

# SenseLab: new developments in disseminating neuroscience information

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## Abstract

This article presents the latest developments in neuroscience information dissemination through the SenseLab suite of databases: NeuronDB, CellPropDB, ORDB, OdorDB, OdorMapDB, ModelDB and BrainPharm. These databases

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include information related to: (i) neuronal membrane properties and neuronal models, and (ii) genetics, genomics, proteomics and imaging studies of the olfactory system. We describe here: the new features for each database, the evolution of SenseLab's unifying database architecture and instances of SenseLab database interoperation with other neuroscience online resources.

**Keywords:** neuroscience; databases; SenseLab; neuroinformatics; Human Brain Project

## INTRODUCTION

The SenseLab suite of databases ([www.senselab.med.yale.edu/senselab](http://www.senselab.med.yale.edu/senselab)), supported in part by the Human Brain Project [1, 2], is an online resource for neuroscience information. SenseLab was developed to disseminate information related to neuronal membrane properties with special emphasis on the olfactory system. SenseLab currently contains seven databases: NeuronDB, CellPropDB, ModelDB, Olfactory Receptor Database (ORDB), OdorDB, OdorMapDB and, most recently, the pilot BrainPharm database. These databases combine to provide neuronal, genomics/genetics, proteomics and imaging information to the neuroscience research community and the public.

Over the years, SenseLab's databases and information pages have garnered several million hits and unique visits. A logging system surveys and analyzes the usage of SenseLab resources (<http://senselab.med.yale.edu/senselab/site/log/reports/>) [3]. Analyses of visitor IP (Internet Protocol) addresses indicate that SenseLab's databases have been accessed extensively by people across the world. These resources have been used in neuroscience research, teaching, thesis-writing and database design. The number of web page requests has significantly increased in the past two years.

One of the unique features of SenseLab is that all the databases are implemented in a unifying database architecture—EAV/CR (Entity Attribute Values with Classes and Relationships) [4]. This architecture helps assure that new types of information can be added to each database with few, if any, programming modifications. In the EAV/CR schema, an 'entity' or object is described by 'attributes' for which 'values' are stored. Complex values can be stored as entities with their own attributes. For example, if a certain laboratory is responsible for work related to olfactory receptors, then **Laboratory**, which is an 'attribute' for the 'entity' **Olfactory Receptor**, is itself stored as an independent entity. This ensures that the **Laboratory** 'entity' can have its own set of 'attributes', such as name, address, phone number, etc. The EAV/CR architecture

has also facilitated the addition of new databases in SenseLab.

Several publications and book chapters have described the evolution of SenseLab over the years [5–18]. This article will describe recent developments in SenseLab's information dissemination, automatic deposition of information into its databases, and interoperation between SenseLab databases and other neuroscience databases.

## EAV/CR: NEW DEVELOPMENTS IN SenseLab ARCHITECTURE

The EAV/CR [4] data storage approach was devised to address the issues of data integration and software maintenance in SenseLab [19], with a view to potential applicability to other bioscience databases. EAV/CR applications have evolved to facilitate data navigation and flexible, *ad-hoc*, metadata searching [11]. In NeuronDB (see next section), for example, one can navigate from a link to a neuron to access that neuron's properties. If a computational neuronal model exists for this neuron (including its properties), then the property page for this neuron provides a link to computational models of the neuron in ModelDB (described later). Each class can also have sub-classes that are stored independently as classes. Adding more classes or categories (data specialization) to any of the classes in the database does not require additional programming. The metadata-driven approach to creating web interfaces (on the fly) in the EAV/CR framework automatically adapts to new classes and to the relationships between these classes. Thus, EAV/CR facilitates database adaptability for the continually evolving domain of neuroscience.

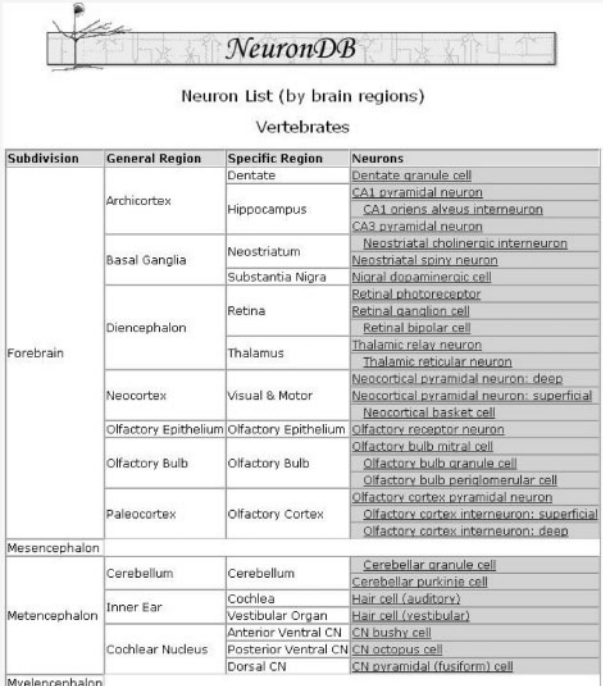
The EAV/CR framework has also been extended to databases outside the SenseLab project. It has been used in the creation of the Neuroscience Database Gateway (NDG) <http://ndg.sfn.org>, a registry of web resources related to neuroscience. SenseLab has been actively participating in database integration experiments with NDG through the development of a knowledge-integration mechanism known as the *ndg.disco* interoperability framework. Use of

ndg.disco involves identifying and creating workflows between databases. These workflows may include integrator systems such as database mediators, ontological servers, text search engines or gateways. Other resources, BIRN-Mediator ([http://www.nbirn.net/research/data\\_integration/data\\_mediation\\_FAQ.shtml](http://www.nbirn.net/research/data_integration/data_mediation_FAQ.shtml)), BIRN Bonfire (<http://www.nbirn.net/research/ontology/index.shtml>) and the BrainML/Metal (<http://brainml.org>), have contributed to this integration project.

One specific use of the ndg.disco framework is seen in the Entrez LinkOut Broker. Entrez is the NCBI information-dissemination web-portal. NCBI houses comprehensive listings of published and deposited information related to genes, proteins, journal articles, etc. The LinkOut Broker allows different databases that provide links to Entrez to be, in return, linked to by Entrez wherever relevant. For example, in SenseLab, ORDB entries for chemosensory receptors are linked to accession numbers in Entrez (PubMed and GenBank entries). In return, when a user accesses a journal article in Entrez, the web page for that journal article in PubMed also provides a link back to the page containing the relevant chemosensory receptor in ORDB. The NDG web resource is used as a mediator for all neuroscience-based databases and Entrez: every database registered at NDG can take advantage of this facility and use the LinkOut Broker utility to define bi-directional links to Entrez.

## NEURONDB AND CELLPROPDB

Both NeuronDB (<http://senselab.med.yale.edu/senselab/NeuronDB>) and CellPropDB (<http://senselab.med.yale.edu/senselab/CellPropDB>) are repositories of published research information related to three neuronal membrane properties: voltage gated conductances, neurotransmitter receptors and neurotransmitter substances. Whereas CellPropDB provides this information with reference to a neuron as a whole, the information in NeuronDB is localized to specific neuronal compartments. The EAV/CR schema methodology allows users of CellPropDB and NeuronDB access to similar information, the differences are only in the granularity of information sought (neuron as a whole versus at the compartmental level). Both databases present information related to 20 neurons and 11, recently added interneurons, which represent every major region on the brain (Figure 1). Information



Subdivision	General Region	Specific Region	Neurons
Forebrain	Archicortex	Dentate	Dentate granule cell
		Hippocampus	CA1 pyramidal neuron
			CA3 pyramidal neuron
	Basal Ganglia	Neostriatum	Neostriatal cholinergic interneuron
		Substantia Nigra	Nigral dopaminergic cell
	Diencephalon	Retina	Retinal photoreceptor
			Retinal ganglion cell
		Thalamus	Retinal bipolar cell
	Neocortex	Visual & Motor	Thalamic relay neuron
			Thalamic reticular neuron
		Olfactory Epithelium	Neocortical pyramidal neuron: deep
			Neocortical pyramidal neuron: superficial
		Olfactory Bulb	Neocortical basket cell
		Paleocortex	Olfactory Epithelium
	Olfactory Bulb		Olfactory bulb mitral cell
Mesencephalon	Cerebellum	Olfactory bulb granule cell	
		Olfactory bulb periglomerular cell	
Metencephalon	Inner Ear	Olfactory cortex pyramidal neuron	
		Olfactory cortex interneuron: superficial	
	Cochlear Nucleus	Olfactory cortex interneuron: deep	
		Cerebellum	Cerebellar granule cell
	Myelencephalon	Cochlea	Cerebellar purkinje cell
Vestibular Organ			Hair cell (auditory)
Dorsal CN		Anterior Ventral CN	Hair cell (vestibular)
	Posterior Ventral CN	CN bushy cell	
			CN octopus cell
			CN pyramidal (fusiform) cell

**Figure 1:** List of neurons and interneurons included in NeuronDB. A similar figure can be found in CellPropDB. The columns in the figure show the region-sub-region-neuron-property hierarchy.

stored in the two databases can be presented to the end user in the brain region-neuron-property hierarchy.

Figure 2 shows the information in NeuronDB presented for each neuronal compartment with annotations for the relevant publication entered by the domain experts. Both CellPropDB and NeuronDB databases are not necessarily repositories of all the published information. They seek to present first-principles perspectives of neuronal membrane properties for a fixed set of neurons.

The continuing maintenance of NeuronDB will be facilitated by information-extraction tools such as NeuroText [13]. NeuroText mines the abstracts of neuroscience journal articles and is designed to help the database curator make a decision as to whether an article should be included in NeuronDB. NeuroText uses indexing, context matching, concept based scoring, hierarchical matching, lexical parsing and supervised and unsupervised learning. Each processed abstract is marked-up to inform the domain expert as to how NeuroText arrived at its suggestion as to whether to populate NeuronDB and CellPropDB. NeuroText also dynamically creates

**NeuronDB**

CA1 pyramidal neuron

Mode: [Overview](#) [Data/Search](#) [plus Connectivity](#) [plus References/Notes](#) [Models](#)

Region: [Dad](#) [Dam](#) [Dap](#) [Dbd](#) [Dbm](#) [Dbp](#) [Soma](#) [AH](#) [A](#) [T](#) [All Compartments](#)

Properties: [Receptors](#) [Channels](#) [Transmitters](#) [All Properties](#)

Interoperation: [Gene and Chromosome](#) [Experimental Data \(neurodatabase.org\)](#) [Microscopy Data \(CCDB\)](#)

Are:  Present  Absent

Neuron type: principal  
Organism: Vertebrates

	Input Receptors	Intrinsic Currents	Output Transmitters
<b>Dad</b>	Perforant pathway entorhinal pyramidal neuron terminals (T) Glutamate is commonly believed to be the primary excitatory neurotransmitter in the hippocampal formation generally (reviewed in Cotman et al., 1995), and in CA1 in particular (Storm-Mathisen J, 1977 <sup>141</sup> , Randall AD and Collingridge GL, 1992 <sup>142</sup> ). CA1 pyramidal neurons increase their firing (recorded extracellularly) in response to ionophoresed Glu within their apical dendritic fields or in the cell body layer (Dudar 1974 PMID#4437726). Magee JC and Cook EP, 2000 <sup>143</sup>	<b>I<sub>L</sub> high threshold</b> Ca fluorescence imaging shows that application of L-channel antagonists reduces the Ca influx associated with backpropagating action potentials, and has a significantly greater effect in the proximal dendrites than in more distal dendrites (Christie BR, 1995 <sup>144</sup> ). <b>I<sub>N</sub></b> Using confocal microscopy, these channels were found to be localized on the soma, dendrites, and a subpopulation of dendritic spines (Mills LR et al, 1994 <sup>145</sup> ). <b>I<sub>IR,Q,h</sub></b> Depolarizing "sag" during larger hyperpolarizing voltage	

**Figure 2:** Information presented in NeuronDB. The columns indicate the receptor, current, transmitter properties for the distal apical dendrite (Dad) compartment of the Cal Pyramidal Neuron.

a form, which the domain expert can use to evaluate the text-mining results, make changes dynamically and directly deposit the information into the databases if desired.

One of the first instances of interoperability in neuroinformatics involved NeuronDB. NeuronDB currently interoperates with CCDB (Cell Centered Data Base—<http://ccdb.ucsd.edu>) housed at the University of California at San Diego. While NeuronDB provides information related to neuronal membrane properties for a fixed set of neurons in specific regions of the brain, CCDB provides microscopy imaging data related to these neurons [8].

A pilot tool NeuroExtract has been developed [20] in conjunction with NeuronDB to perform text-based integrated queries from generalized sources of data, which contain neuroscience concepts only as sub-categories. NeuroExtract uses concepts stored in NeuronDB and CellPropDB to query and extract information from other neuroscience sources and sources that contain neuroscience information as sub-categories.

## ORDB AND ODORDB

ORDB and OdorDB along with OdorMapDB (described in following section) are dedicated to disseminating genetic, genomic, proteomic and imaging information related to the olfactory system. Olfactory Receptors (ORs) are a class of GTP-Binding Protein Coupled Receptors (GPCR). GPCRs are membrane receptors that are responsible

for myriad functions that involve biological cell membranes, and which find direct applications in the pharmaceutical industry [21]. The study of ORs has gained momentum in the decade and a half since the first OR was identified in a seminal paper by Linda Buck and Richard Axel [22]. Buck and Axel received the Nobel Prize in medicine in 2004 for this work and subsequent contributions to the field of chemosensory research. ORDB plays a key role in the olfactory receptor research field. It also serves as a warehouse of information related to fungal receptors, pheromone receptors, insect olfactory receptors and mammalian olfactory and taste receptors. ORDB represents the work of more than 100 laboratories worldwide. It contains information for more than 40 different species. OR-like genes (judging by sequence similarities) can be found in different tissues in different organs.

Functional analyses of olfactory receptors involve experimentally identifying specific odors excite or inhibit specific ORs. Research on OR function has shown [23] that there exists a many-to-many relationship between ORs and odorous molecules (more than one OR is likely to be excited by an odor and more than one odor compound is likely to excite an OR). OdorDB is a repository of odors that have been shown to excite olfactory receptors. ORDB interoperates with OdorDB: OdorDB contains a list of odors with links to the ORs (listed in ORDB) they are known to excite. Similarly, for each OR, the odors that excite these ORs are listed under the attribute 'Ligand'.



The information stored in ORDB and OdorDB is constantly being updated. ORDB has grown from a list of a thousand ORs and other chemosensory receptors that were reported in GenBank to more than thirteen thousand such receptors in early 2007. The large increase in the list of receptors in the last few years has been largely due to the publications of drafts of mammalian genomes: humans, mouse, rat and chimpanzee [24–33]. The continuous and rapid update of ORDB was possible due to AutoPop [15], an automatic information deposition tool that interoperated between sources of olfactory receptors, such as GenBank, SwissProt and EMBL and ORDB. AutoPop is a web-based tool that extracts information relevant to ORDB from web pages using HTML or XML file parsers by mapping the information from the source databases to corresponding attributes (descriptors for each OR or chemosensory receptor) in ORDB and then directly depositing this extracted information into the database.

Since ORDB is the centralized repository of chemosensory receptor information, ORDB curators and scientific coordinators were charged with the task of performing a sequence analysis of OR genes identified from different groups from the mouse and human genomes. Two web pages (<http://senselab/senselab/ORDB/files/humanorseqanal.html>) and (<http://senselab/senselab/ORDB/files/mouseorseqanal.html>) illustrate the results of this

endeavor. The web pages contain different color mark-ups to identify sequences that were full-length, partial and pseudogenetic. Links to GenBank and EMBL web pages (wherever available) are provided for each OR gene.

Functional analysis of olfactory receptors is often a challenging task. Fewer than 50 odor compounds have been identified as having an excitatory or inhibitory effect on ORs. The specific details of the experimental challenges in performing functional studies [34] are beyond the scope of this article. A related difficulty is testing odors out of several thousand known to identify which odor might excite a particular OR. Experimentalists often have to rely on modeling and theoretical binding studies to identify a select number of odor-ligands, which might successfully bind and excite or inhibit OR function. One attribute added to ORDB is ‘OR Model’ which provides a link to a picture or a movie file of a computationally determined OR model and an odor-molecule computationally docked in the OR binding region. A PubMed link to functional studies if any for an OR allows an end user to access all the information for that particular OR or chemosensory receptor. Figure 3 shows the web page for a single OR gene entry.

Recently, a multi-attribute search has been instituted in ORDB, using search capabilities already developed for other SenseLab databases. The EAV/CR schema on which SenseLab is based ensures that

Chemosensory Receptors	
Name:	<b>OR11</b>
Description:	
CR Type:	= OBL(Olfactory Receptor Like) <a href="#">Show other</a>
Organism:	<a href="#">Rattus norvegicus (rat)</a> <a href="#">Show other</a>
Source Tissue:	= olfactory epithelium <a href="#">Show other</a>
Chromosome:	
Genbank:	M64386
Medline:	91191556
Common Name:	I7
Strain:	
Source:	<a href="#">GENBANK</a> <a href="#">Show other</a>
Sequence Lab:	<a href="#">BUCE_L</a> <a href="#">Show other</a> <a href="#">ANEL_E</a> <a href="#">Show other</a>
Length:	= Full Length <a href="#">Show other</a>
Ligand:	<a href="#">OCTANAL</a> <a href="#">Show other</a>
Nucleotide:	ATGGAGCGAAGG AACACAGTGGG AGAGTGAAGTAA TTGTGTGGCTG GGTTCOCAGCT CCTGCCCACTG CGAGTACTACTA TTTTCTTCTT CTCTGGMCTAT GTGTGGTGTG ACTGAAAACATG CTCATCATATA GCAATTAGGAAC CACCCAAACCTC CACAAACCATG TATTTTTCTTG GCTAATATGTCA TTTCTGGAGATT TGGTATGTCAT GTTAAGATCTC AAGATGCTCGCT GGCITCATTTGT TCCAAGGAAAC CATGGACAGCTG ATCTCCTTTGAG GCATGCAAGACA CAACCTACTTT TTTCTGGGCTTG GTTTGCACAGAG TGTGTCTTCTT GCTGTGATGGCC TATGACCGCTAT GTGGCATCTGT CATCCACTCCAC TACCCCGTCATT GTCAGTACCCGG CTATGTGTGACG ATGGCAGCTGGA TCTCGGCTGGA GGTFTTGGTATC TCCATGGTAAA GTTTTCTTATT TCTGGCTGTCT TACTGTGGCCGC AACACCACTAAC CACTTTTCTGT GATGTGTCTCCA TTGCTCAAGCTG TCATGCATGAC ATGCCACAGCA GAGCTACAGAC TTTGCTCTGGCC ATTTTATCTCG CTGGACCCGCTC TCTGTCACTGGG GCATCTCATG GCATACAGAGT GCTGTGATGGC ATGCCCTAGCT GCTGGGCGCAT AAGSCCTTTCA ACTGTGGCTGC CACTCACTGTT GTSATCATCTG TATGACCCAGCT ATTTTCATCTAT CCAGCCCTAAG GCACCTCTAGCT TTTGACACCAAC AAGCTGTCTCT GTACTCAAGCT ATCA7TGTACCG TTGTCAATCC ATCATCTACTGC TTGCCAACCAC GATGTCAAAGA GCCTAGCTGTC ACGCTGCACCTG GCCACGAGCAG GAGGCAATACC AACAAAGGCAGC AAAATGGTTAG
Amino Acids:	MERRRNSGRVSE FVLLGFPAPAPL RVLLFLLSLXV VLVLTENKLIIL AIRNHPHLKPM YFFLANHSFLEI VYVTVTPKHLA GFIOSENHQL ISPEACTQLYF FLGLCTCEVLL AVNAVDRVVAIC HPLHYVPIVSSR LCVQMAAGSWAG GFGISWVKVFLI SRLSYCGPNTIN HFFCDVSPLLNE SICTMSTAEILD FVLAIFLLGLPE SVTGSAMVMTG AVNRPSAAGRH KAFSTCASHLY VIFVYAAISFIY ARPKALSAFDTN KLYSVLYAVIYP LFNPIIYCLRNG DFKRALRRLHL AADQEAETHRGS KIG
Type of Sequence:	= cDNA <a href="#">Show other</a>
Accession Number:	M64386
Receptor 2D (ORDB):	<a href="#">OLF7_RAT_SW.html</a>
Molecular Models:	<a href="#">rx_17.jpg</a>
Functional Analysis Laboratory:	
Functional Analysis Reference:	10781022
Microarray Experiment:	552

**Figure 3:** Entry in ORDB. Rat OR I7 was one of the first cloned and identified. The figure shows the attributes and values for this OR. Values that appear as links are also stored as attributes. The last attribute in the figure provides a link to an entry in ORMicroarrayDB with links to the results of microarray experiments for this OR.

any new feature instituted for one database is easily applicable to other databases. This search feature is critical in a database that has seen an almost exponential increase in deposition of gene information for chemosensory receptors. Figure 4 shows sample search pages for ORDB. The search results are available in HTML (with links to entries), text and XML formats. The search page in ORDB can be accessed at <http://senselab/senselab/ORDB/eavXSearch.asp> and a tutorial describing the use of the program is available at the following web page: [http://senselab/senselab/ORDB/search\\_tutorial.asp](http://senselab/senselab/ORDB/search_tutorial.asp).

The most recent attribute added to ORDB is a link to a microarray experiment for every OR gene-entry, if such a microarray experiment has been performed. The link in the 'Microarray Experiment' attribute leads the user to the Olfactory Receptor Microarray Database (ORMD- <http://neurolab.med.yale.edu/ormd>), which contains descriptions of results from microarrays containing this specific gene.

OdorDB contains a list of 45 odors. As mentioned previously, OdorDB is not a repository of all known odor compounds but tracks the research related to

the functional analysis of olfactory receptors. The list of odors in OdorDB (saved as entities) is also stored in ORDB under the attribute heading 'Ligand'. Clicking on the 'OR by Ligand' link takes the user to a page containing this list of odors with numbers besides them. The numbers indicate how many ORs this odor-ligand is known to excite. By clicking the number-link, the user can access a page with a list of the ORs; clicking each of the OR links takes the user to the OR entry in ORDB. Though these entries are accessed through ORDB, the mark-up and colors appear as if the information is stored separately in OdorDB. Much like the entries that are dynamically presented in CellPropDB and NeuronDB discussed in the previous section, each data source, therefore, appears to operate independently even though the actual data are shared.

Within OdorDB, users can access the odors based on the ORs they are known to excite. Odors are also stored based on specific features of these compounds: hydrocarbon features, cyclic, straight-chain or branched, and by their functional groups. Figure 3 shows the web-page for entry related to octanal. The entity 'octanal' is described in terms of its Chemical

**SenseLab - OrDB Search**

Version 2.0 Help

Searching: Chemosensory Receptors

SN	Del	Parameter	Show	Type	Condition
0		Name	<input type="checkbox"/>	S	
1	<input checked="" type="radio"/>	CR Type	<input checked="" type="checkbox"/>	C	<a href="#">LookUp</a> TPR (Taste Papilla Receptors)
2	<input checked="" type="radio"/>	Sequence Lab	<input checked="" type="checkbox"/>	C	<a href="#">LookUp</a> BUCK_L
3		** New **			

Advanced >>  
Analyze >>

Show results as: HTML

SN	ID	Name	CR Type	Sequence Lab
1	2557	TPR2	TPR (Taste Papilla Receptors)	BUCK_L
2	2558	TPR3	TPR (Taste Papilla Receptors)	BUCK_L
3	2559	TPR4	TPR (Taste Papilla Receptors)	BUCK_L
4	2574	TPR17	TPR (Taste Papilla Receptors)	BUCK_L
5	2575	TPR18	TPR (Taste Papilla Receptors)	BUCK_L
6	2578	TPR21	TPR (Taste Papilla Receptors)	BUCK_L
7	2586	TPR29	TPR (Taste Papilla Receptors)	BUCK_L
8	2821	TPR36	TPR (Taste Papilla Receptors)	BUCK_L
9	2822	TPR37	TPR (Taste Papilla Receptors)	BUCK_L
10	2823	TPR38	TPR (Taste Papilla Receptors)	BUCK_L
11	3140	TPR81	TPR (Taste Papilla Receptors)	BUCK_L

```
rs version= "2.1"
columns
column id= "c1" name= "SN" datatype= "I"
column id= "c2" name= "ID" datatype= "S" URLbase= "/senselab/site/dbData/eavData.asp?o="
column id= "c3" name= "Name" datatype= "S" multi_value= "False"
column id= "c4" name= "CR Type" datatype= "C" multi_value= "False" URLbase= "/senselab/site/dbData/eavData.asp?o="
column id= "c5" name= "Sequence Lab" datatype= "C" multi_value= "True" URLbase= "/senselab/site/dbData/eavData.asp?o="
rows
row id= "o2557"
col idref= "c1" value= "1"
col idref= "c2" value= "2557" URLsuffix= "2557"
col idref= "c3" value= "TPR2"
col idref= "c5" value= "BUCK_L" URLsuffix= "855"
col idref= "c4" value= "TPR (Taste Papilla Receptors)" URLsuffix= "1443"
row id= "o2558"
col idref= "c1" value= "2"
```

**Figure 4:** Results of the multi-attribute search in ORDB. This search feature appears in all SenseLab databases. The end user here wishes to find all taste receptors that have been explored by the laboratory of Dr Linda Buck. The figure also shows partial results in both HTML and XML formats.

Abstracts Service (CAS) number, its chemical formula, its functional group (useful for searches), its hydrocarbon feature designation, a diagram of its structural formula and a link to a map (if available) of glomerular activity in the olfactory bulb. The last attribute allows OdorDB to interoperate with OdorMapDB described in the next section.

## ODORMAPDB

The sense of smell in animals originates in the olfactory sensory neurons (OSNs) in the neuro-epithelium, which is at the roof of the nasal cavity. Axons from OSNs cross the cribriform bone and project onto the olfactory bulb (OB), the first relay station of olfactory signals in the brain. Projections of the sensory neurons have been illustrated in the OB as well as the olfactory cortex [35, 36]. More than a decade before olfactory receptor genes were first identified [22], odor-induced spatial patterns of neural activity in the OB had been discovered by researchers using odor mapping techniques where a series of sequential coronal OB sections were examined and the activity in the roughly spherical glomerular layer was plotted in a 2-dimensional flat map [37]. This technique has since been extended to a broad range of OB activities, including neuronal uptake of 2-deoxyglucose (2DG), expression of immediate early gene *c-fos* and fMRI. [12, 38, 39] Odor maps are a medium by which functional imaging data can be presented. The maps describe the unique spatial activity patterns in the glomerular layer of the main OB in animals exposed to odor stimuli. OdorMapDB (<http://senselab.med.yale.edu/senselab/OdorMapDB>) is a data repository for the odor maps generated by researchers at Yale University and at other laboratories [9].

The goal of archiving odor maps is to create a resource of functional properties of the OB that is available to the olfactory research community as well as the public. OdorMapDB is a web-accessible database. Images are stored as binary data-type in an Oracle database management system. Each odor map 'entity' is described using the 'attributes': species, age, odor type, concentration, mapping method, etc. It is integrated with two other SenseLab olfactory databases, i.e. ORDB and OdorDB (described in the previous section). These three databases taken as a whole provide a multi-faceted knowledge-based informatics tool to help address the mechanisms underlying the olfactory perception.

OdorMapDB continues to evolve in terms of both its content and database schema. The database now contains fMRI odor maps for isoamyl acetate, aliphatic aldehyde homologues, ketones and odor mixtures. In addition to fMRI and 2DG maps, OdorMapDB now archives *c-fos* odor maps [39]. The database schema of OdorMapDB has been expanded to include the original 3D data from which the maps are derived. This allows users to examine the odor-induced neural activity that occurred in the entire bulb. OdorMapDB also archives fMRI data obtained from the accessory-OB. This is a unique bulbar region responsible for pheromone perception. The accessory-OB plays an important role in an organism's social and reproductive behaviors [6].

OdorMapDB interoperates with a large 2DG odor map database developed at the University of California at Irvine [40]. 2DG, *c-fos* and fMRI approaches examine different neuronal properties. Odor maps from these studies are therefore not redundant. They offer different perspectives in an attempt to answer the same questions—the response in the olfactory bulb to olfactory stimuli. Odor map databases face a challenge to archive the different types of odor maps in a cooperative fashion. OdorMapDB serves as a useful informatics tool to help explain the signal encoding mechanism of smell perception.

## MODELDB

Neuroscience investigators computationally recreate published computer models for several reasons: to validate models a models reproducibility, to understand models by comparing effects of parameter changes with intuitive predictions, to explore neuronal processes by using models beyond their original application, to modify models to test alternative hypotheses, or to reuse models or components of models as building blocks in other models. Efforts to facilitate the creation and storage of computational neuronal models on-line in web-based databases<sup>1</sup> [10, 14, 41–45] and in distributed sharing through web resources [46] have been ongoing for at least a decade. ModelDB is the result of one such approach.

One of the strengths of the EAVCR system (described earlier in this work) is the ability for new categories of classes and attributes to be created as the database population grows, with low maintenance requirements for maintaining the existing web pages as the database evolves. ModelDB has expanded

from four models in 2000 to 270 models of neurons, neuronal components and neuronal networks as of early 2007. A partial list of model entries appears in Figure 5. Recently, ModelDB has seen increased usage [47–51]<sup>2</sup> due to the collaborations within the neuroscience community along with a willingness to contribute models to this resource. An editorial in the *Journal of Computational Neuroscience* recommended using ModelDB to store models for all modeling articles published in that journal. Spurred by a data sharing policy adopted by molecular biologists for the last two decades, ModelDB developers recently suggested that computational neuroscientists adopt a policy on model sharing. When a modeling paper is accepted for publication, a request is made to the authors to deposit the model's source code in ModelDB's publicly accessible model repositories.

ModelDB is now also a test database for the Entrez-LinkOut broker. This is illustrated in Figure 6. The original Hodgkin-Huxley computational model can be found in PubMed by entering 'hodgkin a,huxley a, 500' in PubMed. This PubMed

web page also contains 'Links' → 'Link out' (Figure 6 upper left) link. When this link is clicked, the Link-out resources for that journal article are displayed (Figure 6 lower left). Clicking on 'Neuroscience Related Data' shows a link to an NDG (among links to other sources that reference this article, Figure 6 lower right) web page. The NDG page contains links to the Hodgkin-Huxley model in ModelDB. Clicking on this link then shows the model description page (Figure 6 upper right) where the user can download or autolaunch the model using the NEURON neuronal model simulator.

A new area that ModelDB hopes to leverage the EAV/CR framework is by interoperating with databases of journals articles. The 'Publication' class in ModelDB, whose instances contains citations to 31,000 scientific articles [52], allows the browsing of citations associated with model and the citation's bibliographies. One new attribute for ModelDB papers, the digital object identifier (doi), stores a unique code supplied by journals that identifies each paper. We plan on adding new tables that will map

Find Models by Topic	
Click on a Topic to show a list of models that incorporate or demonstrate that Topic.	
<a href="#">Action Potentials</a>	<a href="#">Action Potential Initiation</a>
	<a href="#">Axonal Action Potentials</a>
	<a href="#">Dendritic Action Potentials</a>
<a href="#">Active Dendrites</a>	<a href="#">Bursting</a>
	<a href="#">Oscillations</a>
<a href="#">Activity Patterns</a>	<a href="#">Spatio-temporal Activity Patterns</a>
	<a href="#">Synchronization</a>
	<a href="#">Temporal Pattern Generation</a>
<a href="#">Coincidence Detection</a>	
<a href="#">Detailed Neuronal Models</a>	
<a href="#">Electrotonus</a>	
<a href="#">Influence of Dendritic Geometry</a>	
<a href="#">Invertebrate</a>	
<a href="#">Ion Channel Kinetics</a>	
<a href="#">Methods</a>	
<a href="#">Parameter Fitting</a>	
<a href="#">Pathophysiology</a>	<a href="#">Epilepsy</a>
	<a href="#">Heart disease</a>
	<a href="#">Multiple sclerosis</a>
	<a href="#">Parkinson's</a>
	<a href="#">Therapeutics</a>
<a href="#">Pattern Recognition</a>	
<a href="#">Rate-coding model neurons</a>	
<a href="#">Signaling pathways</a>	
<a href="#">Simplified Models</a>	
<a href="#">Synaptic Integration</a>	
<a href="#">Synaptic Plasticity</a>	<a href="#">Long-term Synaptic Plasticity</a>
	<a href="#">Short-term Synaptic Plasticity</a>
	<a href="#">Depression</a>
	<a href="#">Facilitation</a>
	<a href="#">Post-Tetanic Potentiation</a>

**Figure 5:** A partial list of model Topics in ModelDB.





**Figure 6:** Entrez-LinkOut broker used for ModelDB. When the link to the PUBMED entry in the upper right hand panel is clicked, it opens the page for the original Hodgkin–Huxley computational model in PUBMED shown in the upper left hand panel. The lower left hand panel displays the LinkOut resources in PUBMED for NDG as a link. When that link is clicked, it results in the Hodgkin–Huxley model link in NDG. The lower right panel shows that the Hodgkin–Huxley model is stored in both ModelDB and the SNNAP database housed at University of Texas Medical School in Houston, Texas. Clicking on the link for ModelDB in NDG then results in the original page illustrated in the upper right hand panel.

the name or abbreviated name of the journal as supplied in the citation to the journals URL. The doi, if included in paper attributes, is sufficient to link to at least the abstract of the paper, which journals uniformly supply free of charge. This will allow modelers to view abstracts or the full text of the paper, if available, while browsing citations in ModelDB. With the shift in the field toward open access of articles (usually after a delay of a year) many journals will make papers freely available.

## BRAINPHARM

BrainPharm, a pilot database under development, was recently added to SenseLab. It is primarily concerned with the management of knowledge associated with neurological disorders with emphasis on Alzheimer’s Disease, Parkinson’s Disease and epilepsy. BrainPharm was created to store research-information on drugs for the treatment of different neurological disorders, identify agents that act on neuronal receptors and differentiate between signal transduction pathways in the normal and diseased

brain. The flexibility of the EAV/CR schema that allows users access to all of SenseLab functionality enables searches for drug actions at the level of key molecular constituents, neuronal compartments and individual neurons (in NeuronDB). Also provided are links to ModelDB that allow users to run neuronal model simulation packages that differentiate processes between normal and diseased brains. Much of BrainPharm is still under development. The section on Parkinson’s Disease currently contains information related to drugs that act during several specific stages of the Dopamine neurotransmitter mechanism; the section on Epilepsy section contains links to a table containing of 23 drugs used in Epilepsy treatment and the different types of symptoms of epilepsy that each drug is known to affect. These symptoms range from: Epilepsy without seizures, infantile spasms, Lennox–Gastaut, generalized tonic-clonic seizure, myoclonic seizures and partial seizures.

The most development in BrainPharm is in the area of Alzheimer’s Disease. The next section

describes in detail how by using technologies of the Semantic Web, BrainPharm seeks to interoperate with Alzforum ([www.alzforum.org](http://www.alzforum.org)), a web resource for Alzheimer's Disease information, through a pilot project AlzPharm. BrainPharm interoperates with NeuronDB, which has to this point disseminated information related to properties of healthy neurons, and extends it to include diseased cells in that it describes the extracellular elements such as  $\beta$ -amyloid precursor proteins—the primary constituent of plaques, and intracellular elements such as tau proteins. BrainPharm contains lists of neurons affected by Alzheimer's Disease elements with the information being presented as annotated links to the literature related to the neuronal compartments where these elements are expressed. The EAV/CR schema mentioned earlier in this article allows for the easy updating of information in BrainPharm.

## SEMANTIC WEB DEVELOPMENT IN SenseLab

This section describes the application of the Semantic Web, an evolving extension of the World Wide Web (<http://www.w3.org/2001/sw/>) for knowledge representation in SenseLab. This is being explored as a research project and will aid in extending SenseLab's knowledge environment to become more semantically interoperable with other neuroscience knowledge sources available over the Internet. The EAV/CR schema on which SenseLab's architecture is based bears some resemblance to the RDF (Resource Description Framework) schema. RDF is an ontological language for knowledge representation. Semantic Web supports RDF. When the SenseLab project was initiated (more than 10 years ago), RDF was a relatively new standard and there were not many software tools available for manipulating data stored in RDF format. Both EAV/CR and RDFS model concepts and their instances are in a format called a 'triple'. The following example illustrates an RDF triple:

```
<http://en.wikipedia.org/wiki/Dopamine,  
http://en.wikipedia.org/wiki/Function,  
http://en.wikipedia.org/wiki/Neurotransmitter>
```

The above triple expresses the notion that *Dopamine* has the *Function* of being a *Neurotransmitter*. In the Semantic Web, each component of the triple is identified using a Uniform Resource Identifier (URI) (details can be found at the following web site: <http://www.w3.org/>

Addressing/). When resources have the same URI, they are assumed to be the same entity, and any data about that entity can be merged. In RDF, as triple statements become connected they form a directed labeled graph. The EAV/CR triple, on the other hand, consists of an 'entity' which is described by 'attributes' for which 'values' exist as described earlier in this article (See the first section). RDF may also be extended by another ontology language called Ontology Web Language or OWL (<http://www.w3.org/TR/owl-features/>), which is also supported by the Semantic Web. It extends RDF by adding vocabulary that describes the relations of cardinality and equality among classes and properties. The application of the Semantic Web in the neuroscience domain is actively being pursued by the Semantic Web for Health Care and Life Sciences Interest Group (HCLSIG) (<http://www.w3.org/2001/sw/hcls/>). The HCLSIG is established by the World Wide Web Consortium (W3C) (<http://www.w3.org/>).

## SenseLab in OWL/RDF

We have begun the process of converting some of the SenseLab databases into OWL or RDF. This allows us to explore the representation of knowledge at different levels of expressiveness and use a range of tools to query and integrate knowledge in different representation formats. We converted a subset of NeuronDB into the target OWL ontology that was created manually using the ontology editor Protégé (<http://protege.stanford.edu/>). We mapped NeuronDB from its relational (EAV/CR) form to OWL using a tool called 'D2RQ' (<http://sites.wiwiw.fu-berlin.de/suhl/bizer/D2RQ/>). D2RQ provides a high-level mapping specification language for converting the relational database structure to RDF or OWL structure. To demonstrate the operation of this OWL data set with other related OWL data sets, we also converted a portion of CoCoDat [53] (a relational database based at the University of Dusseldorf, Germany) into OWL using D2RQ. Then we demonstrated the use of OWL's constructs such as 'sameAs' to create a bridge between the NeuronDB and CoCoDat OWL ontologies. We also demonstrated how to use nRQL, which is an OWL query language supported by the OWL reasoner 'Racer' (<http://www.cs.concordia.ca/~haarslev/racer/racer-queries.pdf>), to query bridged

ontologies. In [54], we describe this OWL-based integration approach.

Recently, we have converted the new prototype version of BrainPharm (discussed in the previous section) into RDF. The conversion was implemented using the XML Stylesheet Transformation or XSLT (<http://www.w3.org/TR/xslt>), which was used to transform a portion of BrainPharm data exported in EDSP/XML format into the target RDF/XML structure. In addition, we have manually created an ontology using RDF Schema (RDFS) which is available through Protégé. The ontology represents information about the effect of drugs on pathological (or molecular) mechanisms (which involve neuronal properties such as receptors, currents and neurotransmitters) mediating the pathological changes in various neurological disorders such as Alzheimer's Disease (AD). Figure 7 shows the ontology diagram of BrainPharm. The diagram depicts a class-relationship graph representing the various classes as nodes and their relationships as edges. It also shows examples of class instances. In terms of understanding a drug's effect on the molecular mechanism of Alzheimer's Disease, these example instances tell us the following:

*'the drug Nifedipine reduces the pathological effect of beta Amyloid on the I Calcium current of CA1 pyramidal neuron'.*

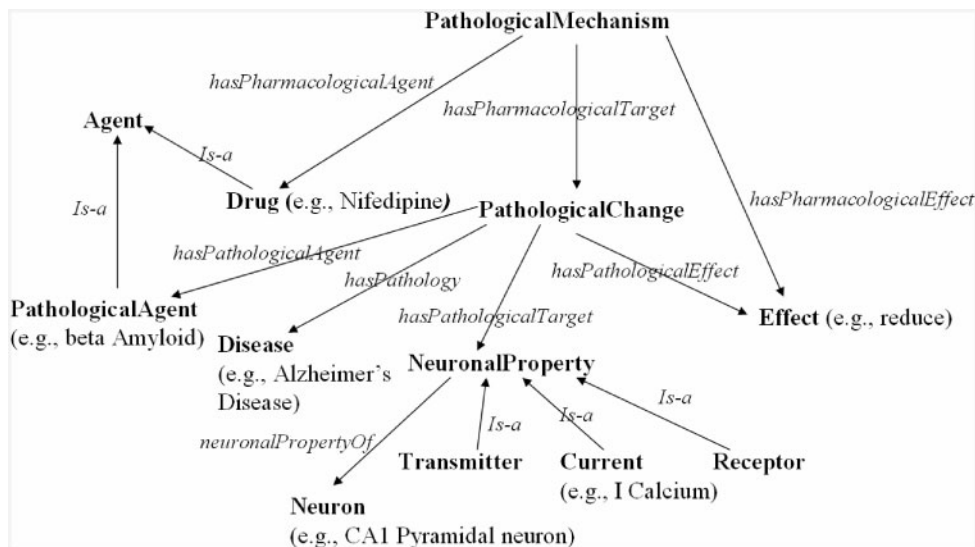
To explore the capabilities provided by RDFS to make inferences, we used Oracle Database 10g's RDF Data Model ([http://www.oracle.com/technology/tech/semantic\\_technologies](http://www.oracle.com/technology/tech/semantic_technologies)). We loaded the converted RDF data set of BrainPharm (and the corresponding RDF Schema) into the Oracle RDF

database. In addition, we loaded into this Oracle RDF database another existing RDF data set (with RDF Schema) provided by the pilot version of SWAN (Semantic Web Applications in Neuromedicine) [55]. The pilot data set contains a small subset of data extracted from AlzForum [56], which has to do with research hypotheses and the associated publications relating to both basic and clinical research studies of Alzheimer's Disease. We have built a Web-based application called 'AlzPharm' [56], which allows the user to access and query the BrainPharm and SWAN RDF data in an integrated fashion. In [56], we described in detail the Semantic Web development of BrainPharm and demonstrated how to use the inference capability provided by Oracle's RDF query language to retrieve from SWAN annotated publications (which is defined as a subclass of publications in the SWAN RDF schema) that are associated with a particular AD drug target.

We plan to continue to expand the Semantic Web development in SenseLab. We will also make our effort visible to HCLSIG, as we have been actively involved in many HCLSIG activities such as teleconferences and face-to-face meetings. In addition, we have made our RDF/OWL data sets accessible through the HCLSIG Wiki site.

## CONCLUSION

SenseLab as a neuroscience information dissemination resource has through its seven database continued to evolve, expand and diversify. SenseLab's involvement in projects such as NDG and NIF,



**Figure 7:** BrainPharm ontology diagram.

interoperability and integrated querying through the web medium will only serve to make neuroscience information to the research community.

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### Notes

- 1 ModelDB:<http://senselab.med.yale.edu/senselab/modeldb>  
Visiome:<http://platform.visiome.org/index.html>  
Biomodels:<http://www.ebi.ac.uk/biomodels/>
- 2 Papers listed here are restricted to those with authors outside the ModelDB development group.

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