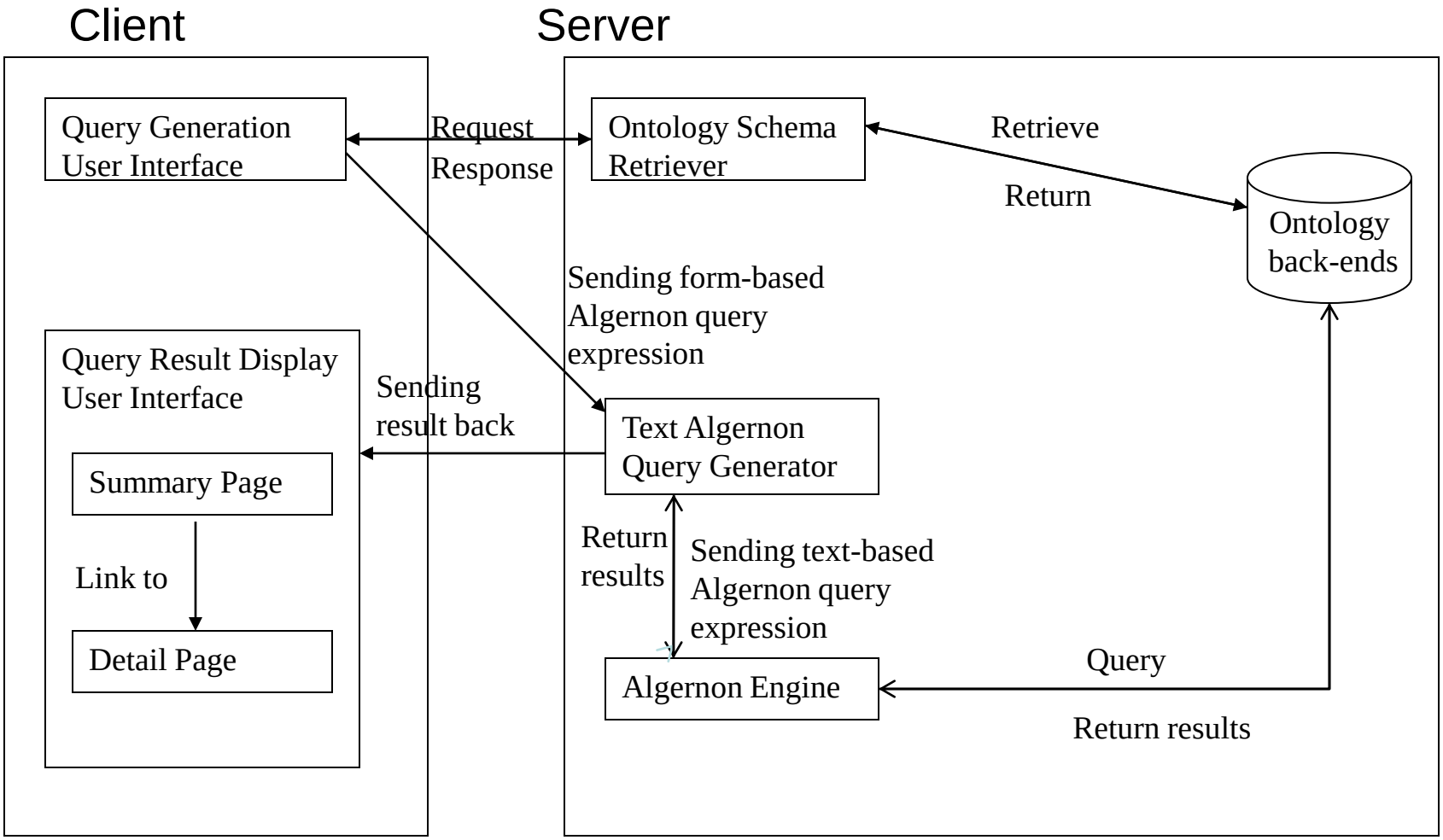
Clients

- Submit Authentication
- Browse to Branch
- Algernon QL Builder
- Custom control
  - QL build
  - Data visualization
  - Data entry

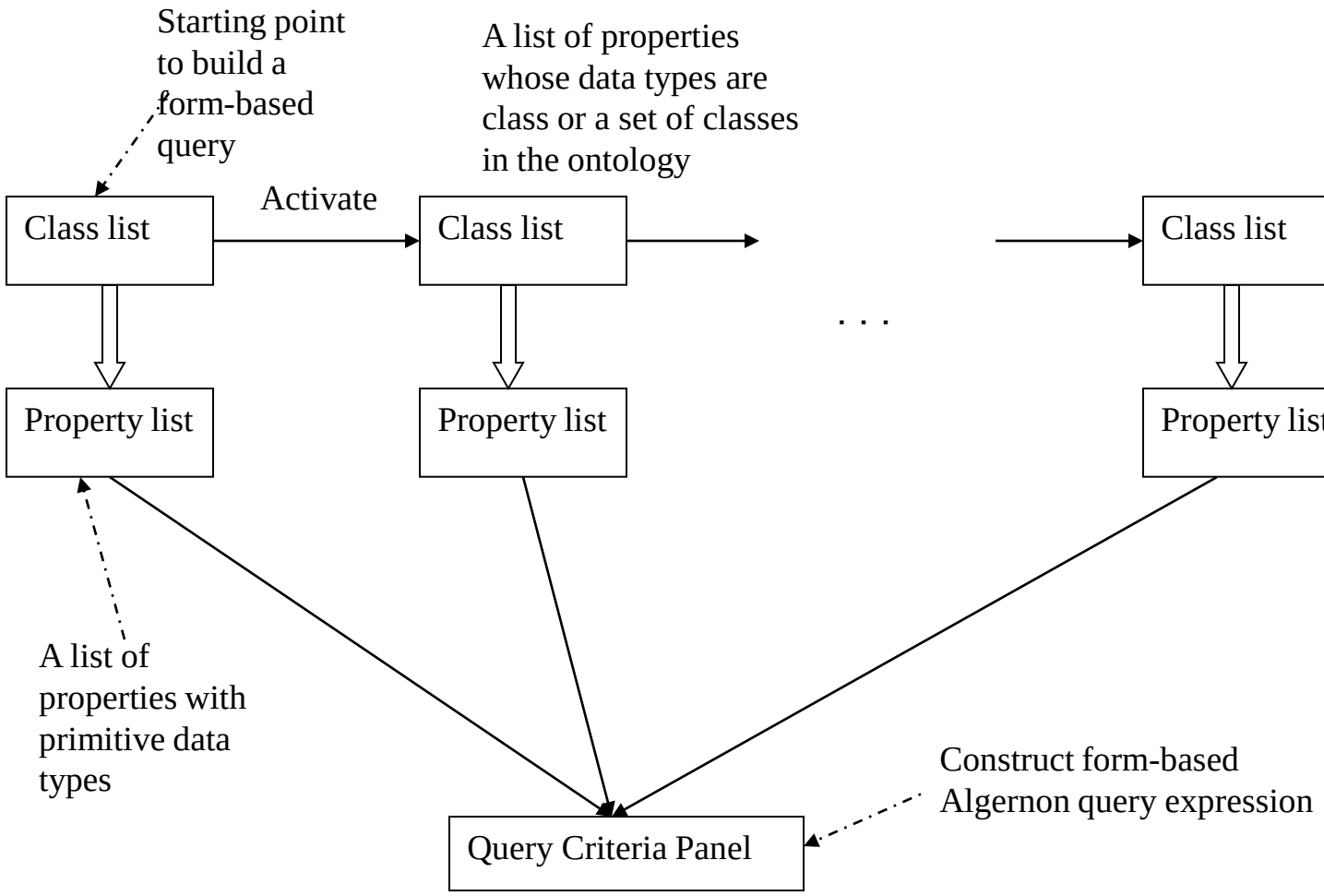
Query component

- ontology-based Web query interface.
- Algernon system on frame-based knowledge bases.
- JavaServer Faces (JSF) technology.
- The form-based query is translated into a textual Algernon query.

Query system architecture



Query generation user interface



- Class lists

(a) The start dropdown menu

(b) Relationship Properties of Selected Class in next Column

- Property list boxes

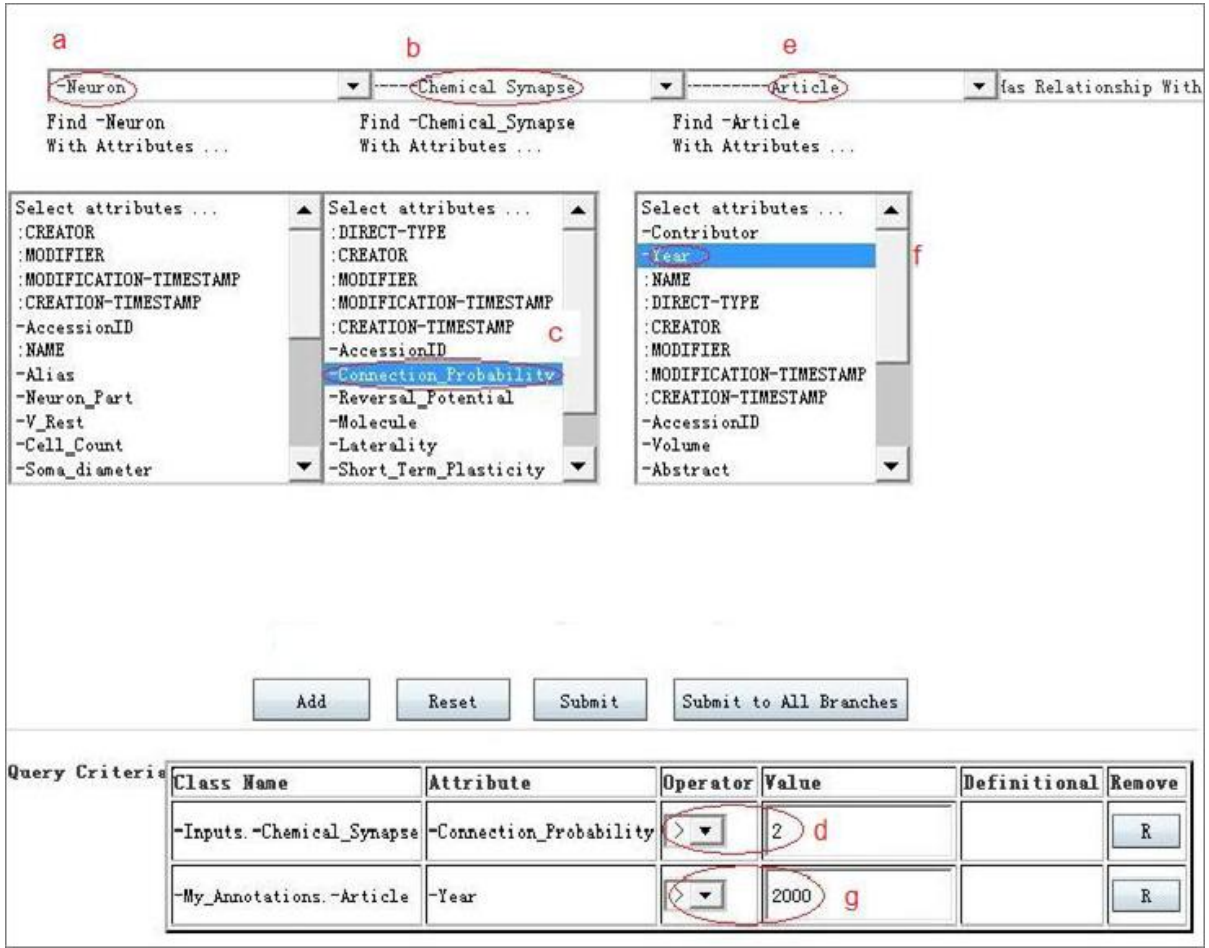
Primitive Properties of Selected Class - in Property List-Box

- Query Criteria Panel
  - a form-based interface
  - construct Algernon query expressions

An Example Form-based Search

Find all neurons which are involved in chemical synapses satisfying the following two properties:

1. the connection probability of the synapse is greater than 2, and
2. the synapse has an article annotation which was published after year 2000.



Query results

- Cross Branch Query Results

Results from

Branch	Query Status	No. of Results
Tritonia	Query Complete	3
SandBox	No results/Branch Unavailable	-
Melibe	No results/Branch Unavailable	-

- Summary Page

No. Of Results:3

List | Location | Network

Query Summary

Sorting

Related Domain

Major Domain

-Neuron	-Inputs.-Chemical_Synapse	-My_Annotations.-Article
S-Cell	-Chemical_Synapse - P19 - S-Cell	{Mongeluzi DL, Hoppe TA, Wang J, Frost WN, Tian LM} (2003)
DRI	-Chemical_Synapse - S-Cell - DRI	{Hoppe TA, Wang J, Frost WN, Tian LM} (2001)
Tr1	-Chemical_Synapse - S-Cell - Tr1	{Hoppe TA, Wang J, Frost WN, Tian LM} (2001)

Your algernon query is: ((:INSTANCE -Neuron ?Col0_Returns)(-Inputs ?Col0_Returns ?Col1_Returns)(:INSTANCE -Chemical_Synapse ?Col1_Returns) (-My_Properties ?Col1_Returns ?Col1_Cond_Prop6)(:CHILD -Connection_Probability ?Col1_Cond_Prop6 ?Col1_Cond6)(-Value ?Col1_Cond6 ?Col1_Cond6_Values)(:test (:lisp (> ?Col1_Cond6_Values 2)))(-My_Annotations ?Col1_Returns ?Col2_Returns)(:INSTANCE -Article ?Col2_Returns)(-Year ?Col2_Returns ?Col2_Cond_Prop12)(:test (:lisp (> ?Col2_Cond_Prop12 2000))))

Query results (Contd)

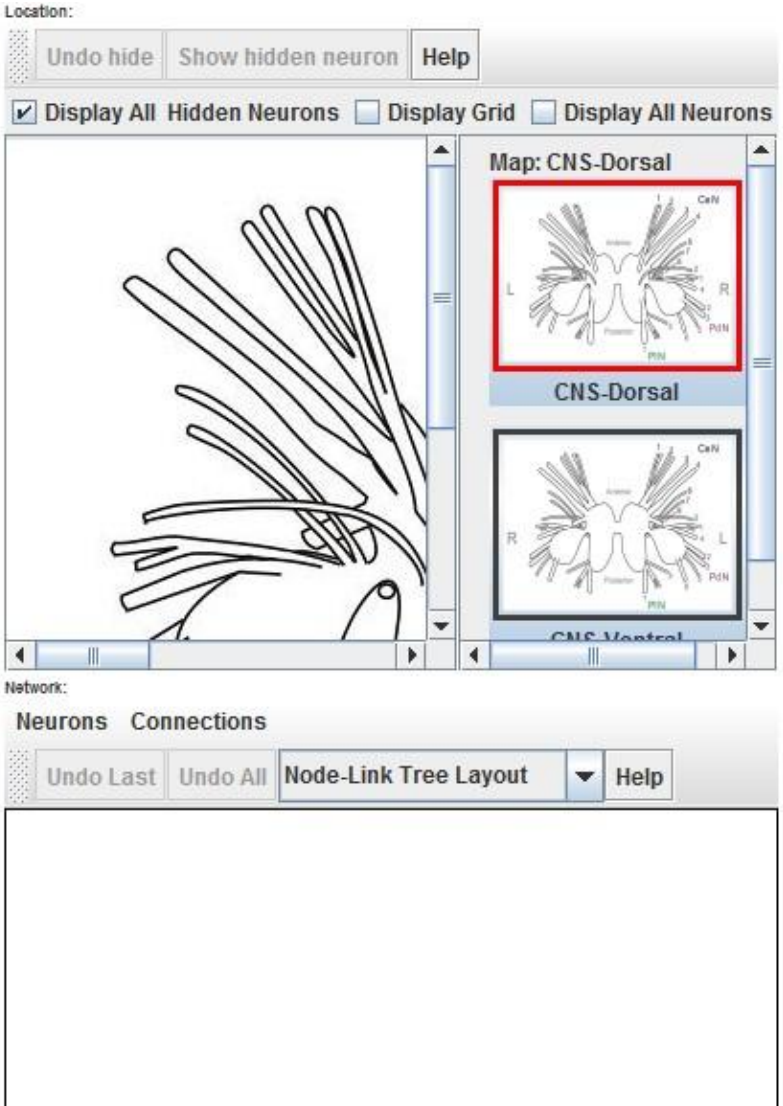
- Detail Page

-Neuron - S-Cell	
Property	**Value**
:CREATOR :MODIFIER	pkatz pkatz
:MODIFICATION-TIMESTAMP	Jun 18, 2007
:CREATION-TIMESTAMP	Mar 30, 2007
-AccessionID	Tri0002367
:NAME -Alias	S-Cell
-Cell_Count	70+/-10 [Annotations: 1]
-Soma_Laterality -Activity_Resting	Bilateral Silent
-Neuron_Type	Sensory_Neuron
-V_Rest -Molecule	mV Glutamate [Annotations: 2]

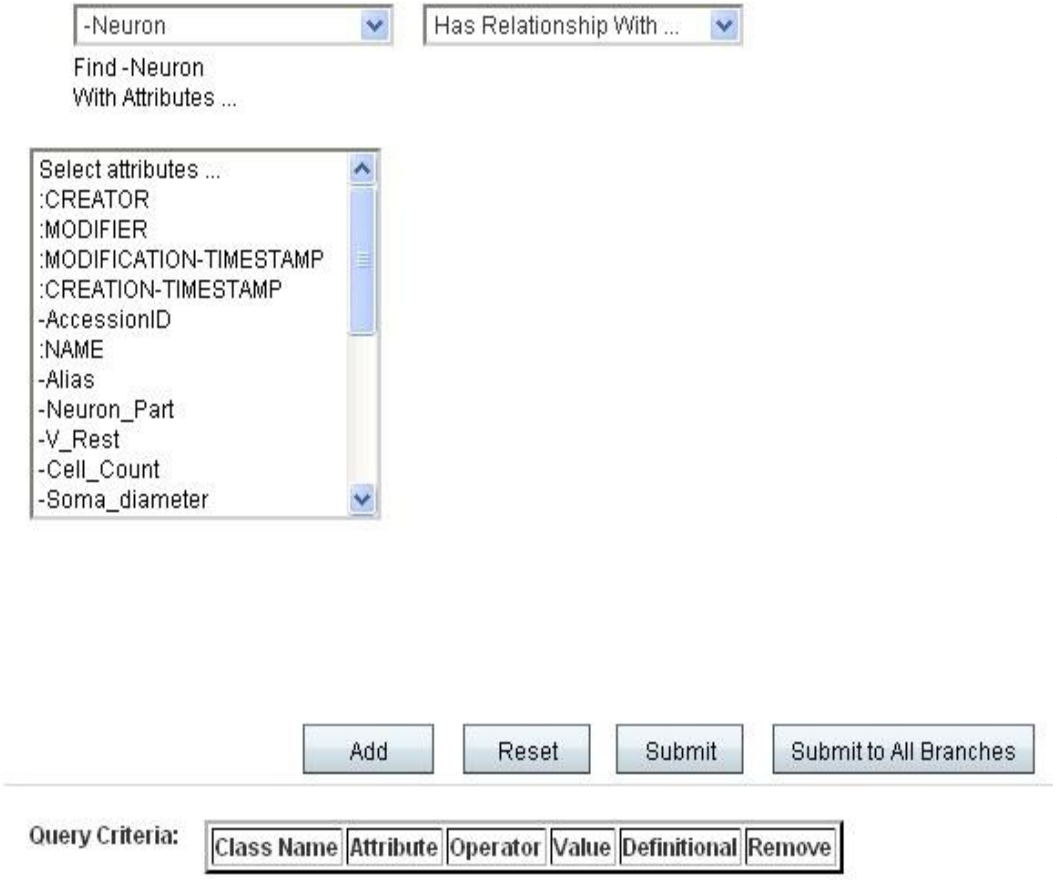
Return URL :
http://test.neuronbank.org/Tri0002367
Wiki URL :
http://www.neuronbank.org/wiki/index.php/Tri0002367

-My_Annotations (3)	
Index	**Values**
1	-Article: Getting PA (1976)
2	-Article: {Megalou EV, Brandon CJ, Frost WN} (2009)
3	-Comment: -Comment: Located under the TGN cell bodies on the dorsal surface of each pleural ganglion. The population of somata runs diagonally across the pleural ganglion with the anterio-medial margin near the central commissure and the posterio-lateral margin near the exit of tn pleural nerve 1.

-Outputs (10)	
Index	**Values**
1	-Chemical_Synapse: -Chemical_Synapse - S-Cell - C2
2	-Chemical_Synapse: -Chemical_Synapse - S-Cell - DRI
3	-Chemical_Synapse: -Chemical_Synapse - S-Cell - Tr1
4	-Chemical_Synapse: -Chemical_Synapse - S-Cell - PI9
5	-Chemical_Synapse: -Chemical_Synapse - S-Cell - PI7

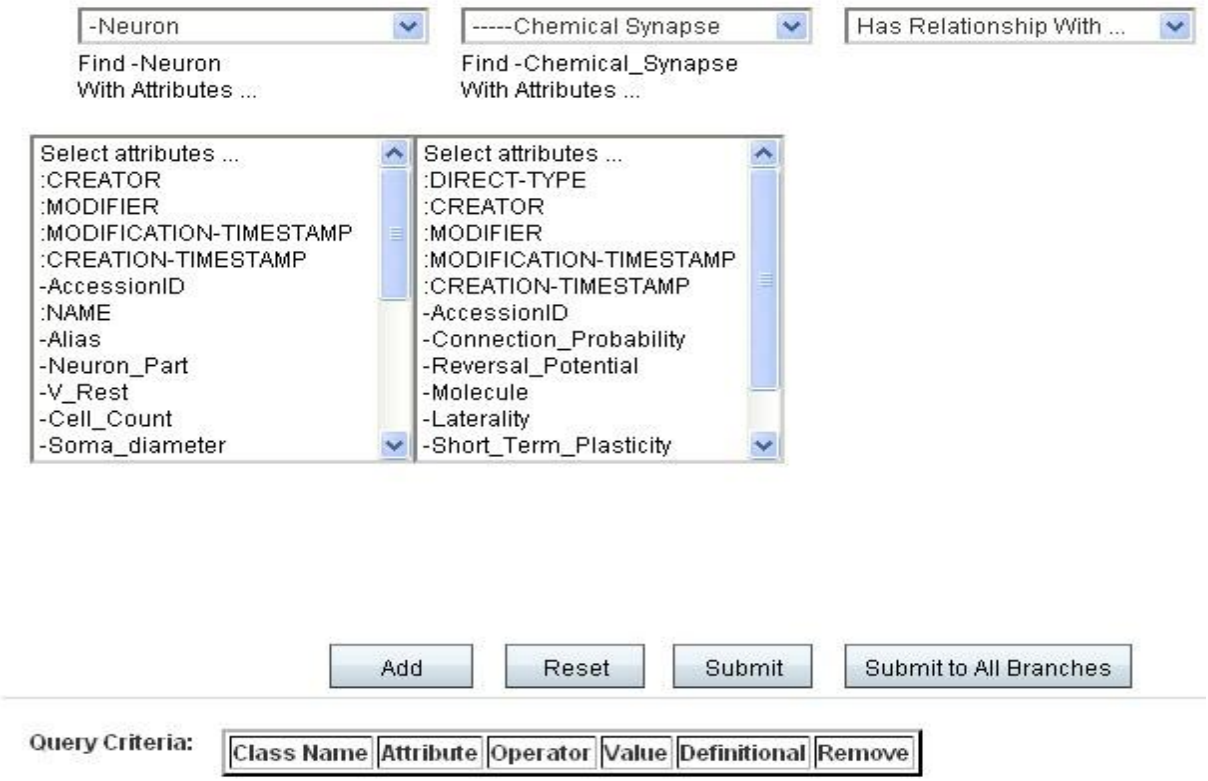


Algernon query generation



- create a query for a neuron

```
(
    (:INSTANCE -Neuron
    ?Col0_Returns)
)
```



- Choose a chemical synapse (whose parent is Inputs), which has relationship with the neuron.

```
(
        (:INSTANCE -Neuron ?Col0_Returns)
        (-Inputs ?Col0_Returns ?Col1_Returns)
        (:INSTANCE –Chemical_Synapse ?Col1_Returns)
)
```

-Neuron

Find -Neuron
With Attributes ...

-----Chemical Synapse

Find -Chemical_Synapse
With Attributes ...

Has Relationship With ...

Select attributes ...
:CREATOR
:MODIFIER
:MODIFICATION-TIMESTAMP
:CREATION-TIMESTAMP
-AccessionID
:NAME
-Alias
-Neuron_Part
-V_Rest
-Cell_Count
-Soma_diameter

Select attributes ...
:DIRECT-TYPE
:CREATOR
:MODIFIER
:MODIFICATION-TIMESTAMP
:CREATION-TIMESTAMP
-AccessionID
-Connection_Probability
-Reversal_Potential
-Molecule
-Laterality
-Short_Term_Plasticity

Add | Reset | Submit | Submit to All Branches

Query Criteria:

Class Name	Attribute	Operator	Value	Definitional	Remove
-Inputs.-Chemical_Synapse	-Connection_Probability	>	2		R

- choose the -Connection Probability property of the Chemical Synapse, whose parent class is - My Properties.
- click the “Add” button
- set the value of that chosen property is larger than 2 in the query criterion.
- The updated Algernon query is:

```
(
    (:INSTANCE -Neuron ?Col0_Returns)

    (-Inputs ?Col0_Returns ?Col1_Returns)
    (:INSTANCE -Chemical_Synapse ?Col1_Returns)

    (-My_Properties ?Col1_Returns ?Col1_Cond_Prop6)
    (:CHILD -Connection_Probability?Col1_Cond_Prop6
    ?Col1_Cond6)
    (-Value ?Col1_Cond6 ?Col1_Cond6_Values)
    (:test (:lisp (> ?Col1_Cond6_Values 2)))
)
```

-Neuron | -----Chemical Synapse | ---------Article | Has Relationship With ...

Find -Neuron With Attributes ...

Find -Chemical_Synapse With Attributes ...

Find -Article With Attributes ...

Select attributes ...
:CREATOR
:MODIFIER
:MODIFICATION-TIMESTAMP
:CREATION-TIMESTAMP
-AccessionID
:NAME
-Alias
-Neuron_Part
-V_Rest
-Cell_Count
-Soma_diameter

Select attributes ...
:DIRECT-TYPE
:CREATOR
:MODIFIER
:MODIFICATION-TIMESTAMP
:CREATION-TIMESTAMP
-AccessionID
-Connection_Probability
-Reversal_Potential
-Molecule
-Laterality
-Short_Term_Plasticity

Select attributes ...
-Contributor
-Year
:NAME
:DIRECT-TYPE
:CREATOR
:MODIFIER
:MODIFICATION-TIMESTAMP
:CREATION-TIMESTAMP
-AccessionID
-Volume
-Abstract

Add | Reset | Submit | Submit to All Branches

Query Criteria:

Class Name	Attribute	Operator	Value	Definitional	Remove
-Inputs.-Chemical_Synapse	-Connection_Probability	>	2		R

- choose the article sub-class from the third pulldown menu of classes which is a relationship property of the chemical synapse. The parent class for the article sub-class is My_Annotations.

```
(
    (:INSTANCE -Neuron ?Col0_Returns)

    (-Inputs ?Col0_Returns ?Col1_Returns)
    (:INSTANCE -Chemical_Synapse ?Col1_Returns)

    (-My_Properties ?Col1_Returns ?Col1_Cond_Prop6)
    (:CHILD -Connection_Probability?Col1_Cond_Prop6
    ?Col1_Cond6)
    (-Value ?Col1_Cond6 ?Col1_Cond6_Values)
    (:test (:lisp (> ?Col1_Cond6_Values 2)))

    (-My_Annotations ?Col1_Returns ?Col2_Returns)
    (:INSTANCE -Article ?Col2_Returns)
)
```

-Neuron

Find -Neuron
With Attributes ...

Select attributes ...
:CREATOR
:MODIFIER
:MODIFICATION-TIMESTAMP
:CREATION-TIMESTAMP
-AccessionID
:NAME
-Alias
-Neuron_Part
-V_Rest
-Cell_Count
-Soma_diameter

-----Chemical Synapse

Find -Chemical_Synapse
With Attributes ...

Select attributes ...
:DIRECT-TYPE
:CREATOR
:MODIFIER
:MODIFICATION-TIMESTAMP
:CREATION-TIMESTAMP
-AccessionID
-Connection_Probability
-Reversal_Potential
-Molecule
-Laterality
-Short_Term_Plasticity

---------Article

Find -Article
With Attributes ...

Select attributes ...
-Contributor
-Year
:NAME
:DIRECT-TYPE
:CREATOR
:MODIFIER
:MODIFICATION-TIMESTAMP
:CREATION-TIMESTAMP
-AccessionID
-Volume
-Abstract

Has Relationship With ...

Add | Reset | Submit | Submit to All Branches

Query Criteria:

Class Name	Attribute	Operator	Value	Definitional	Remove
-Inputs.-Chemical_Synapse	-Connection_Probability	>	2		R
-My_Annotations.-Article	-Year	>	2000		R

- choose the primitive property -Year of the article class.
- Upon clicking the “Add” button, the system introduces a second row in the query criteria panel.
- enter the value of the year property as larger than 2000.
- The final Algernon query is generated:

```
(
    (:INSTANCE -Neuron ?Col0_Returns)

    (-Inputs ?Col0_Returns ?Col1_Returns)
    (:INSTANCE -Chemical_Synapse ?Col1_Returns)

    (-My_Properties ?Col1_Returns ?Col1_Cond_Prop6)
    (:CHILD -Connection_Probability?Col1_Cond_Prop6 ?Col1_Cond6)
    (-Value ?Col1_Cond6 ?Col1_Cond6_Values)
    (:test (:lisp (> ?Col1_Cond6_Values 2)))

    (-My_Annotations ?Col1_Returns ?Col2_Returns)
    (:INSTANCE -Article ?Col2_Returns)

    (-Year ?Col2_Returns ?Col2_Cond_Prop12)
    (:test (:lisp (> ?Col2_Cond_Prop12 2000)))
)
```

Comparison

- Web-based.
- Retrieving ontology schema on demand and facilitating to construct a query expression with the minimal database knowledge.
- Returning not only the final results, but also all intermediate results.

Conclusion and future work

- Web query sub-system of NeuronBank.
  - Primitive properties of classes can be queried by the users as well as relationships with other classes.
  - The user can follow a chain of relationships to formulate complex queries.
- Future work:
  - query arbitrary Ontologies that are stored in Protege Frames.
  - modified to work with RDF/OWL Ontologies as well. SPARQL queries will have to be generated in this case.

Thank You for your time and attention

Questions?