The Brain Architecture Management System: User Manual

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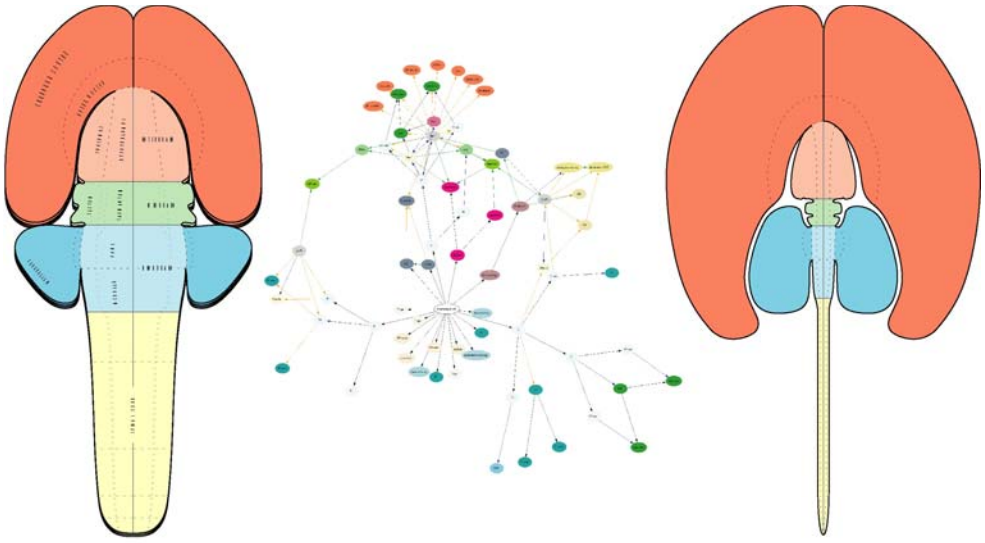
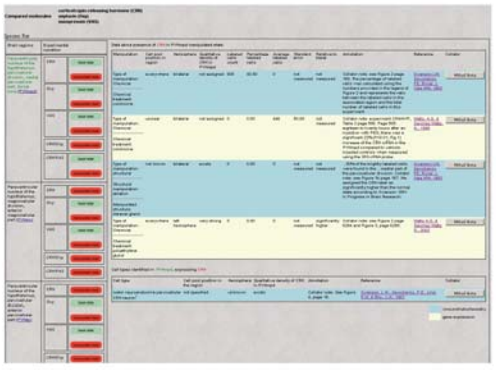
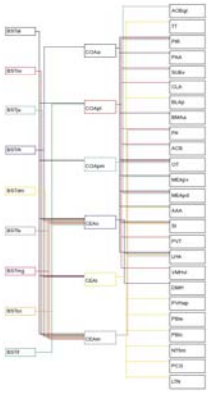






Summary

1. What is the Brain Architecture Management System

The Brain Architecture Management System (BAMS; URL: http://brancusi.usc.edu/bkms) is an online knowledge management system designed to handle neurobiological information at different levels of organization of the vertebrate nervous system (NS).

BAMS handles data and metadata collated from original literature, or inserted by scientists that is associated to four levels of organization of the vertebrate NS: expressed molecules, neuron types and classes, brain regions, and networks of brain regions.

Structurally, BAMS consists of a relational MySQL database and several modules of middle-layer applications written in PHP for querying the backend database and web display of data and metadata.

1.1 BAMS: general structure

The structure of BAMS is modular (the general structure is shown in Figure 1), with the *Brain Parts* module as the center of the system. Brain parts are uniquely defined by a tuplet made of the name of the part, the nomenclature used to identify and name it, the nomenclature version, and species. A brain nomenclature is defined as an internally consistent set of terms used to name a part of the CNS. The number of terms included in a nomenclature is variable (at least one), and the nomenclature version uniquely specifies the set. Usually a brain nomenclature is associated with a brain atlas, but this does not constitute a constraint for inserting it. The constraints that are taken into account are the internal consistency of terms, whether the reference is original research, and the brain region names are associated with textual definitions, or at least depicted on a brain atlas.

The other modules of BAMS are *Connections*, *Relations*, *Cell Types*, and *Molecules*.

Connections module of BAMS holds data and metadata about macroscopic neuroanatomical projections between brain regions. Any neuroanatomical projection can be represented in BAMS by a set of more than 40 attributes. Details about this module can be found in Bota et al. 2005.

The *Relations* module stores qualitative spatial relations between brain regions, as well as cited references.

The *Cell Types* module allows insertion of names and definitions of neuron types and classes, as well as relations between them, as collated from references. The module also records neuron populations attributes, such as position within brain region, density and pattern of staining. It also includes a neurons classification schema, which allows specification of criteria used to hierarchically organize neuron nomenclatures. See Bota & Swanson, 2007 for details.

The *Molecules* module represents data and metadata as collated from the literature and pertaining to brain regions or neurons that are recorded in different physiological states: “normal” and “manipulated”. Molecules are classified in two general classes: “cell associated” and “releasable by neurons”. The “cell

associated" class is further divided in classes accepted by the IUPHAR nomenclature (http://www.iuphar-db.org/index.jsp).

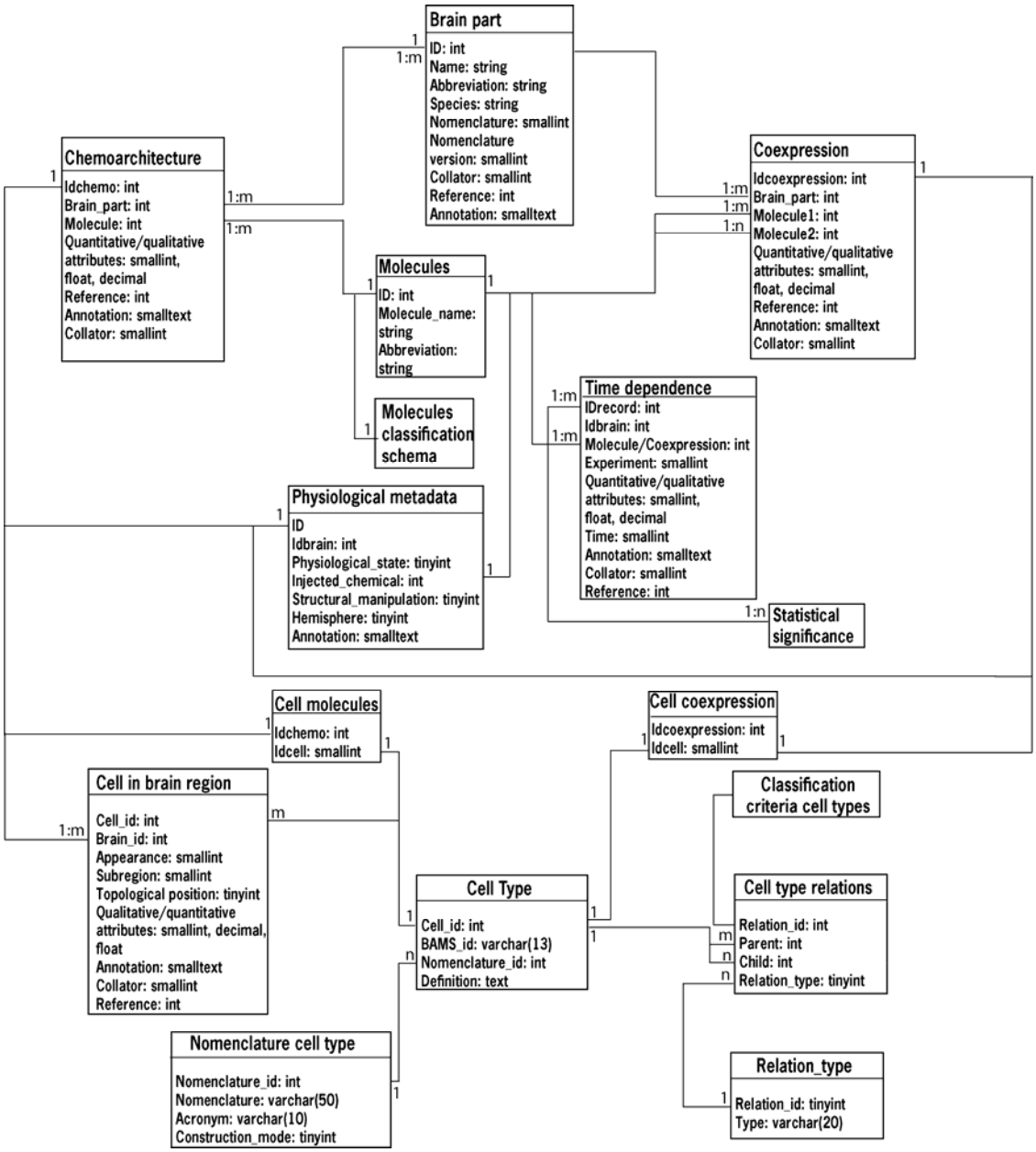


Figure 1. The relational structure of BAMS, emphasizing the *Molecules* and *Cell Types* modules. For detailed description of BAMS *Connections* and *Relations* modules see Bota et al. 2005.

The *Molecules* module allows insertion of quantitative and qualitative attributes as identified using radioactive tracers, immunohistochemistry, or gene expression. It also includes a comprehensive schema for metadata representation (see Figure 1). A full description of this module can be found in Bota & Swanson, 2006.

2. BAMS: web interface

BAMS interface was designed to handle data and metadata in different ways, and is organized in modules, matching the structure of the backend database of the system.

2.1 BAMS Menu – Main Features

The options for online search and manipulation of data and metadata can be found in the **Menu** of BAMS, which has the following structure:

***Search* Brain Parts** by
- Name
- Species
- Nomenclature

References

Cells

Molecules

Evaluate Connections Reports
- Outputs
- Inputs

Nomenclatures

Networks of Brain Regions

3. Searching for information in BAMS

3.1 Search Brain Parts by Name

The search of brain parts by name (direct link: http://brancusi.usc.edu/bkms/brain/search_bname_con.php) can be performed in four different ways: search name of brain regions, search of abbreviations of brain regions, choosing an abbreviation from a scroll-down list and full text string search, as shown in Figure 2.

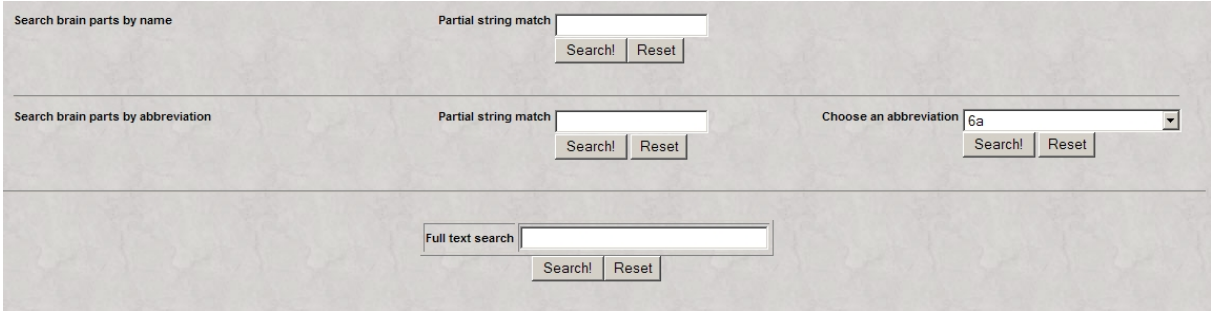


Figure 2. The options of search brain regions by string match with their name, abbreviations, and full text search of their descriptions.

The general result of any search of brain regions by string match is similar to that shown in Figure 3. It includes the name, type (gray matter, fiber tract, or ventricle) and abbreviation of retrieved brain parts, the nomenclature and the version used to identify those, species (strain),

9 exact maches and 369 partial matches

Exact matches:

Brain Part	Type	Abbreviation	Nomenclature	Nomenclature version	Species	General Description	BAMS associated information
Bed nuclei of the stria terminalis	gray matter	BST	Swanson	Swanson-1998	Rat	According to Ju and Swanson 1989.	projections molecules
Bed nuclei of the stria terminalis	gray matter	BST	Swanson	Swanson-2004	Rat	Based on extensive connectional data (see Dong et al. 2001; and Dong and Swanson, in preparation) we have simplified the nomenclature originally proposed by Ju and Swanson (1989). In essence, the anterodorsal, anteroventral, and dorsolateral areas of the anterior division have been combined into an anteromedial area, and the subcommissural zone has been merged with the anterolateral area of the anterior division. In addition, the rostral end of the dorsomedial nucleus has been added to the anteromedial area, and the caudal tip of the principal nucleus of the posterior division has been assigned to the interfascicular nucleus instead.	projections
Bed nuclei of the stria terminalis	gray matter	BST	Swanson	Swanson-1992	Rat	None provided	
bed nucleus of the stria terminalis	gray matter	BST	Paxinos	Paxinos/Watson-1998	Rat	No description provided. The nomenclature was adapted from atlas, pages 150-159	
bed nucleus of the stria terminalis	gray matter	BST	Mai	Mai-1997	Human	No description provided. The nomenclature was adapted from the atlas, pages 313-328	
Bed nucleus of the stria terminalis	gray matter	BST	Hof	Hof et al.-2000	Mouse	No description provided.	
Bed nuclei of the stria terminalis	gray matter	BST	Dong	Dong-2007	Mouse	No description provided	
Bed nucleus of the stria terminalis	gray matter	BST	Moga	Moga-1989	Rat	The bed nucleus of the stria terminalis (BST) is a rostral forebrain structure closely related to the amygdala, its major source of afferent input (Weller and Smith, 1982; De Olmos et al., 1985).	
Bed nuclei of the stria terminalis	gray matter	BST	de Olmos	de Olmos	Rat	..generally classified as a member of the caudal group of septal nuclei. The BST forms the floor of the lateral ventricle and is bounded dorsomedially by the ventral aspect of the lateral septal nucleus, and laterally by the internal capsule which separates it from caudate-putamen and globus pallidus (Figs. 3A; 4A; 5A, B, C; 6A to E; 7F). Caudally, it is successively bounded by the stria medullaris and in part by the columns of the fornix. Rostrally, it is bounded by the nucleus accumbens, while ventrally it merges with the preoptic area. Collator note: this term is not captured in a hierarchy; its subparts are components of the different amygdaloid nuclei.	

Partial matches:

Brain Part	Type	Abbreviation	Nomenclature	Nomenclature version	Species	General Description	BAMS associated information
Bed nuclei of the stria terminalis oval nucleus	gray matter	BSTov	Swanson	Swanson-1998	Rat	According to Ju and Swanson 1989.	cells projections molecules
Bed nuclei of the stria terminalis	gray matter	BSTju	Swanson	Swanson-1998	Rat	According to Ju and Swanson 1989.	cells projections

Figure 3. The result of search by brain parts by abbreviations. In this example, the searched string was “BST”. The retrieved records of brain parts are associated to the part type, abbreviation, nomenclature and its version, species,

description that usually includes the definition of the brain part, according to the authors nomenclature. Additionally, this page includes a metadata field called “BAMS associated information” which summarizes the types of data and metadata that are registered in the system and are associated with the retrieved part.

The retrieved list of brain parts is organized according to two criteria. The first listed are those brain parts that match exactly the searched string. Inside of each of the two sets of records (exact matches and partial matches), the first listed are those regions that are associated to cell, molecules or connectivity information in BAMS.

The result of free text search is split in two steps. The first step retrieves those nomenclatures and nomenclatures versions that include brain parts with names partially matching or descriptions where searched text was found. An example is shown in Figure 4.

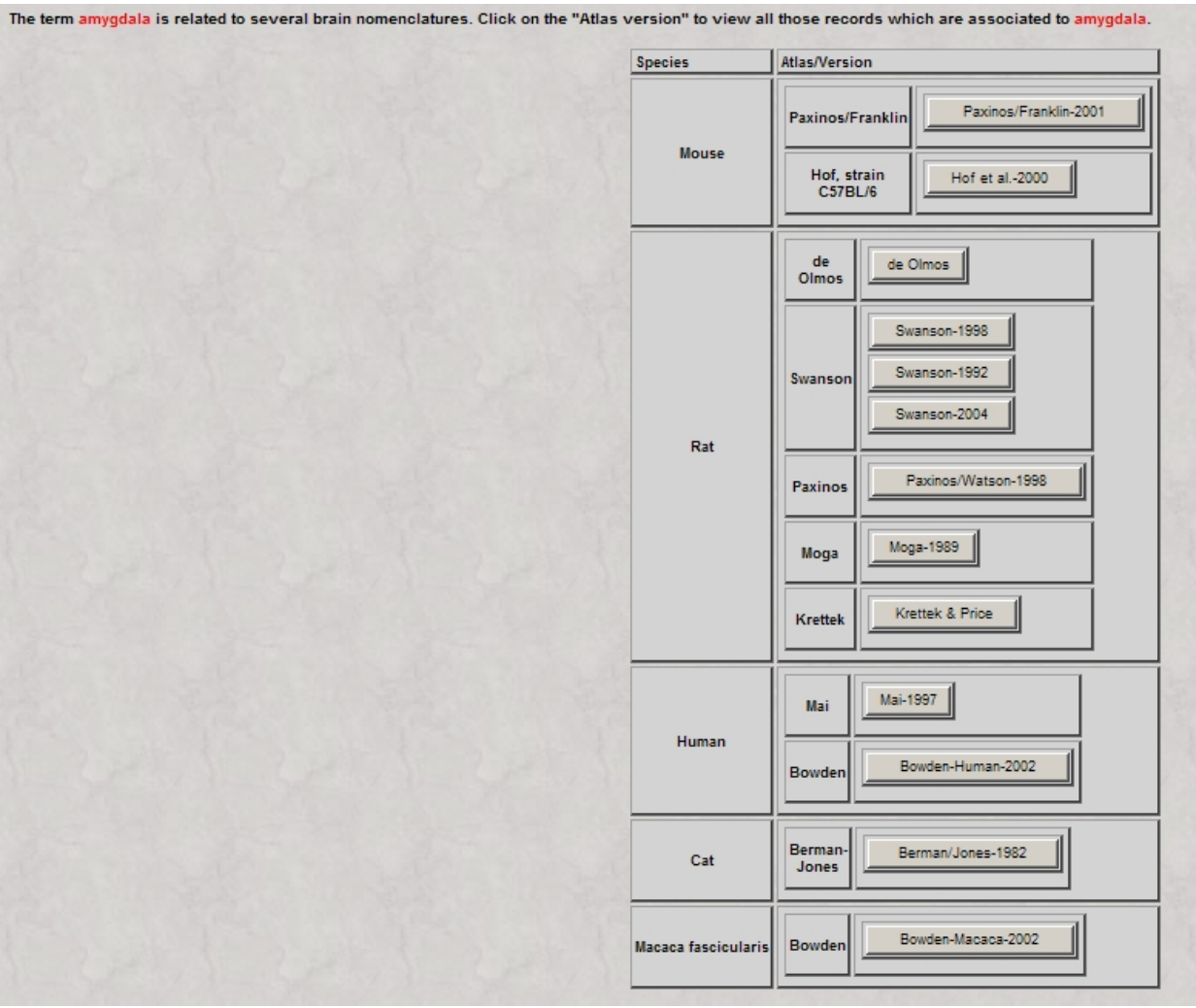
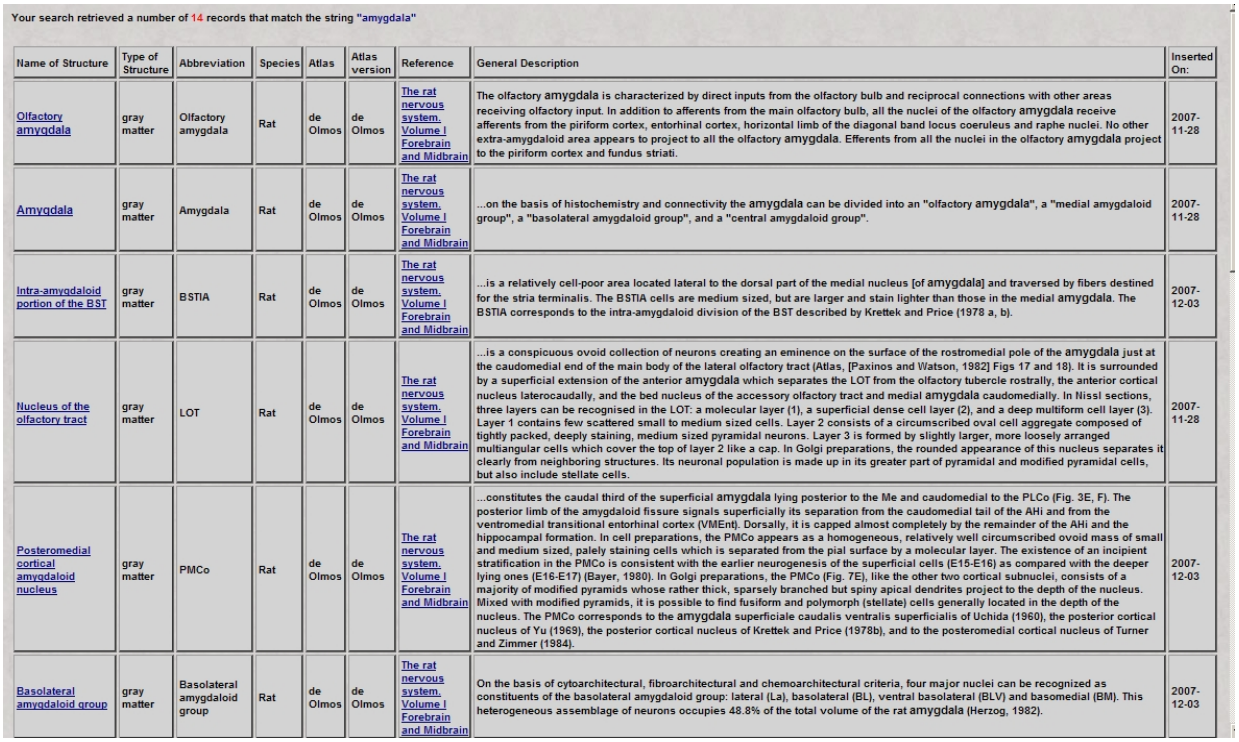


Figure 4. The list of nomenclatures and their versions (Atlas/Version), arranged by species, which include brain parts that have in the term “amygdala” in their description.

This additional step was introduced just to reduce the number of records, which can be big for strings like “amygdala”, and thus increasing the processing and display time for each user. Once a nomenclature is chosen, the associated set of results will be posted as shown in Figure 5.



Your search retrieved a number of 14 records that match the string "amygdala"

Name of Structure	Type of Structure	Abbreviation	Species	Atlas	Atlas version	Reference	General Description	Inserted On:
Olfactory amygdala	gray matter	Olfactory amygdala	Rat	de Olmos	de Olmos	The rat nervous system. Volume I Forebrain and Midbrain	The olfactory amygdala is characterized by direct inputs from the olfactory bulb and reciprocal connections with other areas receiving olfactory input. In addition to afferents from the main olfactory bulb, all the nuclei of the olfactory amygdala receive afferents from the piriform cortex, entorhinal cortex, horizontal limb of the diagonal band locus coeruleus and raphe nuclei. No other extra-amygdaloid area appears to project to all the olfactory amygdala. Efferents from all the nuclei in the olfactory amygdala project to the piriform cortex and fundus striati.	2007-11-28
Amygdala	gray matter	Amygdala	Rat	de Olmos	de Olmos	The rat nervous system. Volume I Forebrain and Midbrain	...on the basis of histochemistry and connectivity the amygdala can be divided into an "olfactory amygdala", a "medial amygdaloid group", a "basolateral amygdaloid group", and a "central amygdaloid group".	2007-11-28
Intra-amygdaloid portion of the BST	gray matter	BSTIA	Rat	de Olmos	de Olmos	The rat nervous system. Volume I Forebrain and Midbrain	...is a relatively cell-poor area located lateral to the dorsal part of the medial nucleus [of amygdala] and traversed by fibers destined for the stria terminalis. The BSTIA cells are medium sized, but are larger and stain lighter than those in the medial amygdala. The BSTIA corresponds to the intra-amygdaloid division of the BST described by Krettek and Price (1978 a, b).	2007-12-03
Nucleus of the olfactory tract	gray matter	LOT	Rat	de Olmos	de Olmos	The rat nervous system. Volume I Forebrain and Midbrain	...is a conspicuous ovoid collection of neurons creating an eminence on the surface of the rostromedial pole of the amygdala just at the caudomedial end of the main body of the lateral olfactory tract (Atlas, [Paxinos and Watson, 1982] Figs 17 and 18). It is surrounded by a superficial extension of the anterior amygdala which separates the LOT from the olfactory tubercle rostrally, the anterior cortical nucleus laterocaudally, and the bed nucleus of the accessory olfactory tract and medial amygdala caudomedially. In Nissl sections, three layers can be recognised in the LOT: a molecular layer (1), a superficial dense cell layer (2), and a deep multiform cell layer (3). Layer 1 contains few scattered small to medium sized cells. Layer 2 consists of a circumscribed oval cell aggregate composed of tightly packed, deeply staining, medium sized pyramidal neurons. Layer 3 is formed by slightly larger, more loosely arranged multiangular cells which cover the top of layer 2 like a cap. In Golgi preparations, the rounded appearance of this nucleus separates it clearly from neighboring structures. Its neuronal population is made up in its greater part of pyramidal and modified pyramidal cells, but also include stellate cells.	2007-11-28
Posteromedial cortical amygdaloid nucleus	gray matter	PMCo	Rat	de Olmos	de Olmos	The rat nervous system. Volume I Forebrain and Midbrain	...constitutes the caudal third of the superficial amygdala lying posterior to the Me and caudomedial to the PLCo (Fig. 3E, F). The posterior limb of the amygdaloid fissure signals superficially its separation from the caudomedial tail of the AHi and from the ventromedial transitional entorhinal cortex (VMEnt). Dorsally, it is capped almost completely by the remainder of the AHi and the hippocampal formation. In cell preparations, the PMCo appears as a homogeneous, relatively well circumscribed ovoid mass of small and medium sized, palely staining cells which is separated from the pial surface by a molecular layer. The existence of an incipient stratification in the PMCo is consistent with the earlier neurogenesis of the superficial cells (E15-E16) as compared with the deeper lying ones (E16-E17) (Bayer, 1980). In Golgi preparations, the PMCo (Fig. 7E), like the other two cortical subnuclei, consists of a majority of modified pyramids whose rather thick, sparsely branched but spiny apical dendrites project to the depth of the nucleus. Mixed with modified pyramids, it is possible to find fusiform and polymorph (stellate) cells generally located in the depth of the nucleus. The PMCo corresponds to the amygdala superficiale caudalis ventralis superficialis of Uchida (1960), the posterior cortical nucleus of Yu (1969), the posterior cortical nucleus of Krettek and Price (1978b), and to the posteromedial cortical nucleus of Turner and Zimmer (1984).	2007-12-03
Basolateral amygdaloid group	gray matter	Basolateral amygdaloid group	Rat	de Olmos	de Olmos	The rat nervous system. Volume I Forebrain and Midbrain	On the basis of cytoarchitectural, fibroarchitectural and chemoarchitectural criteria, four major nuclei can be recognized as constituents of the basolateral amygdaloid group: lateral (La), basolateral (BL), ventral basolateral (BLV) and basomedial (BM). This heterogeneous assemblage of neurons occupies 48.8% of the total volume of the rat amygdala (Herzog, 1982).	2007-12-03

Figure 5. The list brain parts that have in their description the term “amygdala”, and are associated with “de Olmos” brain nomenclature. See text for details.

The table shown in Figure 5 includes two types of links: one that is associated with the retrieved brain parts, and one associated with the cited reference. The link associated with the cited reference leads to a page that displays details about it, which includes URL to the Pubmed abstract, if the reference is an article published in journal indexed by this database.

The link associated with the retrieved brain parts leads to a page that summarizes the data and metadata associated in BAMS. The example shown in Figure 6 represents a summary of the data and metadata associated with a nucleus of the rat paraventricular hypothalamic nucleus, identified in the Swanson-1998 nomenclature. The minimal displayed information is the list of identical terms identified in other species/nomenclatures and the definition, and the reference details of the brain part, which can be accessed by clicking on the button “More”. An example of the metadata that can be accessed through the “More” button is shown in Figure 7. This includes the criteria used to include the associated brain part in an internally consistent hierarchy.

If the retrieved brain part is captured in a hierarchical tree, then the tree of super-parts (parents) including it and the set of substructures that lie immediately under it are returned. Users can navigate along the

hierarchy of a nomenclature by accessing any structures that are either superstructures or substructures of the retrieved brain region. If the searched region's hierarchical tree is reconstructed up to the root (the CNS for the rat brain nomenclature, Swanson-1998), then users can view the position of the retrieved region in the reconstructed hierarchical tree by clicking the button "Tree," as shown in Fig. 6.

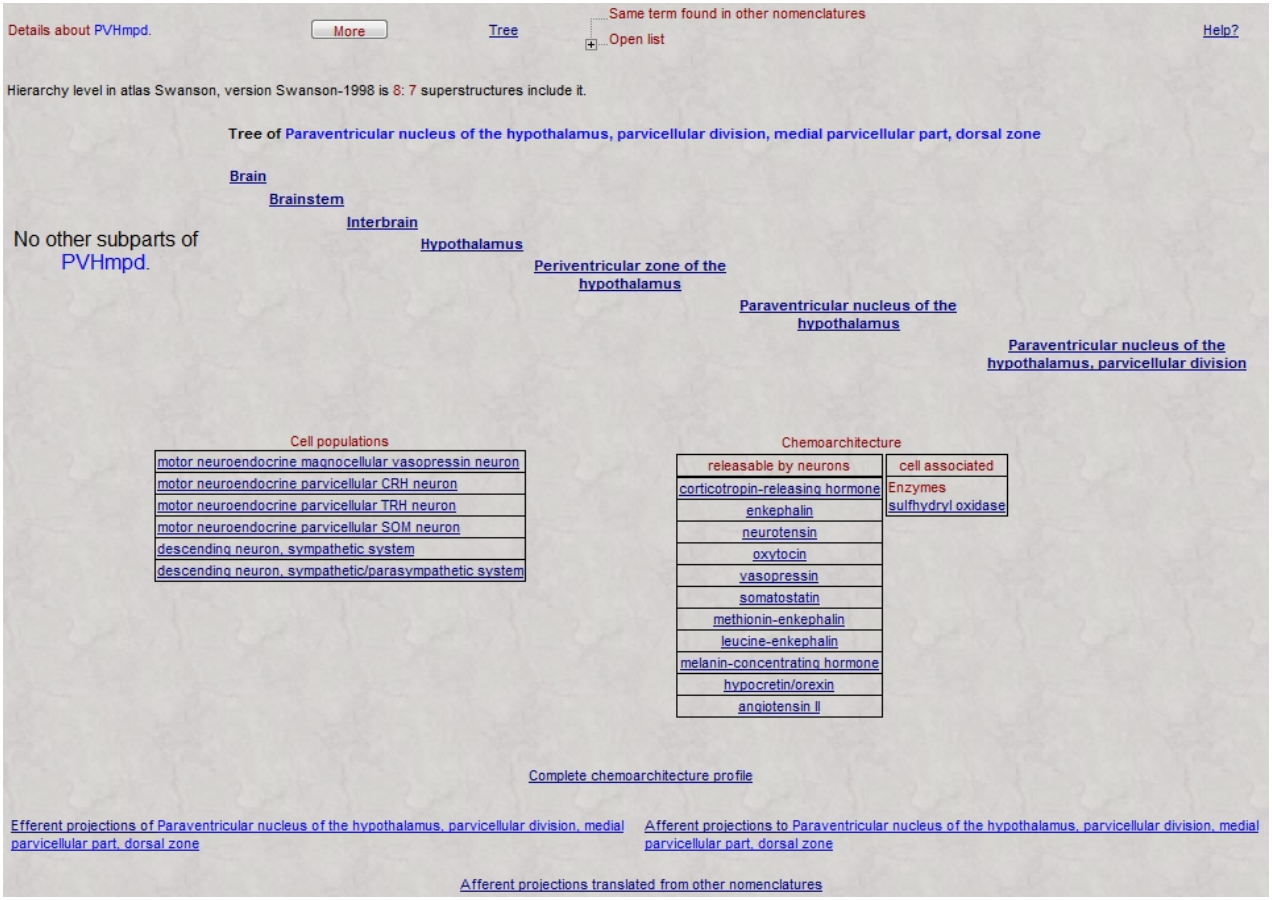
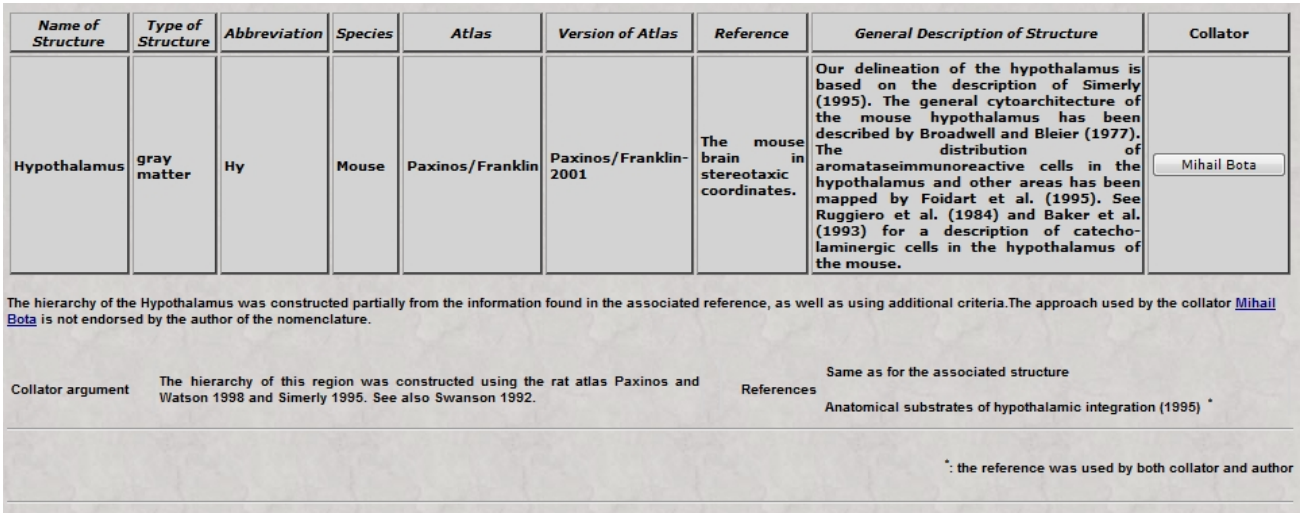


Figure 6. The output page that summarizes the data and metadata associated to a brain part in BAMS. See the text for detailed explanation of each displayed category.



Name of Structure	Type of Structure	Abbreviation	Species	Atlas	Version of Atlas	Reference	General Description of Structure	Collator
Hypothalamus	gray matter	Hy	Mouse	Paxinos/Franklin	Paxinos/Franklin-2001	The mouse brain in stereotaxic coordinates.	Our delineation of the hypothalamus is based on the description of Simerly (1995). The general cytoarchitecture of the mouse hypothalamus has been described by Broadwell and Bleier (1977). The distribution of aromataseimmunoreactive cells in the hypothalamus and other areas has been mapped by Foidart et al. (1995). See Ruggiero et al. (1984) and Baker et al. (1993) for a description of catecho-laminergic cells in the hypothalamus of the mouse.	Mihail Bota

Figure 7. The details about a brain region of interest that can be accessed by clicking on the button “More” shown in Fig. 6. The displayed metadata include the description (definition) of the region, and the method of including it in a internally consistent hierarchy.

In this example, the position in the hierarchy of the brain region “Hypothalamus” identified in the mouse and defined in the neuroanatomical atlas Paxinos/Franklin-2001 (Paxinos and Franklin, 2001), is based on a reference cited by the authors of the nomenclature and on a reference used by the collator. Users can thus view the modes of hierarchy construction for the brain region of interest, as well as arguments and references used by collators, in a textual format, along with references that were used.

The output web page containing information about the searched brain region (Fig. 6) also includes links to several BAMS inference engines associated with the *Cells* and *Molecules* modules. Each of these inference engines will be discussed below.

Search of brain parts can be performed in two additional ways (see the general structure of the Menu, page 4): search parts by species (direct link http://brancusi.usc.edu/bkms/brain/search_bspecies.php), and search by nomenclature (direct link http://brancusi.usc.edu/bkms/brain/search-nomenclature.php).

The interface for search brain parts by species lists the distinct species, or genera, which are recorded in BAMS. So far, there are five distinct species (genera) recorded in BAMS: human, macaque (general), Macaca fascicularis, cat, rat, and mouse. The various rat and mice strains are displayed in the output pages of different queries. As for the free text search option, the result of search by species is first limited by the nomenclature, and this type of encoding was made for the same reason: the reduction of time of processing of queries, which can become important if the computational load is big. Different of the free text search, the intermediary step of choosing a nomenclature includes graphically encoded metadata, that specify whether a nomenclature is hierarchically organized, and its brain parts are associated with connectivity reports. An example is shown in Fig.8, which is the display of nomenclatures associated in BAMS with species rat.

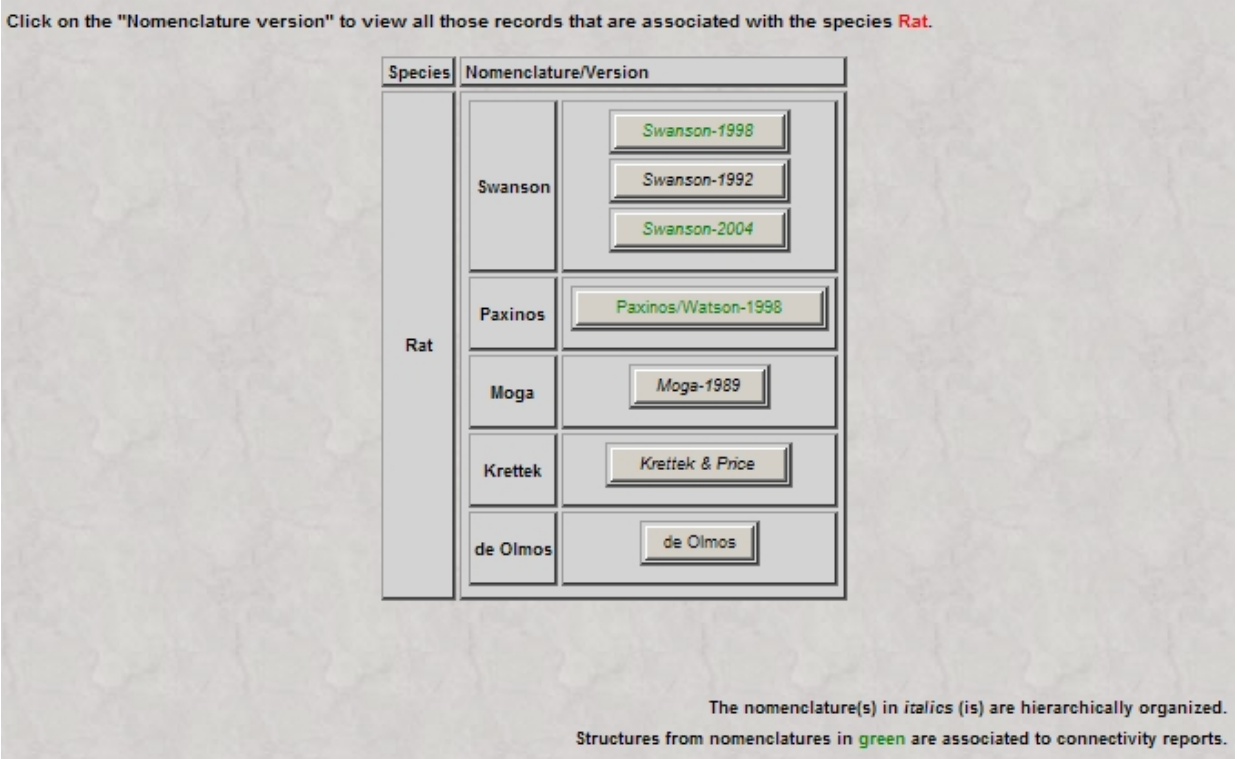


Figure 8. The intermediary step of choosing a nomenclature, which is a part of the query of search of brain regions by species. The nomenclatures that are hierarchically organized and include brain regions that are associated with connectivity reports, are graphically labeled (italics fonts, and font color green, respectively).

After a nomenclature is chosen, the system returns the brain parts included in it, alphabetically arranged. If the nomenclature includes more than 50 terms, then the returned page will include only the first 50 ones, an alphabetical index, and a search by name option. The structure of this output page was designed in such way that will be processed and displayed as fast as possible. An example of the output of search brain parts by species is shown in Figure 9.

Species: Rat, Atlas: Swanson, Reference: Brain Maps: Structure of the Rat Brain

Your search will retrieve more than 50 names. You may want to narrow the search, or view the names of brain structures alphabetically.

Search by name of structure [ ] Search!

A B C D E F G H I J K L M N O P R S T U V Z

The first 50 structures retrieved by your query. Click on any below to see details about them

Name of Structure	Type of Structure	Abbreviation	General Description of Brain Part
Abducens nerve	fiber tract	VIn	According to Hebel and Stromberg 1986
Abducens nucleus	gray matter	VI	According to Glicksmann 1980.
Abducens nucleus proper	gray matter	VI_p	This is the remaining part of the abducens nucleus after eliminating the accesory abducens nucleus
Accesory abducens nucleus	gray matter	ACVI	According to Szekely and Matesz 1982.
Accessory facial nucleus	gray matter	ACVII	According to Szekeley and Matesz 1982.
Accessory olfactory bulb	gray matter	AOB	According to Gurdjian 1925, Shipley et al. 1996.
Accessory olfactory bulb, glomerular layer	gray matter	AOBgl	None provided
Accessory olfactory bulb, granular layer	gray matter	AOBgr	None provided

Figure 9. The result of search of brain regions by species. This search is initially restricted by nomenclature, as shown in Fig. 8.

The result of search of brain regions by nomenclature is very similar to that of search by species (Fig. 9). The option of search is made of a pull-down list of available nomenclature versions, as shown in Figure 10.

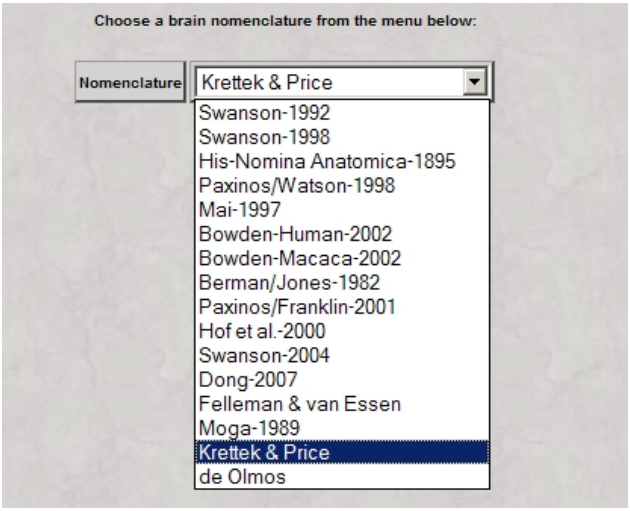


Figure 10. The list of neuroanatomical nomenclatures included in BAMS, arranged in a pull-down list, which can used for brain parts searches.

3.2 Manipulation of neuroanatomical projections in BAMS

Neuroanatomical projections are modeled in BAMS by a complex backend database schema that includes more than 40 variables (Bota et. al. 2005). The interfaces that have been developed range from simple display of experimental data and metadata, to inference engines that construct possible brain regions networks, or qualitatively translate projection reports across different nomenclatures.

The simplest way to view the pattern of connectivity of a brain region is to search for it (see section 3.2), and the result of the search will be a page similar to Fig. 6. If the brain region is associated with projections reports in BAMS, then two links become available to the user: “Efferent projections to” and “Afferent projections from”.

The link “Efferent projections to” becomes visible to the user whenever the brain region is associated with projections reports that originate from it and terminate in other regions. The output page of this link will list all brain regions that receive neuroanatomical projections from the region of interest, and are recorded in BAMS. If the associated brain nomenclature is hierarchically organized, then the list of inputs will be organized accordingly. An example of such output is shown in Fig. 11.

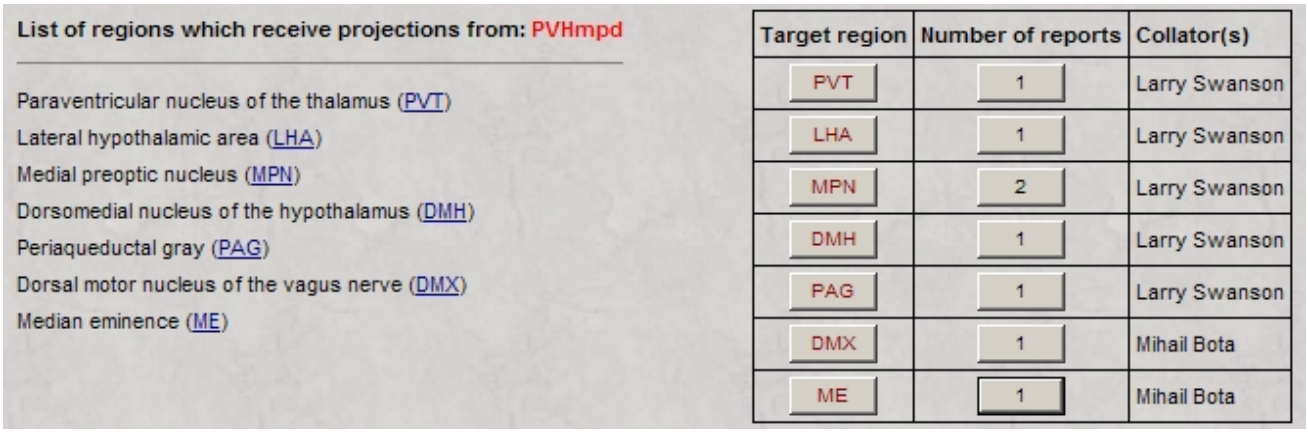
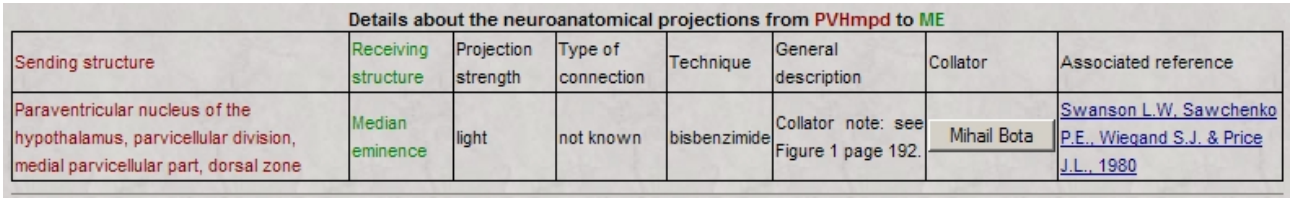


Figure 11. The hierarchically organized list of brain regions that receive projections from the rat PVHmpd, identified in the Swanson-98 nomenclature, together with associated number reports in BAMS and collators.

The output page does not only display the list of regions that receive projections from the brain region of interest, but also the associated number of reports and collators. Clicking on the link associated with the target region abbreviation will lead the user to the summary page shown in Fig. 6. Clicking on the buttons included in the right-hand side table, under the field “Target region” will bring details about the target region, as shown in Fig. 7. The details of connectivity reports that are associated to each target region can be accessed by clicking on the buttons under the field “Number of reports”. The details of the projection from the rat PVHmpd to the median eminence (ME) are shown in Figure 12.



Details about the neuroanatomical projections from PVHmpd to ME

Sending structure	Receiving structure	Projection strength	Type of connection	Technique	General description	Collator	Associated reference
Paraventricular nucleus of the hypothalamus, parvicellular division, medial parvicellular part, dorsal zone	Median eminence	light	not known	bisbenzimide	Collator note: see Figure 1 page 192.	Mihail Bota	Swanson L.W. Sawchenko P.E., Wiegand S.J. & Price J.L., 1980

Figure 12. Projection reports details that can be accessed by clicking on the buttons that display the numbers of reports, shown in Fig. 11. Displayed metadata include the assessed qualitative strength of the projection, the connection type (in terms of neurotransmitters), the used technique, an annotation which can be used to associate the text most relevant to the presence or absence of the projection, the collator's name, and the associated reference. If the reference is a published journal article, the URL to the PubMed abstract will also be displayed.

The link "Afferent projections from" shown in Figure 6 becomes available when the brain region of interest is associated in BAMS with reports of regions that send neuroanatomical connections to it. The display of sources that project to the brain region of interest and of the associated metadata is very similar to Figs. 11 and 12.

Whenever a brain region, captured in a hierarchy, is composed of subparts, and at least one of these is associated with connectivity reports in BAMS, then two additional links become available in the summary web page (Fig. 6): "Inferred efferent projections", and "Inferred afferent projections" (Fig. 13).

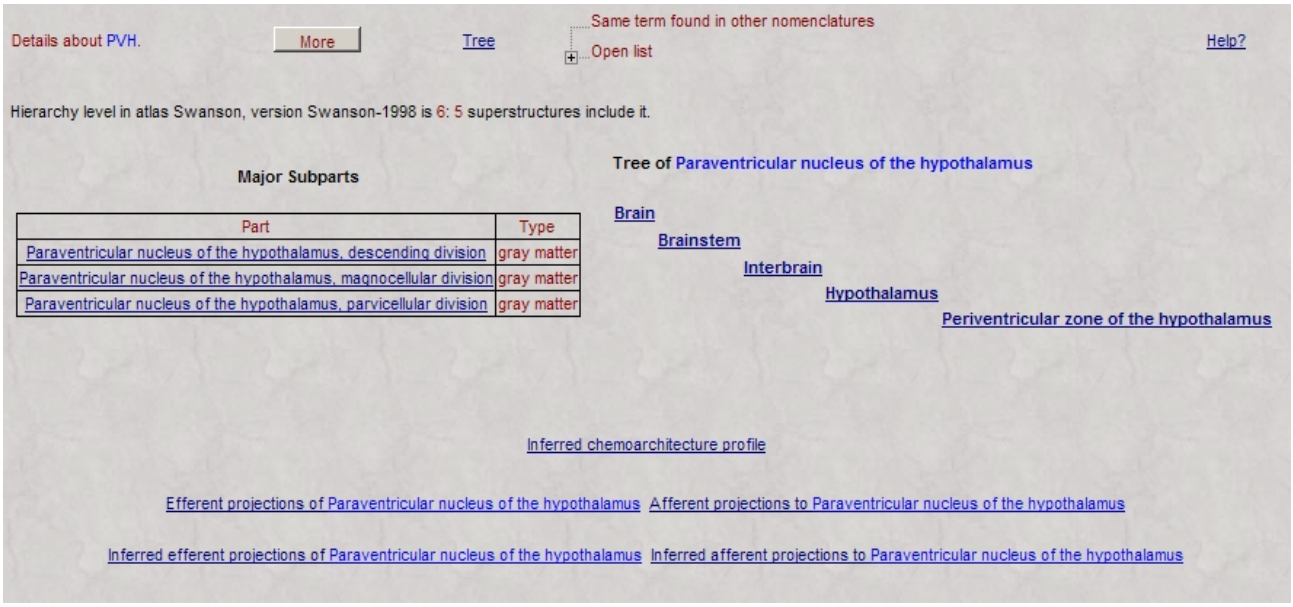
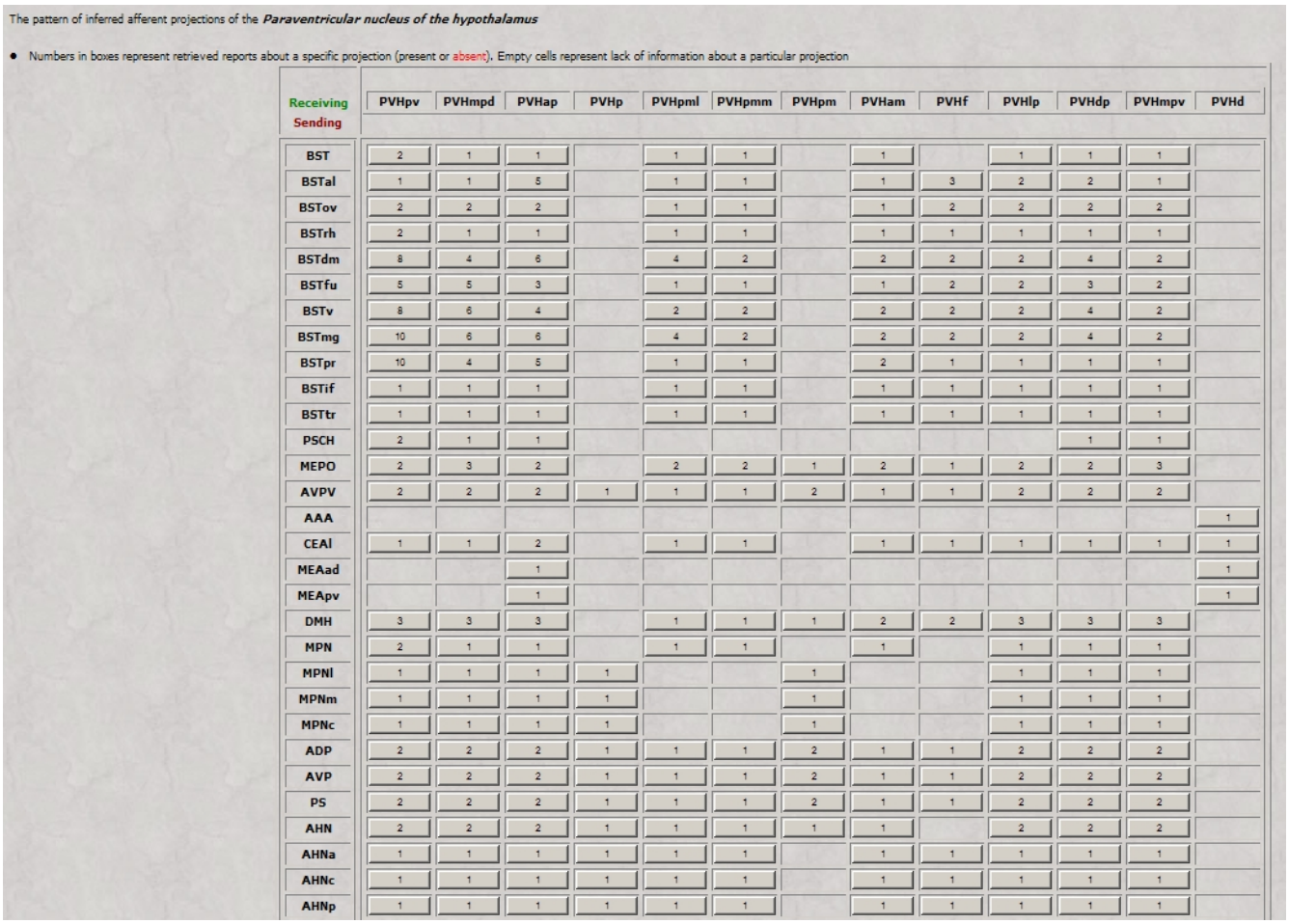


Figure 13. The BAMS page that displays summary information about the paraventricular nucleus of the hypothalamus (PVH). If a brain regions, such as PVH, is made of a set of subregions, and at least one of these is associated with reports of efferent or afferent projections, then two additional links will become available to the user: "Inferred efferent projections" and "Inferred afferent projections". These links lead to pages that reconstruct the output, and input respectively", projections patterns of the brain region (PVH) from the projection reports associated to its subregions.

The output pages of either of these links reconstruct in tabular formats the connectivity patterns of the brain region of interest from the connection patterns of the component subparts. The inferred pattern of inputs to the rat PVH is shown in Figure 14.



The pattern of inferred afferent projections of the ***Paraventricular nucleus of the hypothalamus***

- Numbers in boxes represent retrieved reports about a specific projection (present or absent). Empty cells represent lack of information about a particular projection

Receiving / Sending	PVHpv	PVHmpd	PVHap	PVHp	PVHpml	PVHpmm	PVHpm	PVHam	PVHf	PVHlp	PVHdp	PVHmpv	PVHd
BST	2	1	1		1	1		1		1	1	1	
BSTal	1	1	5		1	1		1	3	2	2	1	
BSTov	2	2	2		1	1		1	2	2	2	2	
BSTrh	2	1	1		1	1		1	1	1	1	1	
BSTdm	8	4	6		4	2		2	2	2	4	2	
BSTfu	5	5	3		1	1		1	2	2	3	2	
BSTv	8	6	4		2	2		2	2	2	4	2	
BSTmg	10	6	6		4	2		2	2	2	4	2	
BSTpr	10	4	5		1	1		2	1	1	1	1	
BSTif	1	1	1		1	1		1	1	1	1	1	
BSTtr	1	1	1		1	1		1	1	1	1	1	
PSCH	2	1	1								1	1	
MEPO	2	3	2		2	2	1	2	1	2	2	3	
AVPV	2	2	2	1	1	1	2	1	1	2	2	2	
AAA													1
CEAl	1	1	2		1	1		1	1	1	1	1	1
MEAad			1										1
MEApv			1										1
DMH	3	3	3		1	1	1	2	2	3	3	3	
MPN	2	1	1		1	1		1		1	1	1	
MPNl	1	1	1	1			1			1	1	1	
MPNm	1	1	1	1			1			1	1	1	
MPNc	1	1	1	1			1			1	1	1	
ADP	2	2	2	1	1	1	2	1	1	2	2	2	
AVP	2	2	2	1	1	1	2	1	1	2	2	2	
PS	2	2	2	1	1	1	2	1	1	2	2	2	
AHN	2	2	2	1	1	1	1	1		2	2	2	
AHNa	1	1	1	1	1	1		1	1	1	1	1	
AHNc	1	1	1	1	1	1		1	1	1	1	1	
AHNp	1	1	1	1	1	1		1	1	1	1	1	

Figure 14. The inferred afferent pattern of projections of the PVH, online reconstructed in BAMS. The pattern is displayed in a tabular format. Numbers in boxes represent reports about a specific projection (present or absent). The empty cells of the matrix represent lack of information about those particular projections.

3.3. Construction of brain regions networks in BAMS

The web interface of BAMS allows online construction of brain region networks from recorded connectivity reports.

The first way of creating brain regions networks is to use the “Outputs” option from the Menu (path: Menu→Evaluate→Connections→Outputs). This option will first create the matrix of output connections of a set of brain regions that is chosen by the user. Therefore, users have to choose the set of brain regions of interest from the set of all regions that are recorded in BAMS with at least one projection. In order to do this,

they first have to choose the brain nomenclature they will be working with, from the list displayed by the system (Fig. 15).

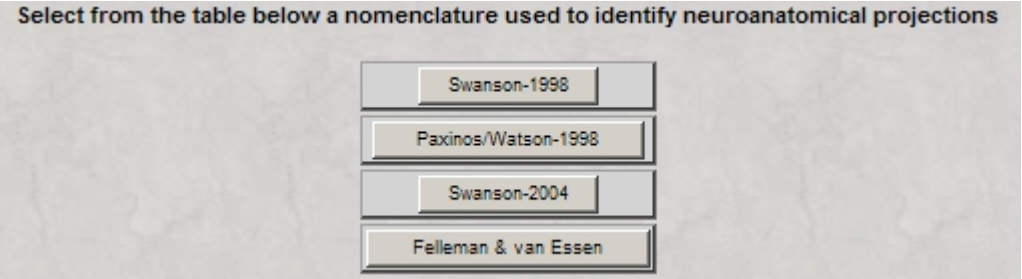


Figure 15. The set of brain nomenclatures, from which the user has to chose in order to construct the connectivity matrix of interest.

Once the nomenclature is chosen, the system will display all the brain regions that are associated with efferent projections reports in BAMS, in a tabular checkboxes format as shown in Fig. 16.

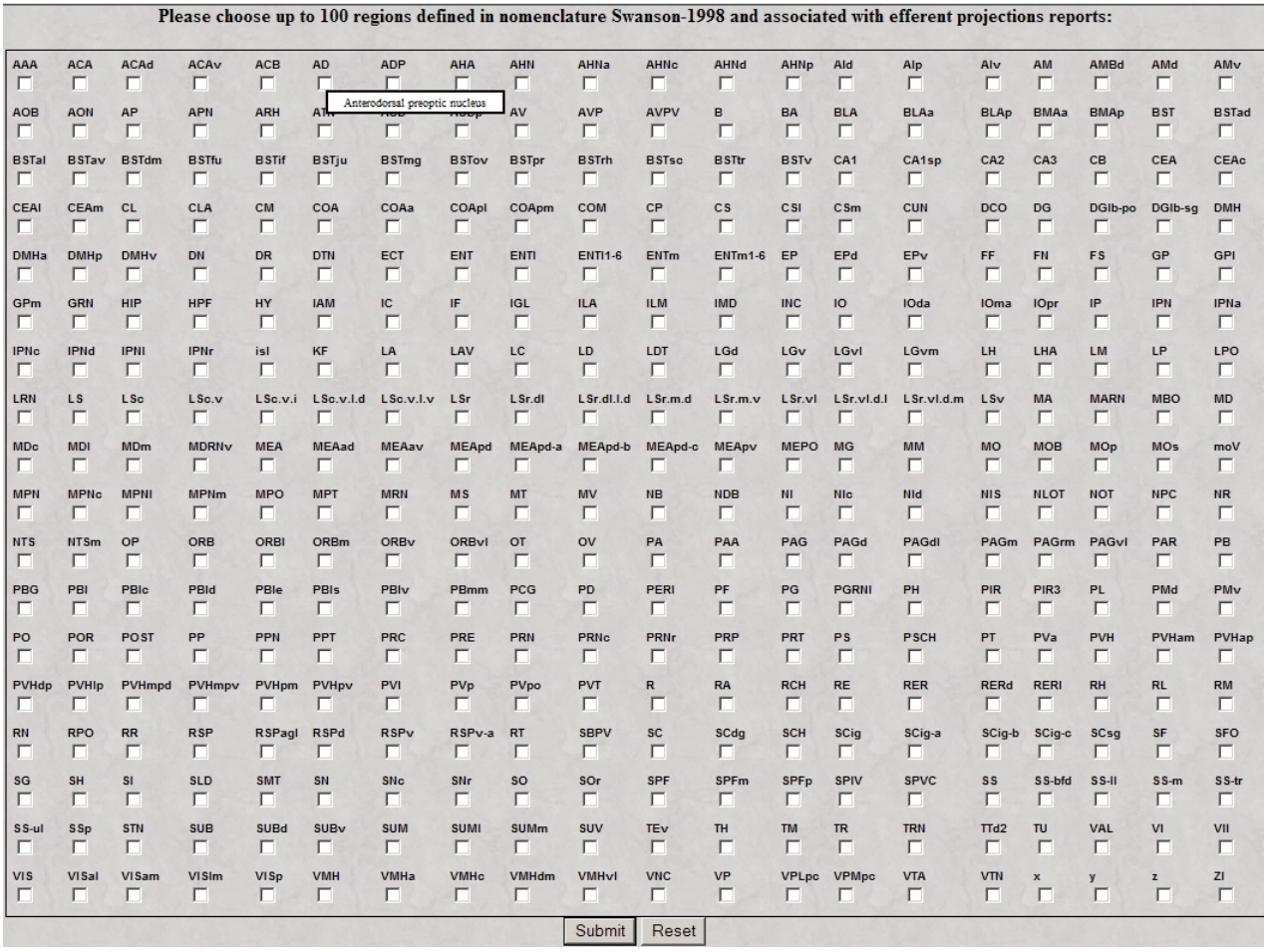


Figure 16. Once users choose a brain nomenclature, the set of brain regions that are associated with efferent projections reports are displayed checkboxes labeled with the regions' abbreviations. The name of each brain region will be displayed if the mouse is over the abbreviation. Users can choose up to 100 regions, to create the matrix of interest.

Once the user chose the set of brain regions of interest, the system will display all the regions that receive connections, and are recorded in BAMS. The user can choose of subset from these targets, or all of them. Once these regions have been chosen, the system will create the corresponding matrix of projections in a tabular format. Figure 17 shows the connectiviy matrix between several amygdalar nuclei and the components of the bed nuclei of the stria terminalis (BST), all of them identified in the rat nomenclature Swanson-1998.

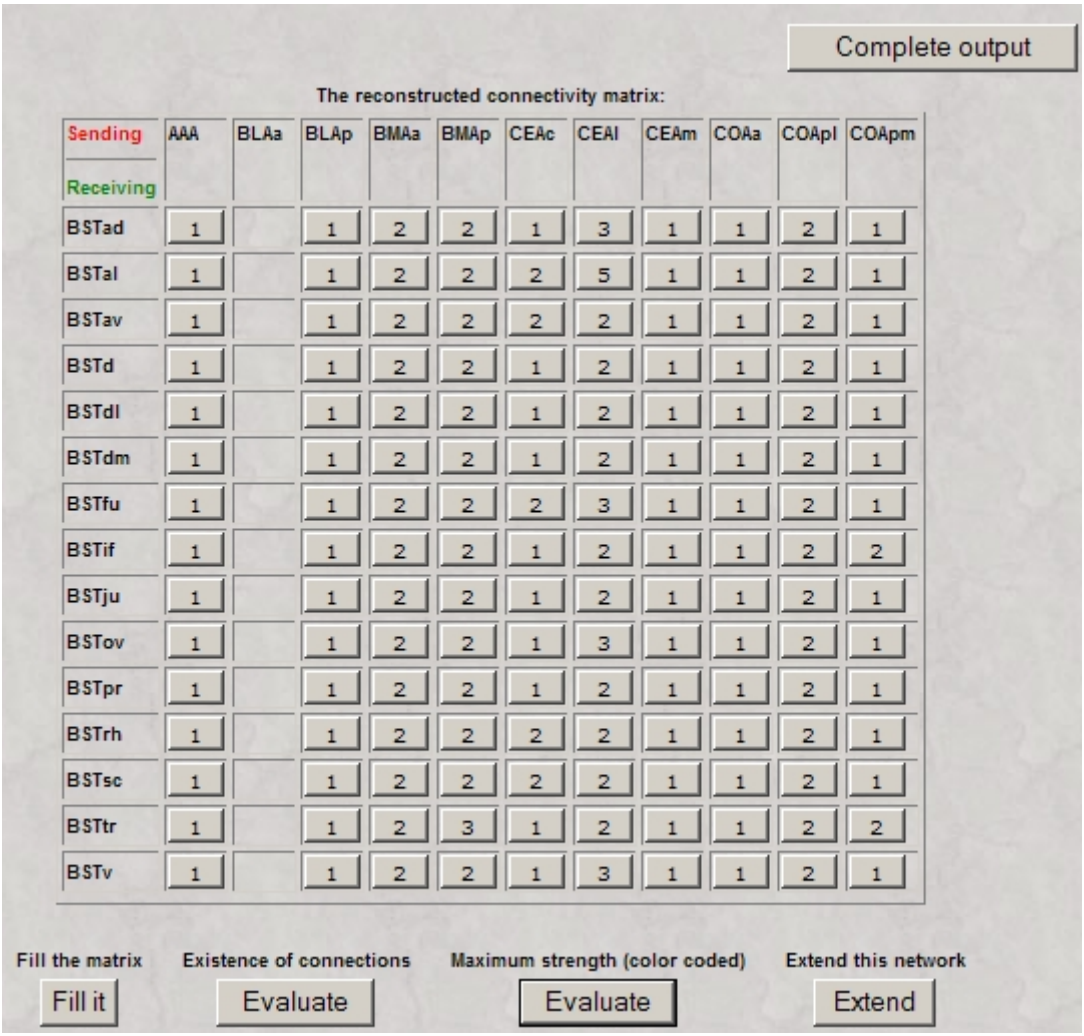


Figure 17. The user-created matrix of projections of several nuclei of the rat amygdala to the parts of the BST. Users have several options of further processing and organizing this matrix, trough the buttons displayed.

The reconstructed connectivity matrix shown in Figure 1 is similar with the matrix shown in Figure 14, with empty elements that mean lack of information about that particular connection. Details about each of connection (each element of the matrix) can be accessed by clicking on the corresponding buttons. As in Figure 14, the numbers displayed on each button mean the number of reports associated with a particular connection. This output display includes several options for further processing and display of projections

data. The button “Fill the data” becomes available whenever there is an empty cell in the reconstructed matrix. In this situation, the system will attempt to fill the “missing” information with connectivity data translated from other nomenclatures. The button “Existence of connections” will re-display the reconstructed connectivity matrix in a Boolean fashion: existent projections, absent projections and “missing” information. The “Maximum strength” button leads to a page that re-evaluates the matrix in terms of qualitative assessments of connections reports. This matrix will also be reordered if the brain regions are captured in a hierarchy. The color coded matrix from Fig. 17 is shown in Fig. 18

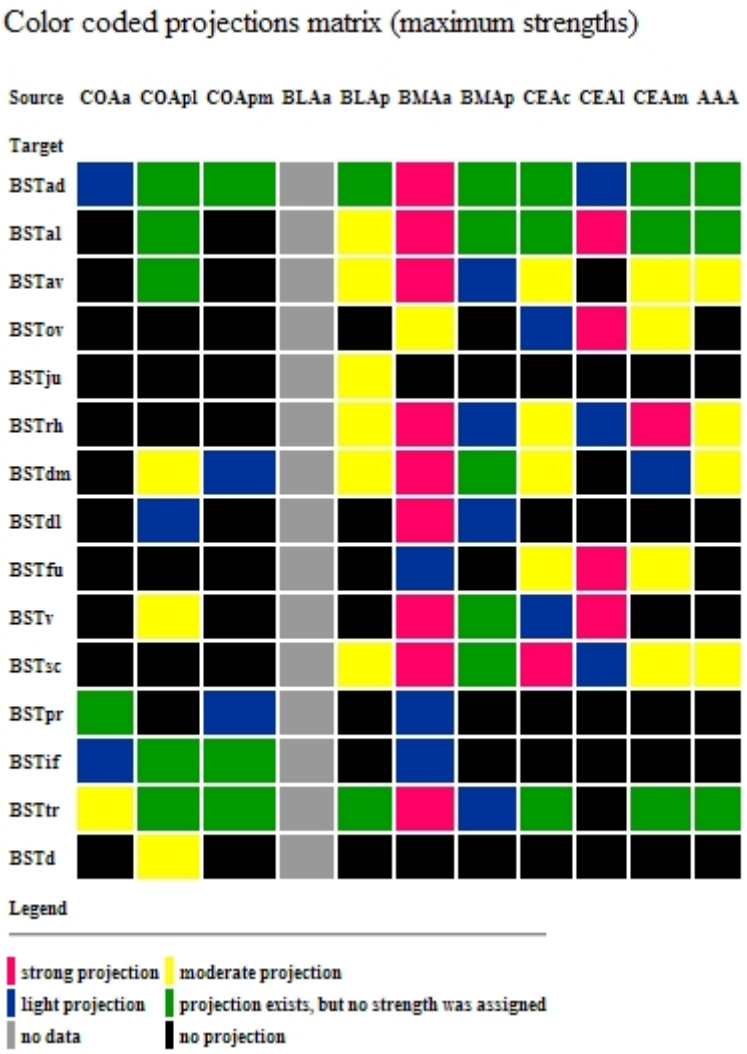


Fig 18. The matrix of outputs of several amygdalar nuclei to BST, graphically displayed as qualitative assessments of projections strengths. The matrix is also rearranged according to the hierarchy of the rat brain nomenclature Swanson-98.

The button “Complete output”, shown in Fig. 17, leads to the page that will display the output matrix of the chosen set of brain regions with all brain regions included in the associated nomenclature. The processing

time of this matrix can be significant, especially if the set of chosen output regions is large, and the computational of the server is high.

Finally, the button “Extend this network” shown in Figure 17 becomes visible whenever the set of target regions is associated in BAMS with reports of their efferents. Thus, this button allows users to create networks of brain regions from the inserted connectivity reports. Clicking on this button will retrieve those brain regions that receive projections from the targets shown in Figs. 17 and 18. Therefore, this set of targets becomes the second set of outputs for the brain regions shown in Fig. 19.

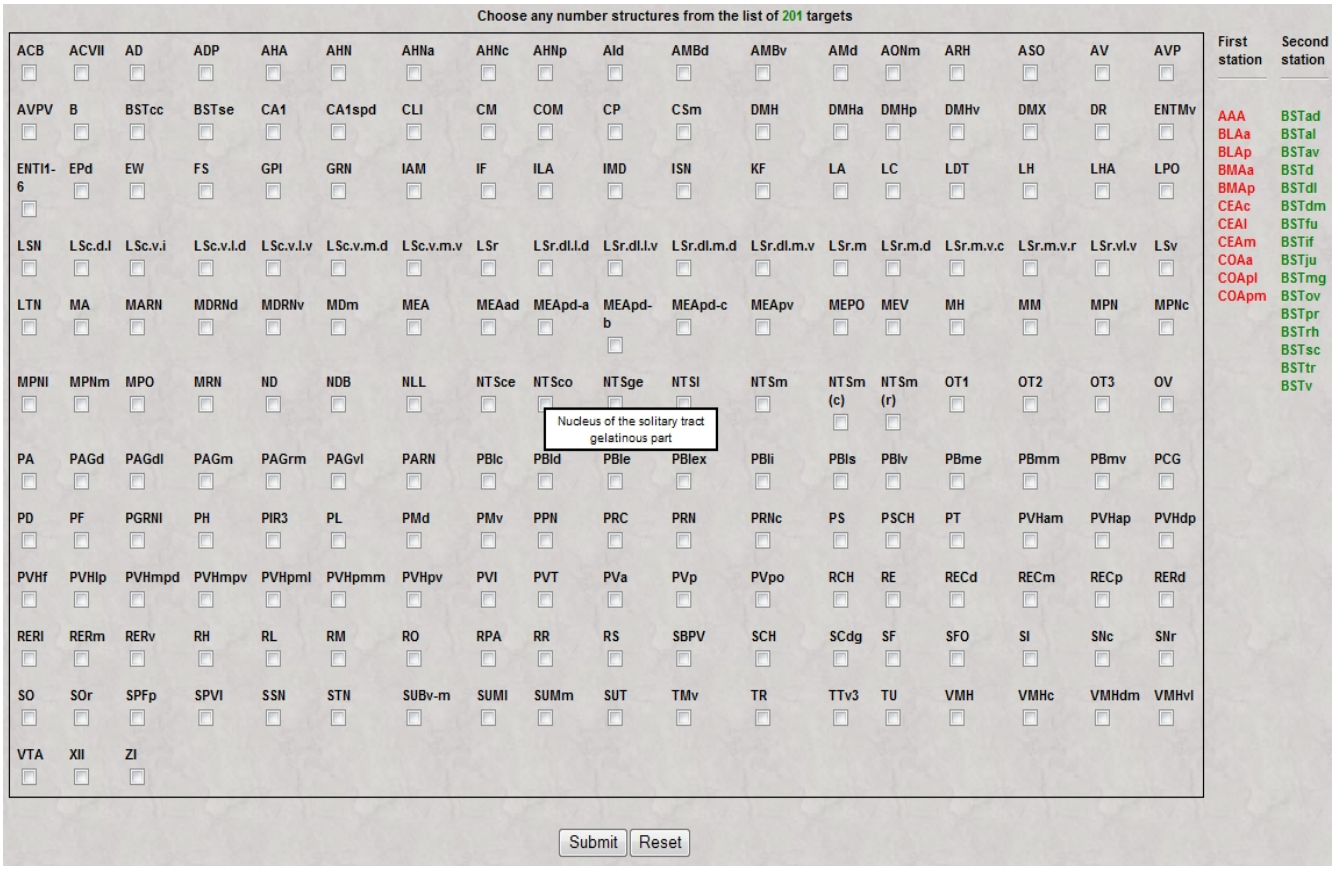


Figure 19. The screen that can be used to choose the third set of regions for creation of customized networks. This screen is very similar to the one shown in Fig. 16.

The network of regions that will be constructed by BAMS will be displayed in a tree-like format, with the first column made of the first station regions, the second made of the second station regions, listed for each of the first-order region. The third column, which is designed in the form of an expandable trees, called “Targets” in Figure 20. These trees are made of the third-order set of regions that receive projections from each of the second-order regions. Users have therefore the option of expanding only those trees with outputs of interest and view the associated details, which are provided through URL’s. Figure 20 shows the example of the network constructed from regions used in Figs. 17-19, and a small set of motor output regions of the rat brain that are the targets of the BST nuclei.

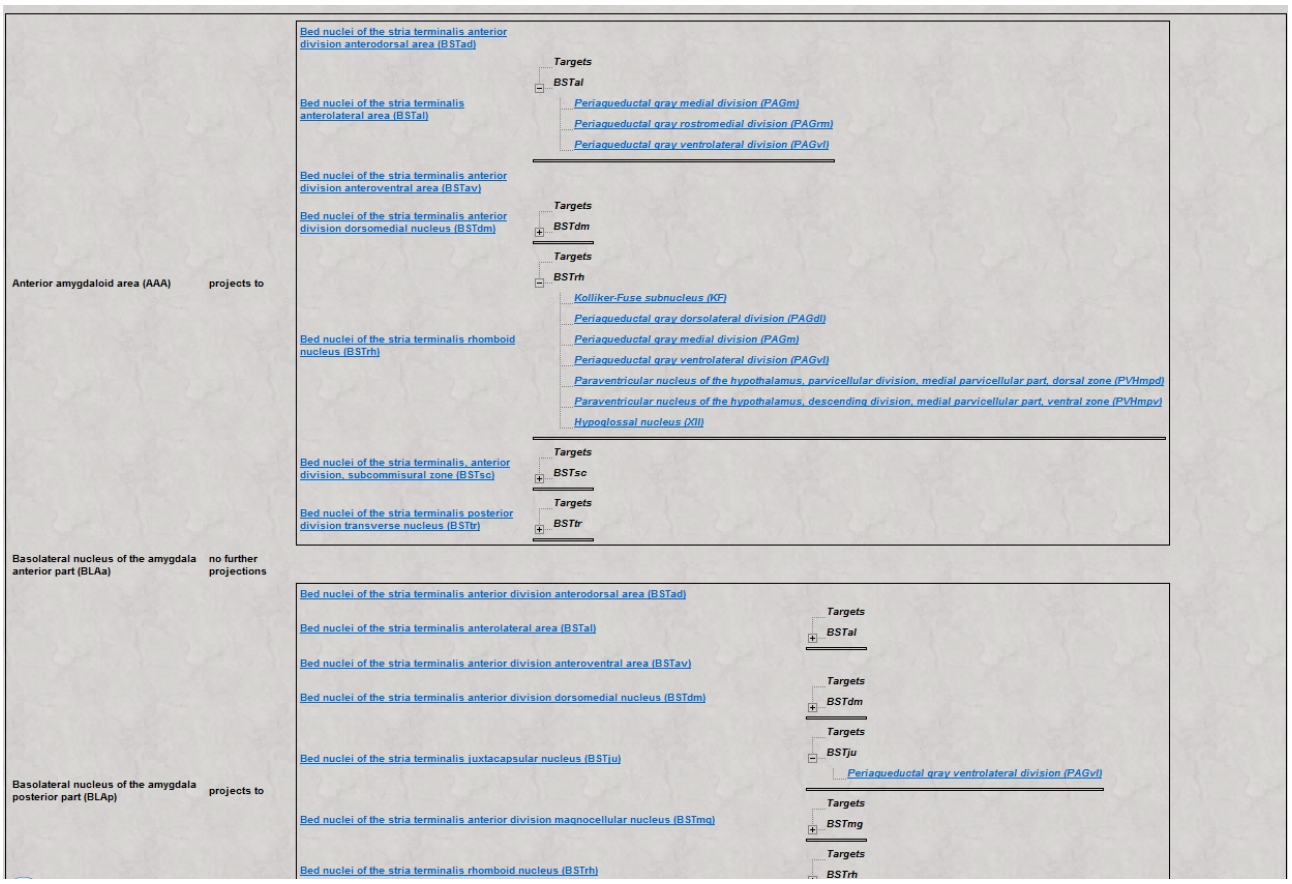


Fig. 20. The network resultant from the matrix shown in Fig. 17 and the third set of regions chosen from the screen shown in Fig. 19. The first set of regions is made of several nuclei of the amygdala, the second from the BST nuclei, and the final from motor hypothalamic and brainstem regions that receive connections from the BST. The displayed links lead to pages that include details about retrieved projections.

This matrix organized in a tabular format as shown in Fig. 20 also includes a button called “Create graph” that will lead to a script which will construct the graphical version of it. The brain regions network shown in Figure 21 is thus the graphical version of the matrix constructed in Figure 20 and is constructed online.

This feature of BAMS, to construct online brain regions networks, from recorded in the backend database of the system, represents a unique feature it. BAMS is the first system that allows users to reconstruct the networks of the brain regions of interest.

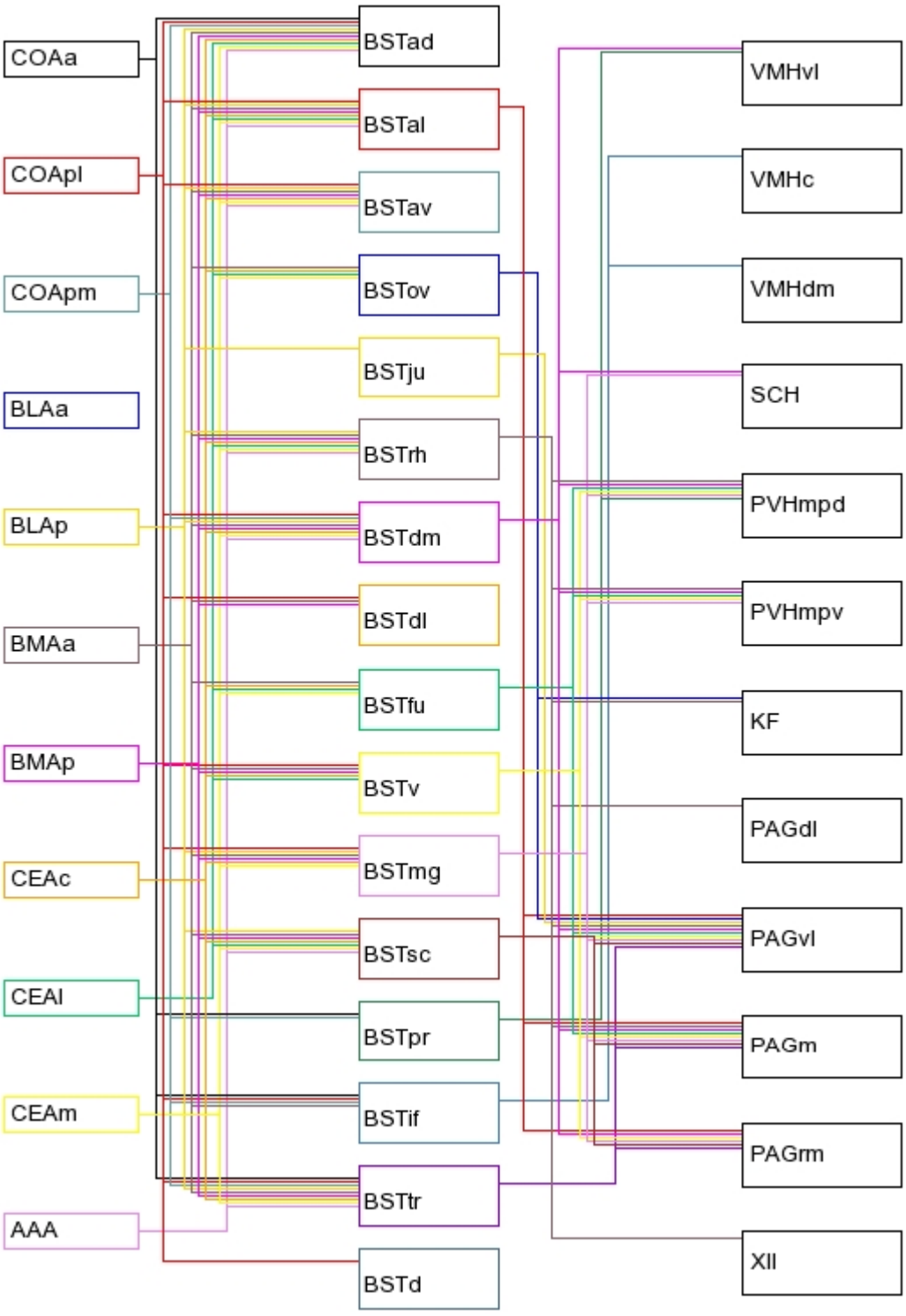


Figure 21. The network displayed in Fig. 19, in a graphical format. This network can be saved by users in an image format (.png).

BAMS includes the options of creating user-customized projections matrices and networks, starting from the inputs of a set of regions of interest. The interface and method of constructing projection matrices and networks are very similar to those described above. The pathway of accessing "Inputs" is Menu→Evaluate→Connections→Inputs.

3.4. Inference of possible networks in BAMS.

A second way of creating online brain regions networks in BAMS is the "Networks" option of the Menu (pathway: Menu→Evaluate→Connections→Networks). This method differs from the one described in the previous sections, in how the networks are created. A complete description of the employed inference engine and of the adopted formalism can be found in Bota et al., 2005.

The first step in creating possible networks of brain regions is to choose the brain nomenclature where the regions have been identified, or defined. Therefore, a screen very similar to Fig. 15 will ask the user to choose one of the nomenclatures associated in BAMS with projection reports.

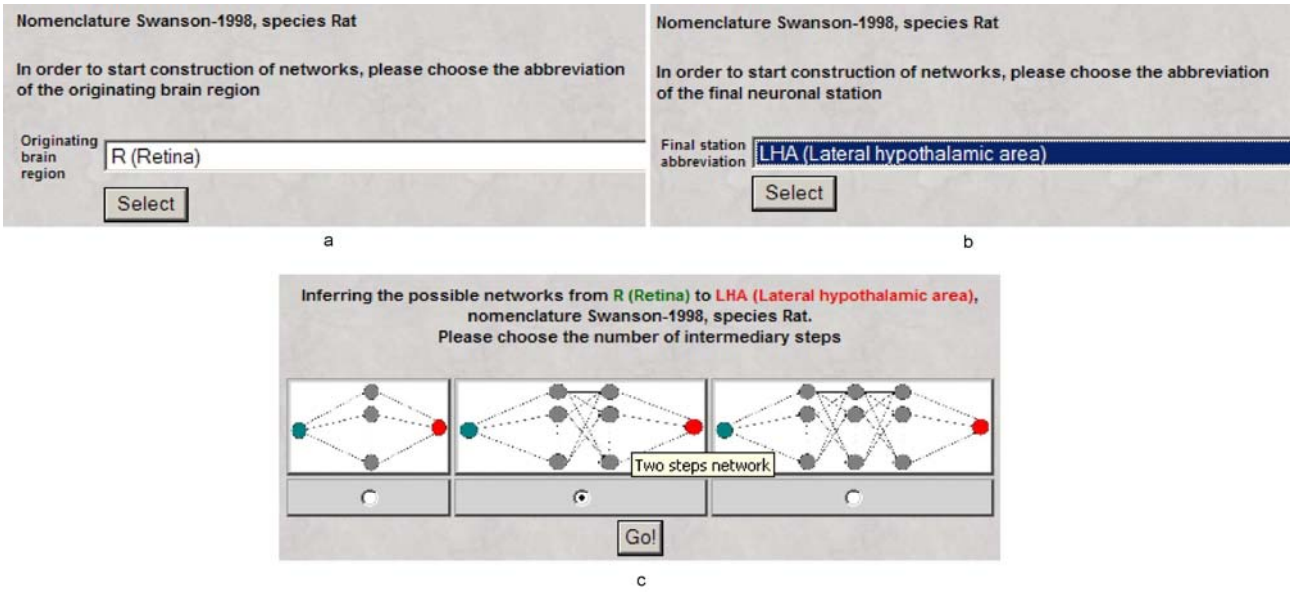
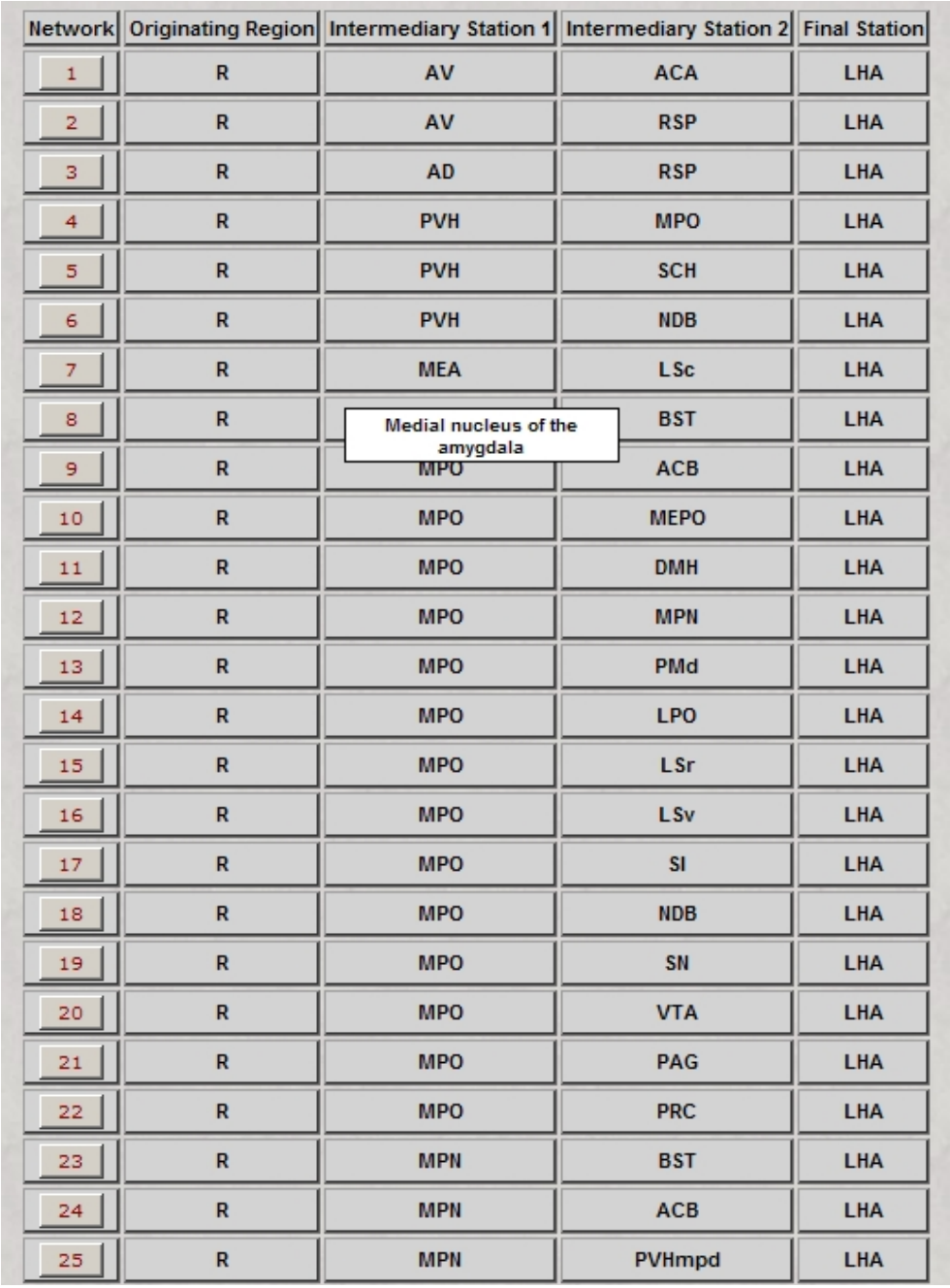


Figure 22. Users have to choose the starting point of the inferred networks (a), the ending point of them (b), and the number of intermediary steps (brain regions) between them (c).

Once the nomenclature was chosen, users will have to choose the originating brain region (Fig. 22a), the final neuronal station of the network (Fig. 22b), and how many intermediary steps (layers of regions) will have the inferred networks (between 1 and 3; Fig. 22 c). After the originating and final stations, and the number of steps, were chosen, the system will display the inferred networks in a tabular format. If the connectivity data inserted in BAMS is not sufficient, the system will suggest the increase of the number of intermediary layers, or choosing another pair of brain regions. An example of the possible networks that can

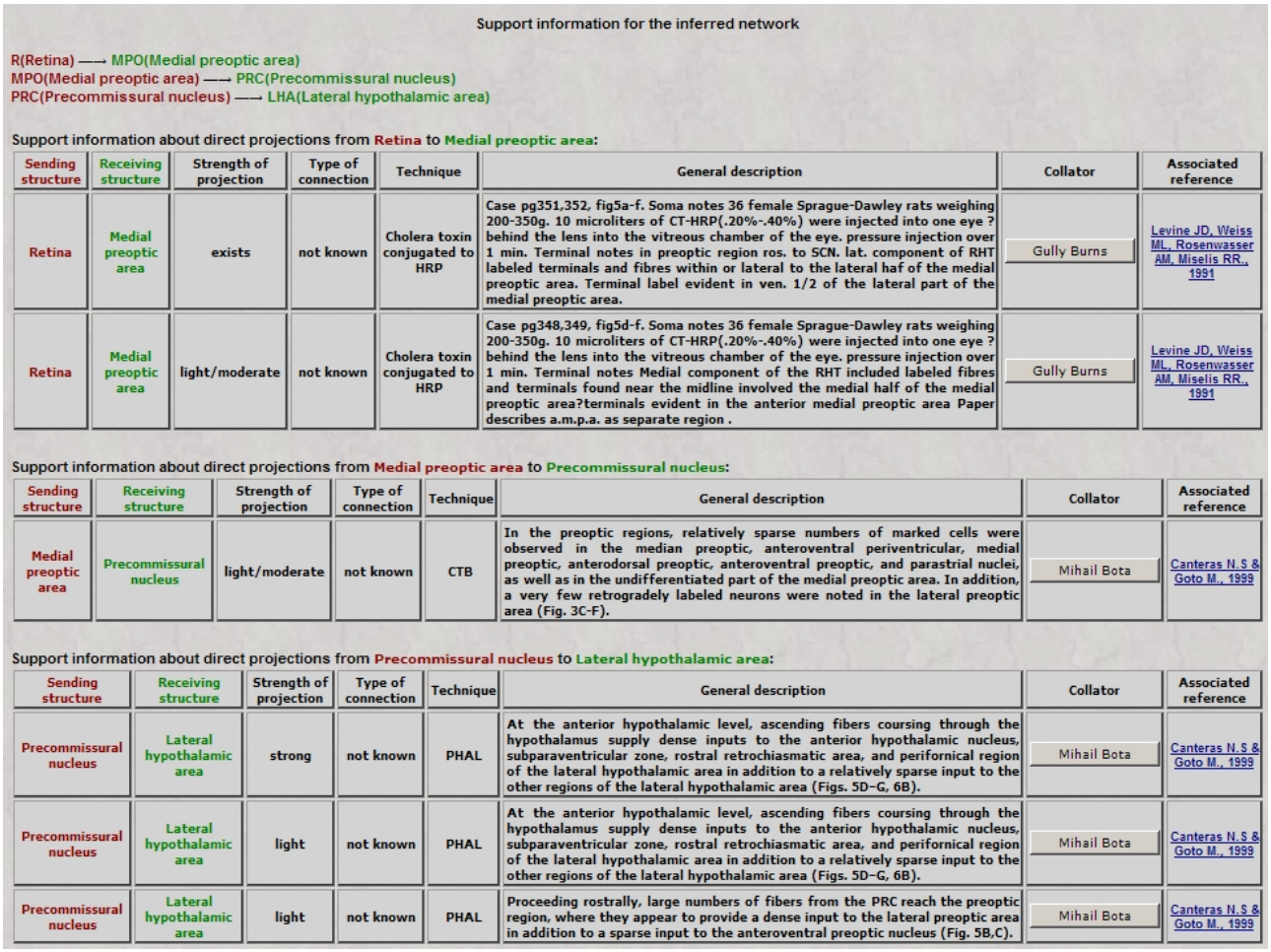
be inferred between the retina (R) and the lateral hypothalamus (LHA), with two intermediary steps, is shown in Figure 23.



Network	Originating Region	Intermediary Station 1	Intermediary Station 2	Final Station
1	R	AV	ACA	LHA
2	R	AV	RSP	LHA
3	R	AD	RSP	LHA
4	R	PVH	MPO	LHA
5	R	PVH	SCH	LHA
6	R	PVH	NDB	LHA
7	R	MEA	LSc	LHA
8	R	Medial nucleus of the amygdala	BST	LHA
9	R	MPO	ACB	LHA
10	R	MPO	MEPO	LHA
11	R	MPO	DMH	LHA
12	R	MPO	MPN	LHA
13	R	MPO	PMd	LHA
14	R	MPO	LPO	LHA
15	R	MPO	LSr	LHA
16	R	MPO	LSv	LHA
17	R	MPO	SI	LHA
18	R	MPO	NDB	LHA
19	R	MPO	SN	LHA
20	R	MPO	VTA	LHA
21	R	MPO	PAG	LHA
22	R	MPO	PRC	LHA
23	R	MPN	BST	LHA
24	R	MPN	ACB	LHA
25	R	MPN	PVHmpd	LHA

Figure 23. The first networks inferred between the rat retina and lateral hypothalamic area, with two intermediary layers. As with other displayed abbreviations, users can also view the CNS region name.

The projections reports associated with each of the inferred networks can be accessed by clicking on the buttons with the network numbers. An example of the data and metadata associated with each network is shown in Figure 24.



Support information for the inferred network

R(Retina) ⟶ MPO(Medial preoptic area)
MPO(Medial preoptic area) ⟶ PRC(Precommissural nucleus)
PRC(Precommissural nucleus) ⟶ LHA(Lateral hypothalamic area)

Support information about direct projections from Retina to Medial preoptic area:

Sending structure	Receiving structure	Strength of projection	Type of connection	Technique	General description	Collator	Associated reference
Retina	Medial preoptic area	exists	not known	Cholera toxin conjugated to HRP	Case pg351,352, fig5a-f. Soma notes 36 female Sprague-Dawley rats weighing 200-350g. 10 microliters of CT-HRP(.20%-.40%) were injected into one eye ? behind the lens into the vitreous chamber of the eye. pressure injection over 1 min. Terminal notes in preoptic region ros. to SCN. lat. component of RHT labeled terminals and fibres within or lateral to the lateral haf of the medial preoptic area. Terminal label evident in ven. 1/2 of the lateral part of the medial preoptic area.	Gully Burns	Levine JD, Weiss ML, Rosenwasser AM, Miselis RR., 1991
Retina	Medial preoptic area	light/moderate	not known	Cholera toxin conjugated to HRP	Case pg348,349, fig5d-f. Soma notes 36 female Sprague-Dawley rats weighing 200-350g. 10 microliters of CT-HRP(.20%-.40%) were injected into one eye ? behind the lens into the vitreous chamber of the eye. pressure injection over 1 min. Terminal notes Medial component of the RHT included labeled fibres and terminals found near the midline involved the medial half of the medial preoptic area?terminals evident in the anterior medial preoptic area Paper describes a.m.p.a. as separate region .	Gully Burns	Levine JD, Weiss ML, Rosenwasser AM, Miselis RR., 1991

Support information about direct projections from Medial preoptic area to Precommissural nucleus:

Sending structure	Receiving structure	Strength of projection	Type of connection	Technique	General description	Collator	Associated reference
Medial preoptic area	Precommissural nucleus	light/moderate	not known	CTB	In the preoptic regions, relatively sparse numbers of marked cells were observed in the median preoptic, anteroventral periventricular, medial preoptic, anterodorsal preoptic, anteroventral preoptic, and parastrial nuclei, as well as in the undifferentiated part of the medial preoptic area. In addition, a very few retrogradely labeled neurons were noted in the lateral preoptic area (Fig. 3C-F).	Mihail Bota	Canteras N.S & Goto M., 1999

Support information about direct projections from Precommissural nucleus to Lateral hypothalamic area:

Sending structure	Receiving structure	Strength of projection	Type of connection	Technique	General description	Collator	Associated reference
Precommissural nucleus	Lateral hypothalamic area	strong	not known	PHAL	At the anterior hypothalamic level, ascending fibers coursing through the hypothalamus supply dense inputs to the anterior hypothalamic nucleus, subparaventricular zone, rostral retrochiasmatic area, and perifornical region of the lateral hypothalamic area in addition to a relatively sparse input to the other regions of the lateral hypothalamic area (Figs. 5D–G, 6B).	Mihail Bota	Canteras N.S & Goto M., 1999
Precommissural nucleus	Lateral hypothalamic area	light	not known	PHAL	At the anterior hypothalamic level, ascending fibers coursing through the hypothalamus supply dense inputs to the anterior hypothalamic nucleus, subparaventricular zone, rostral retrochiasmatic area, and perifornical region of the lateral hypothalamic area in addition to a relatively sparse input to the other regions of the lateral hypothalamic area (Figs. 5D–G, 6B).	Mihail Bota	Canteras N.S & Goto M., 1999
Precommissural nucleus	Lateral hypothalamic area	light	not known	PHAL	Proceeding rostrally, large numbers of fibers from the PRC reach the preoptic region, where they appear to provide a dense input to the lateral preoptic area in addition to a sparse input to the anteroventral preoptic nucleus (Fig. 5B,C).	Mihail Bota	Canteras N.S & Goto M., 1999

Figure 24. Users can view details of each of the connections recorded in BAMS and used to infer networks. The associated connections reports are listed for each component of the inferred network.

3.5 Handling molecule reports in BAMS

BAMS includes a fully developed *Molecules* module, which allows users to handle data and metadata in different ways. The knowledge representation schema of BAMS's *Molecules* module follows the general organization and presentation of experimental data in published neuroscience research articles. Any reference inserted in BAMS's *Molecules* module can be associated with multiple experiments. An experiment is defined as an experimental paradigm applied to a group of animals or human subjects. Each experiment may consist of several experimental series, which are defined by the specific procedures (for example, different antibodies or nucleic acid probes) that were applied. Each experimental series is associated with a set of experimental data that include mapped brain regions and measured variables. The conceptual design of BAMS's *Molecules* module completely separates experimental data from metadata collated from the reference, or inserted by collators. Metadata classes associated with data and experiments inserted in

BAMS's *Molecules* module include: mapping, experimental series, experiment, data presentation, and physiological state. A complete description of this module can be found in Bota & Swanson, 2006.

The page that includes several ways of searching for information in molecules data and metadata is shown in Fig. 25, and can be accessed following the path Menu→Molecules.

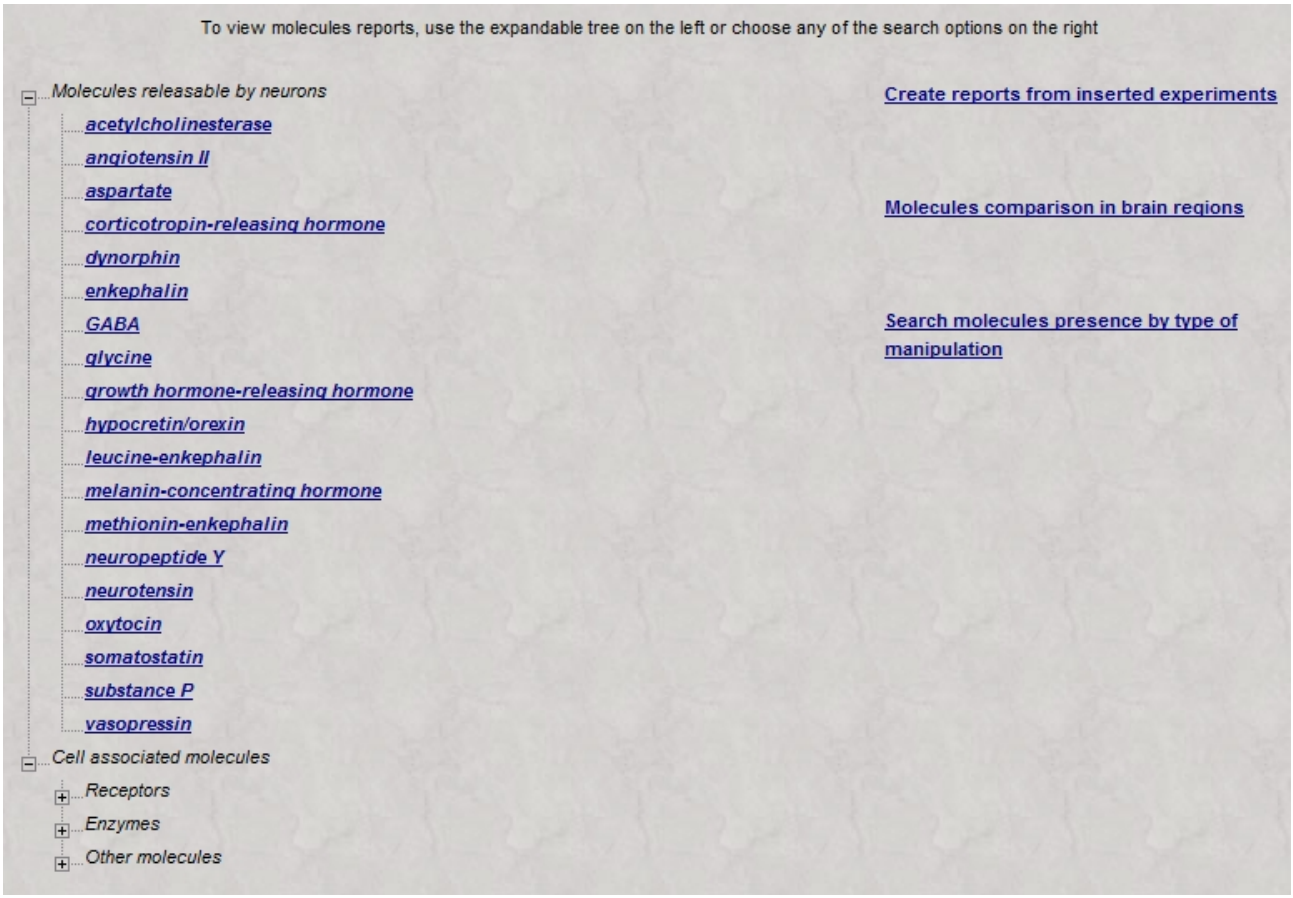
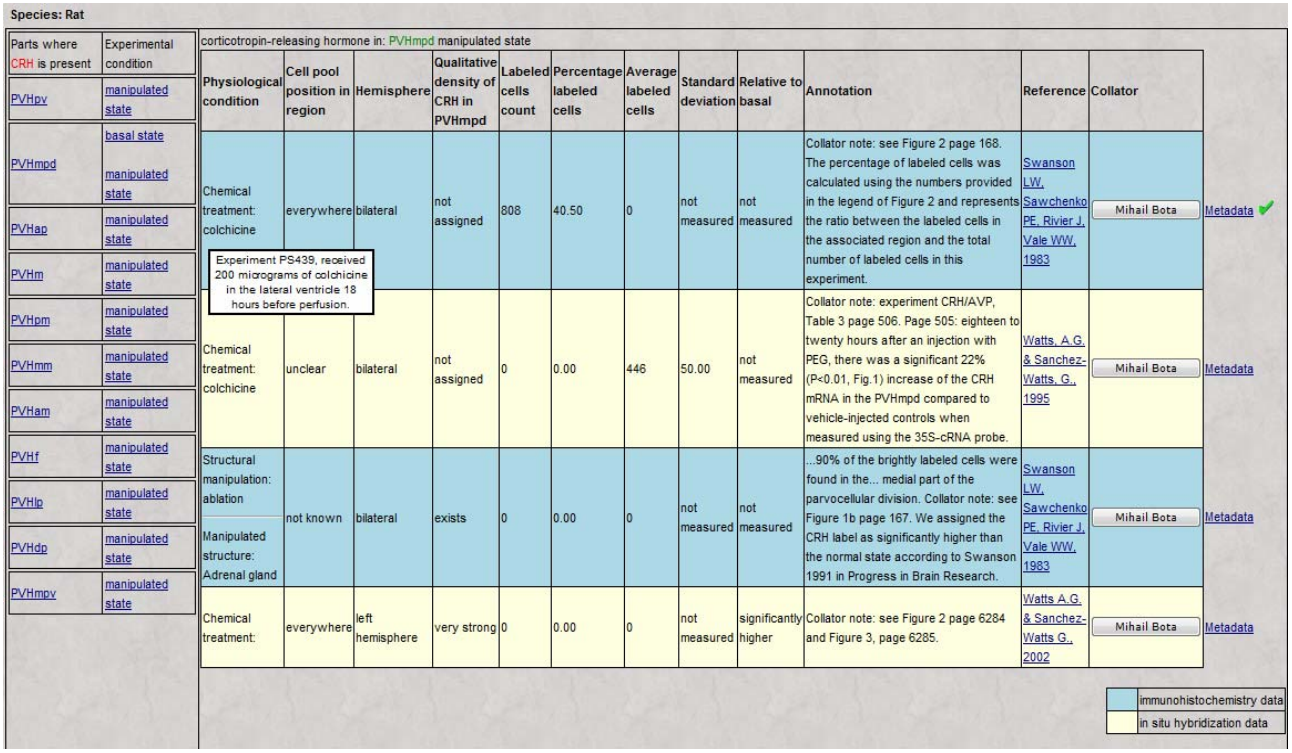


Figure 25. The search options of molecules included in BAMS menu. Users can choose between the expandable tree constructed from the molecules registered in BAMS, in the left hand side of the screen, or any of the three options in the right hand of the screen.

Users can search for molecules either using the expandable tree on the left hand side in Fig. 25, or use one of the search options listed on the right hand half of the figure.

The expandable tree is created dynamically from the molecules classification schema included in the BAMS backend database. The links associated to each of the molecules captured in this tree leads to the list of central nervous system (CNS) regions that express it, and the corresponding physiological state of the animal. Clicking on the physiological state will retrieve the reports that state the presence of the molecule of interest in the brain region chosen by users. The list of brain regions (rat, Swanson-98 brain nomenclature) that express corticotrophin releasing hormone (CRH), the corresponding physiological states of the animals, and the data stating CRH presence in PVHmpd, manipulated state, are shown in Fig. 26.



Species: Rat

Parts where CRH is present	Experimental condition
PVHpv	manipulated state
PVHmpd	basal state / manipulated state
PVHap	manipulated state
PVHm	manipulated state
PVHpm	manipulated state
PVHmm	manipulated state
PVHam	manipulated state
PVHf	manipulated state
PVHlp	manipulated state
PVHdp	manipulated state
PVHmpv	manipulated state

corticotropin-releasing hormone in: PVHmpd manipulated state

Physiological condition	Cell pool position in region	Hemisphere	Qualitative density of CRH in PVHmpd	Labeled cells count	Percentage labeled cells	Average labeled cells	Standard deviation	Relative to basal	Annotation	Reference	Collator	
Chemical treatment: colchicine	everywhere	bilateral	not assigned	808	40.50	0	not measured	not measured	Collator note: see Figure 2 page 168. The percentage of labeled cells was calculated using the numbers provided in the legend of Figure 2 and represents the ratio between the labeled cells in the associated region and the total number of labeled cells in this experiment.	Swanson LW, Sawchenko PE, Rivier J, Vale WW, 1983	Mihail Bota	Metadata ✔
Chemical treatment: colchicine	unclear	bilateral	not assigned	0	0.00	446	50.00	not measured	Collator note: experiment CRH/AVP, Table 3 page 506. Page 505: eighteen to twenty hours after an injection with PEG, there was a significant 22% (P<0.01, Fig.1) increase of the CRH mRNA in the PVHmpd compared to vehicle-injected controls when measured using the 35S-cRNA probe.	Watts, A.G. & Sanchez-Watts, G., 1995	Mihail Bota	Metadata
Structural manipulation: ablation / Manipulated structure: Adrenal gland	not known	bilateral	exists	0	0.00	0	not measured	not measured	...90% of the brightly labeled cells were found in the... medial part of the parvocellular division. Collator note: see Figure 1b page 167. We assigned the CRH label as significantly higher than the normal state according to Swanson 1991 in Progress in Brain Research.	Swanson LW, Sawchenko PE, Rivier J, Vale WW, 1983	Mihail Bota	Metadata
Chemical treatment:	everywhere	left hemisphere	very strong	0	0.00	0	not measured	significantly higher	Collator note: see Figure 2 page 6284 and Figure 3, page 6285.	Watts A.G. & Sanchez-Watts G., 2002	Mihail Bota	Metadata

Experiment PS439, received 200 micrograms of colchicine in the lateral ventricle 18 hours before perfusion.

immunohistochemistry data
in situ hybridization data

Figure 26. The result of search of CNS regions where CRH was identified. Users can view details of records associated with each retrieved CNS region, including qualitative density, cell counts, statistical measurements, spatial characteristics of cells expressing the molecule, and associated annotations by clicking on links associated with experimental conditions. For reports associated with manipulated state, users can also view type of manipulation, injected chemicals, and details about experimental procedure. Users may also access metadata associated with retrieved records. Records verified by original authors of collated references will also have a check mark associated with them.

The information that can accessed through the “Metadata” link, which is associated in Fig. 26 with each retrieved record includes all three major classes described in Bota and Swanson, 2006. The table with experimental method, anatomy and mapping metadata is shown in Fig. 27.

Experiment acronym	Annotation	Collator	Author checked
PS439	Mapping of CRH neurons in the ardrenalectomized rat brain.	Mihail Bota	no

Animals (subjects)
Sex: M **Number of animals:** 3 **Age:** not specified **Mass:** not specified **Unit of mass:** not specified **Housing conditions:** normal housing **Annotation:** The third group was bilaterally adrenalectomized and allowed to survive for 3 days, 1 month and 2 months before perfusion (n=3).

Experimental method

Experiment type: immunohistochemistry
Neuron/glia identification method: not specified
Staining frequency: 1:4 or 1:8

Experimental details:

Antigen: CRF
Antigen species: sheep
Source (producer): not specified
Primary antibody: 24 ([Try22. Gly23]-CRF (1-23)
Primary antibody species: rabbit
Antibody type (monoclonal, polyclonal): polyclonal
Secondary antibody: not specified
Secondary antibody species: not specified
Immunoglobulin class: Alpha globulin
Control: not specified
Visualization method: fluorescence
Visualization medium: slide
Annotation: Seven different antisera to synthetic ovine CRF (or to a fragment of CRF), which were raised in rabbits [7], were tested and all but one were found to stain cells and fibers in the rat. Since antiserum 24 ([Try^{22}. Gly^{23}]-CRF (1-23) conjugated to human alpha-globulin with bis-diazetized benzidine] has been found to interact with rat CRF particularly well in radioimmunoassays [Vale, unpublished observations], it was used extensively for the mapping studies reported here.

Anatomy and histology

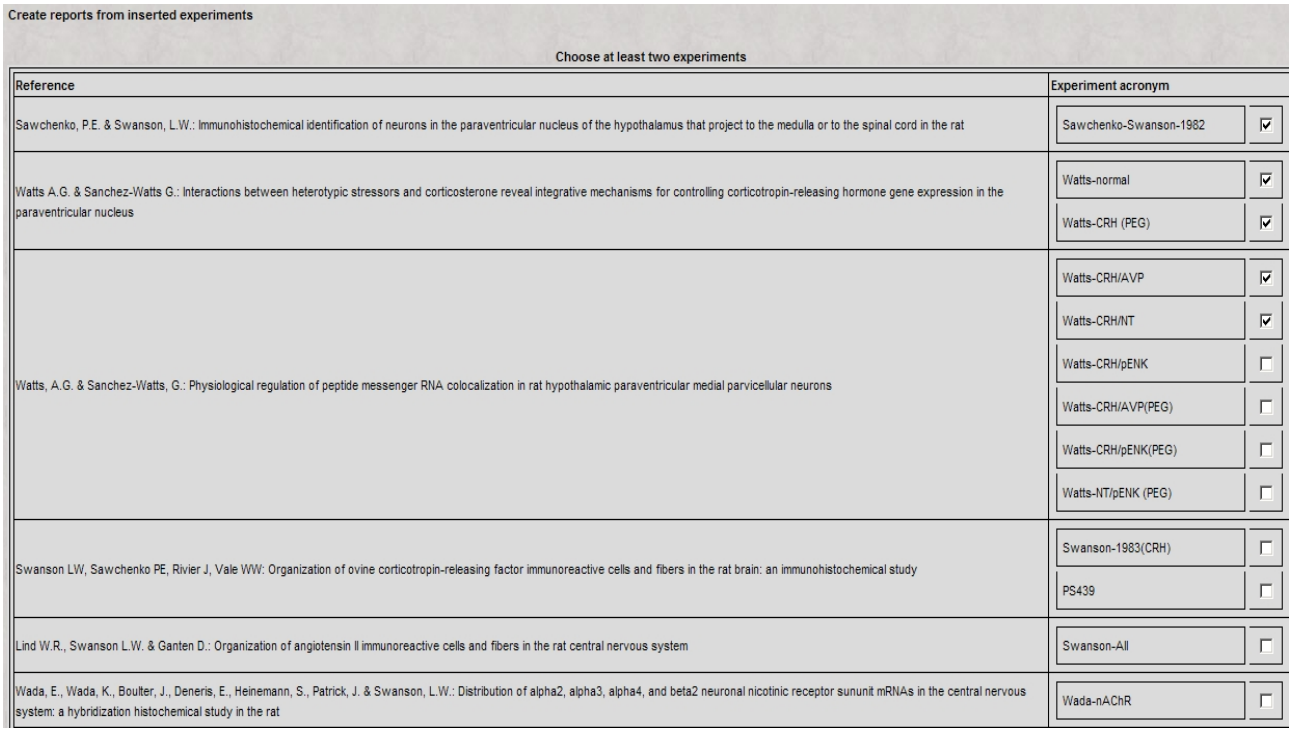
Section plane: coronal	**Angle:** not specified	**Cutting method:** not specified	**Preservation:** freezing	**Thickness:** 30 micrometer
Staining type: thionin	**Sampling:** 1:4 or 1:8	**Annotation:** In general, 1-in-4 or 1-in-8 serios of sections through the brain were stained for immunofluorescence. In addition, an adjacent series of sections from each brain was cut and stained with thionine.		

Mapping details

Coordinates: none	**Data presentation:** text representative labeled images drawings or template mappings of all sections	**Mapping approach:** brain region is captured in a BAMS nomenclature other than that used in the original publication

Figure 27. Users can access experimental method, anatomy and mapping metadata, associated with retrieved experimental data.

The option “Create reports from inserted experiments” can be used to create composite tables with data from several references. This option will bring to the user the list of the molecules experiments that are registered in BAMS and are associated with the collated references. Users can choose any number of these, to create a composite table of the presence or absence of reported molecules. The interface that allows users to choose the experiments of interest is shown in Figure 28.



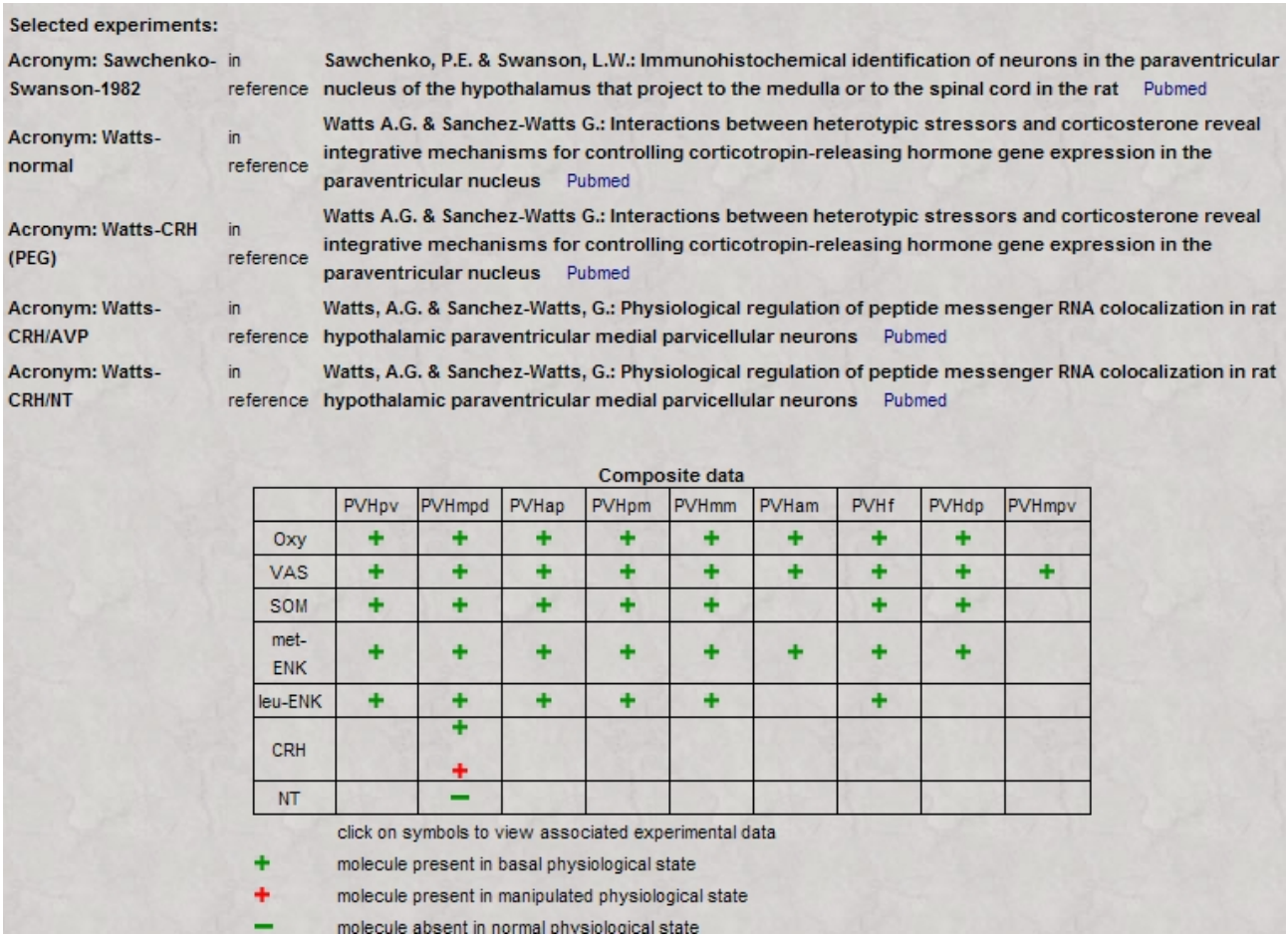
Create reports from inserted experiments

Choose at least two experiments

Reference	Experiment acronym	
Sawchenko, P.E. & Swanson, L.W.: Immunohistochemical identification of neurons in the paraventricular nucleus of the hypothalamus that project to the medulla or to the spinal cord in the rat	Sawchenko-Swanson-1982	☑
Watts A.G. & Sanchez-Watts G.: Interactions between heterotypic stressors and corticosterone reveal integrative mechanisms for controlling corticotropin-releasing hormone gene expression in the paraventricular nucleus	Watts-normal	☑
	Watts-CRH (PEG)	☑
Watts, A.G. & Sanchez-Watts, G.: Physiological regulation of peptide messenger RNA colocalization in rat hypothalamic paraventricular medial parvicellular neurons	Watts-CRH/AVP	☑
	Watts-CRH/NT	☑
	Watts-CRH/pENK	☐
	Watts-CRH/AVP(PEG)	☐
	Watts-CRH/pENK(PEG)	☐
	Watts-NT/pENK (PEG)	☐
Swanson LW, Sawchenko PE, Rivier J, Vale WW: Organization of ovine corticotropin-releasing factor immunoreactive cells and fibers in the rat brain: an immunohistochemical study	Swanson-1983(CRH)	☐
	PS439	☐
Lind W.R., Swanson L.W. & Ganten D.: Organization of angiotensin II immunoreactive cells and fibers in the rat central nervous system	Swanson-All	☐
Wada, E., Wada, K., Boulter, J., Deneris, E., Heinemann, S., Patrick, J. & Swanson, L.W.: Distribution of alpha2, alpha3, alpha4, and beta2 neuronal nicotinic receptor sununit mRNAs in the central nervous system: a hybridization histochemical study in the rat	Wada-nAChR	☐

Figure 28. A subset of the molecules experiments recorded in BAMS. The experiments are grouped by reference, and users can choose any number of them, to create reports of presence/absence of molecules in different CNS regions (*see* text below and Fig. 29)

Once a set of experiments was chosen by users, the system will display data from all of them in a composite tabular format, together with reference information, as shown in Figure 29.



Selected experiments:

Acronym: Sawchenko-Swanson-1982	in reference	Sawchenko, P.E. & Swanson, L.W.: Immunohistochemical identification of neurons in the paraventricular nucleus of the hypothalamus that project to the medulla or to the spinal cord in the rat Pubmed
Acronym: Watts-normal	in reference	Watts A.G. & Sanchez-Watts G.: Interactions between heterotypic stressors and corticosterone reveal integrative mechanisms for controlling corticotropin-releasing hormone gene expression in the paraventricular nucleus Pubmed
Acronym: Watts-CRH (PEG)	in reference	Watts A.G. & Sanchez-Watts G.: Interactions between heterotypic stressors and corticosterone reveal integrative mechanisms for controlling corticotropin-releasing hormone gene expression in the paraventricular nucleus Pubmed
Acronym: Watts-CRH/AVP	in reference	Watts, A.G. & Sanchez-Watts, G.: Physiological regulation of peptide messenger RNA colocalization in rat hypothalamic paraventricular medial parvicellular neurons Pubmed
Acronym: Watts-CRH/NT	in reference	Watts, A.G. & Sanchez-Watts, G.: Physiological regulation of peptide messenger RNA colocalization in rat hypothalamic paraventricular medial parvicellular neurons Pubmed

Composite data

	PVHpv	PVHmpd	PVHap	PVHpm	PVHmm	PVHam	PVHf	PVHdp	PVHmpv
Oxy	+	+	+	+	+	+	+	+	
VAS	+	+	+	+	+	+	+	+	+
SOM	+	+	+	+	+		+	+	
met-ENK	+	+	+	+	+	+	+	+	
leu-ENK	+	+	+	+	+		+		
CRH		+ +							
NT		−							

click on symbols to view associated experimental data

\+ molecule present in basal physiological state

\+ molecule present in manipulated physiological state

− molecule absent in normal physiological state

Figure 29. The result of combining data and metadata from several experiments. First, the experiments, together with the associated reference information are listed. Below, the composite table shows graphically the presence or absence of molecules in both normal and manipulated experimental conditions. Users can view details of the associated reports by clicking on the symbols in each cell. Empty cells represent absence of information.

The option “Molecule comparison in brain regions” processes the query type “What are the CNS parts where all the molecules of interest have been identified?” This engine returns a list of CNS parts where all the chosen molecules have been identified, and the associated physiological states. This engine also returns records of coexpression data for any pair of molecules in the chosen set. The interface for choosing the molecules is shown in Fig. 30, and an example of the reconstruction of the molecular composition of CNS parts is shown in Fig. 31.

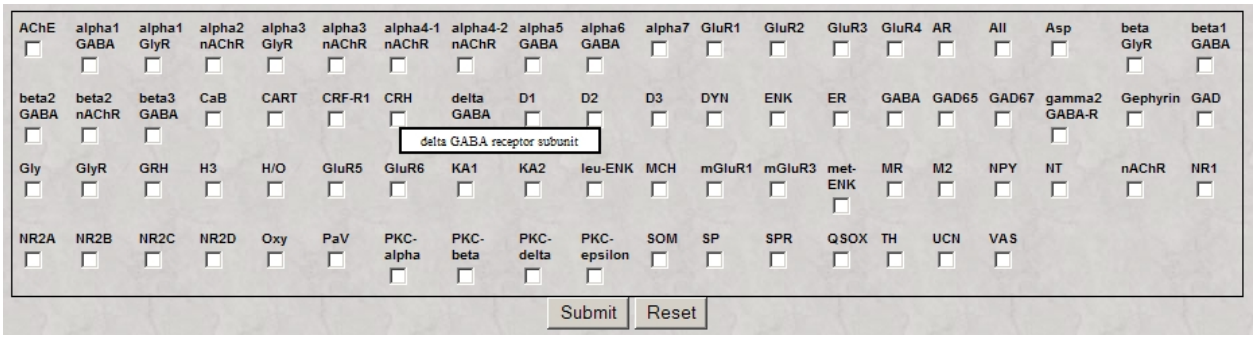


Fig. 30. The user interface that allows users to choose any number of molecules to be compared in terms of presence/absence in CNS regions. As with the other checklist interfaces, users can view the name of the molecules by going with mouse over the corresponding abbreviation.

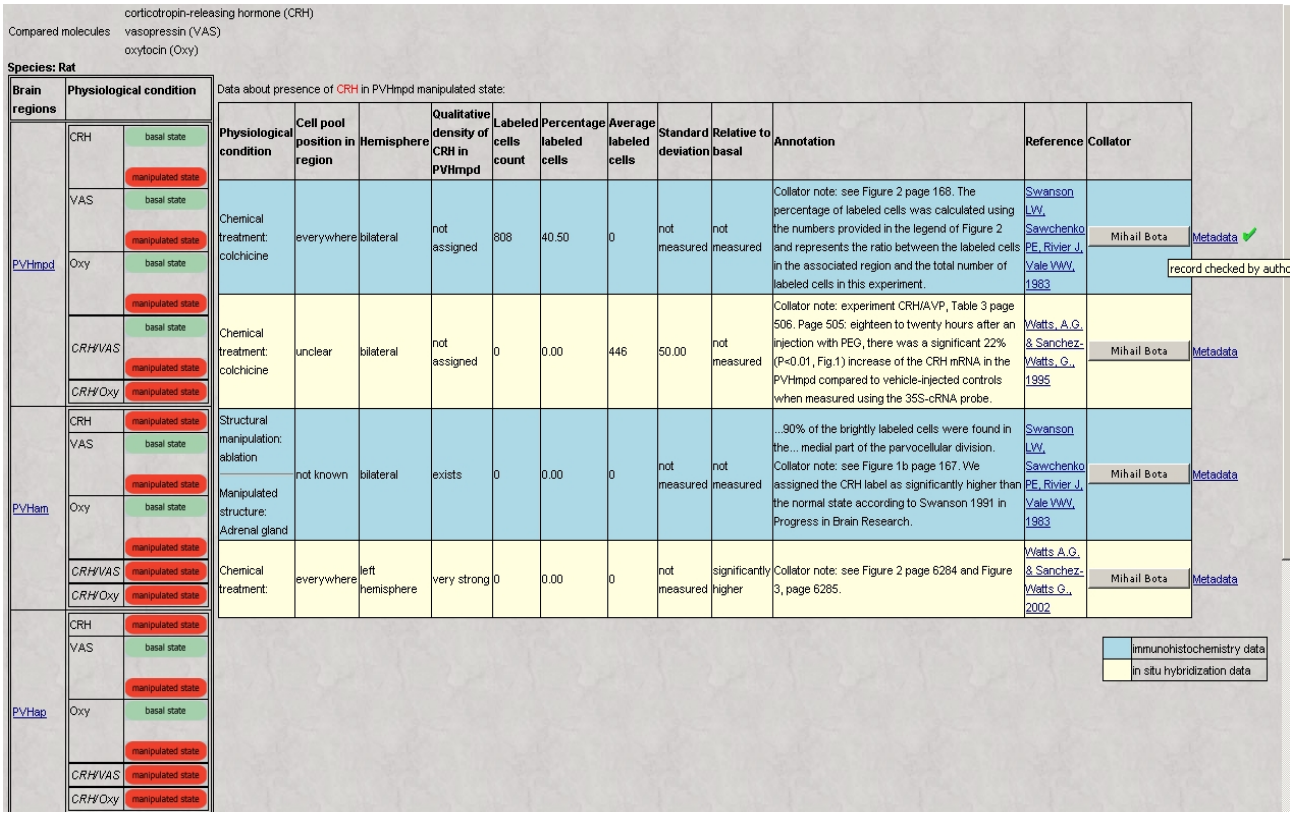


Fig 31. Users may compare the existence of particular molecules in different CNS regions (in this example, the rat PVHmpd). The result is a list of regions that are associated in BAMS with reports of all the searched molecules (corticotrophin releasing hormone [CRH], oxytocin [Oxy], and vasopressin [VAS]), in either basal physiological state or manipulated state. Coexpression data is also returned for all pairs of molecules in the set of interest. Users can access reports of molecule presence in the retrieved CNS regions.

The third option shown in the right half of Fig. 25, called “Search by type of manipulation,” processes the query type “Show identified molecules and CNS parts that are associated with a specific molecule or structural manipulation.” This engine returns the list of CNS parts and molecules associated with the searched type of manipulation, as well as basal state data for each retrieved molecule. If any retrieved experimental data is associated with statistical information, it also will be displayed in graphical format. An example of the online retrieval of chemoarchitectonic data associated with systemic injection of polyethylene glycol is shown in Fig. 32.

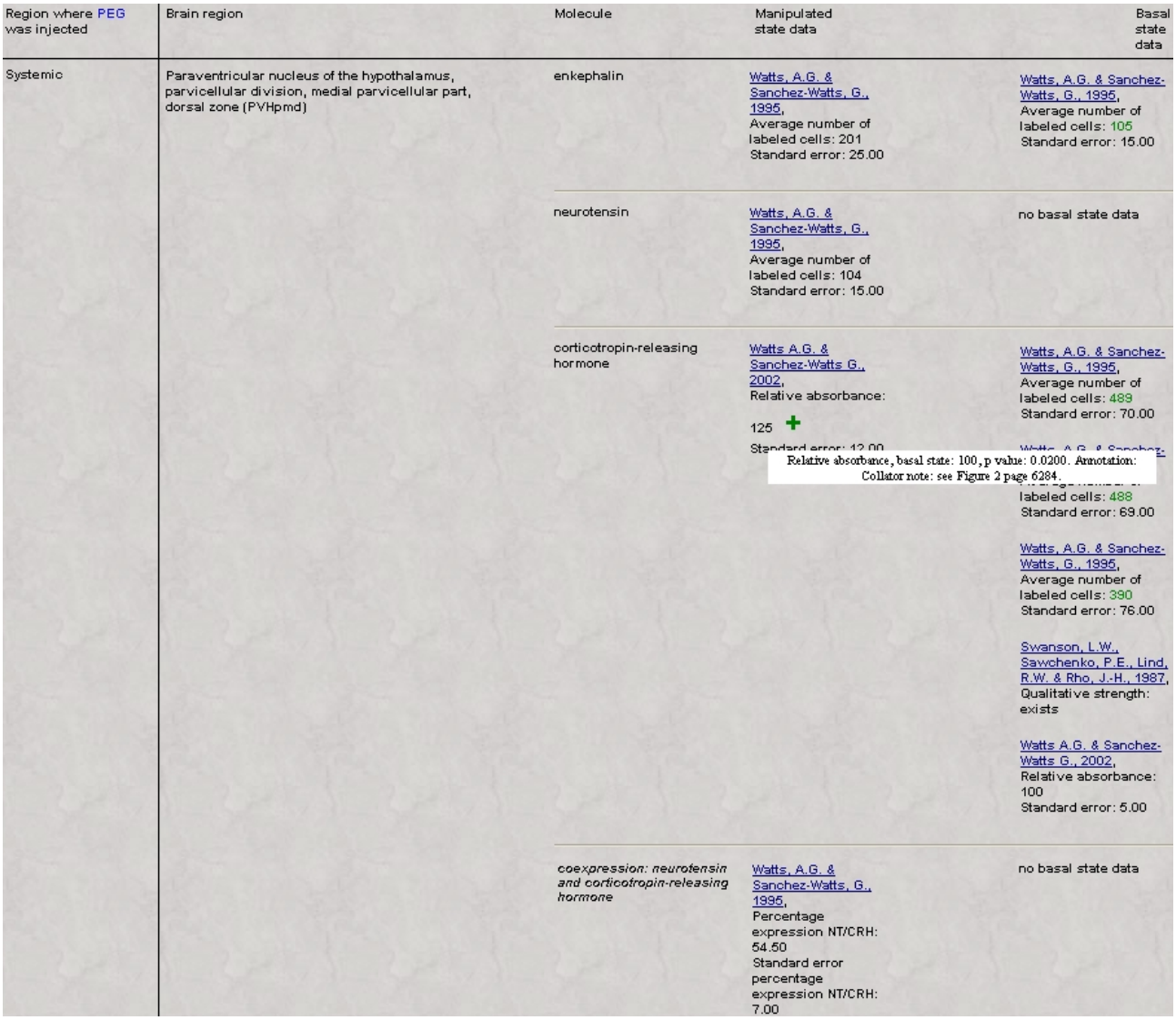


Fig. 32. Users can retrieve chemoarchitectonic data associated with a chemical or structural manipulation and compare the presence of molecules in basal and manipulated states. Additional data and metadata can be viewed by going with the mouse over the graphical symbols that represent statistical changes relative to the basal state.

Molecules that are expressed in CNS regions or neurons, as well as several other inference engines, can be accessed by users from the page that displays the summary of regions (Figs 6 and 13). Another example is shown in Fig.33, the summary information about the rat cerebellar cortex identified in the Swanson-98 nomenclature.

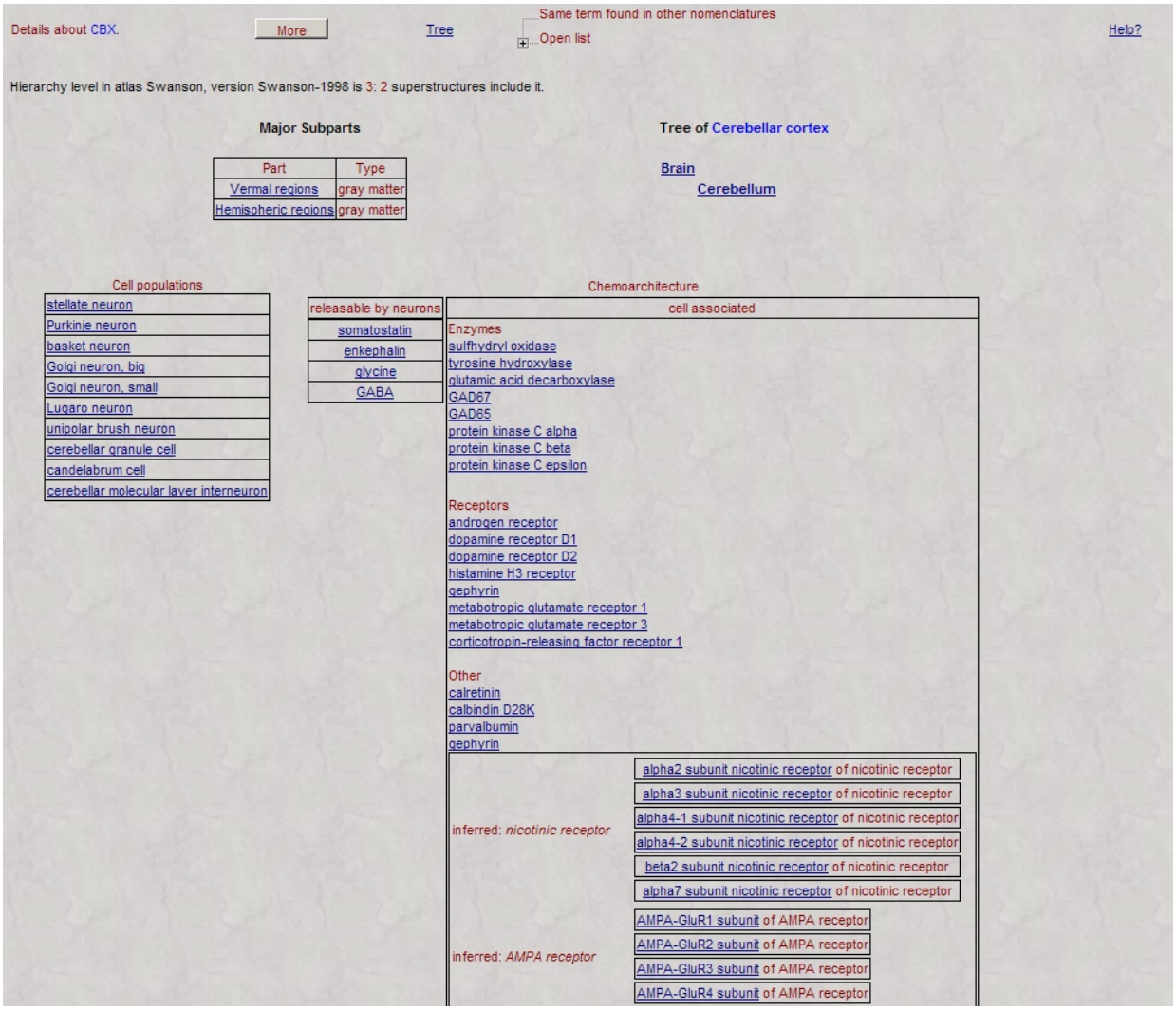
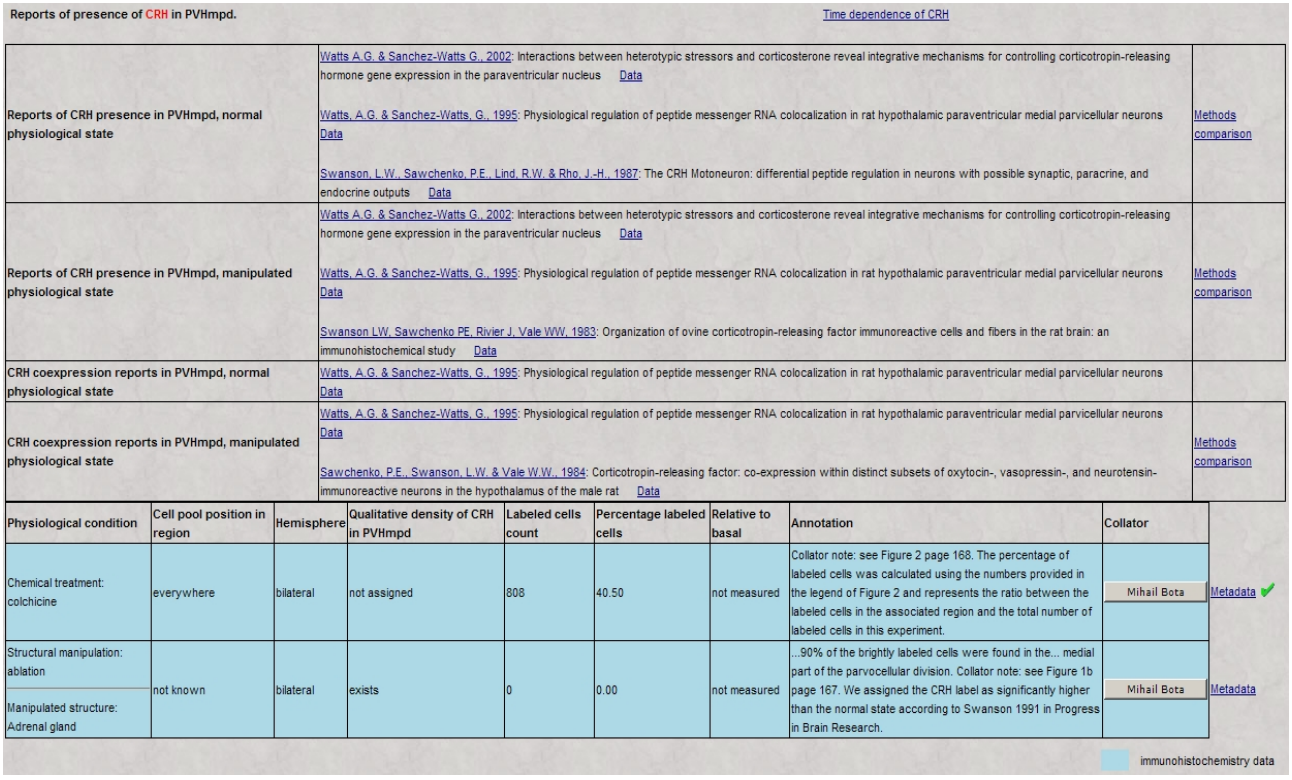


Figure 33. The summary page of the rat cerebellar cortex, Swanson-98 nomenclature. The chemoarchitecture profile of the CNS region is divided in the molecules classes implemented in BAMS.

The molecules that are expressed in the CNS region of interest are displayed according to the molecules schema implemented in BAMS. Clicking on the links associated with each of the retrieved molecules will display the data and metadata inserted in BAMS, which are related to the CNS region, and with the molecule (Fig. 34).



Reports of presence of CRH in PVHmpd. Time dependence of CRH

Reports of CRH presence in PVHmpd, normal physiological state	Watts A.G. & Sanchez-Watts G., 2002: Interactions between heterotypic stressors and corticosterone reveal integrative mechanisms for controlling corticotropin-releasing hormone gene expression in the paraventricular nucleus Data Watts, A.G. & Sanchez-Watts, G., 1995: Physiological regulation of peptide messenger RNA colocalization in rat hypothalamic paraventricular medial parvicellular neurons Data Swanson, L.W., Sawchenko, P.E., Lind, R.W. & Rho, J.-H., 1987: The CRH Motoneuron: differential peptide regulation in neurons with possible synaptic, paracrine, and endocrine outputs Data	Methods comparison
Reports of CRH presence in PVHmpd, manipulated physiological state	Watts A.G. & Sanchez-Watts G., 2002: Interactions between heterotypic stressors and corticosterone reveal integrative mechanisms for controlling corticotropin-releasing hormone gene expression in the paraventricular nucleus Data Watts, A.G. & Sanchez-Watts, G., 1995: Physiological regulation of peptide messenger RNA colocalization in rat hypothalamic paraventricular medial parvicellular neurons Data Swanson LW, Sawchenko PE, Rivier J, Vale WW, 1983: Organization of ovine corticotropin-releasing factor immunoreactive cells and fibers in the rat brain: an immunohistochemical study Data	Methods comparison
CRH coexpression reports in PVHmpd, normal physiological state	Watts, A.G. & Sanchez-Watts, G., 1995: Physiological regulation of peptide messenger RNA colocalization in rat hypothalamic paraventricular medial parvicellular neurons Data	
CRH coexpression reports in PVHmpd, manipulated physiological state	Watts, A.G. & Sanchez-Watts, G., 1995: Physiological regulation of peptide messenger RNA colocalization in rat hypothalamic paraventricular medial parvicellular neurons Data Sawchenko, P.E., Swanson, L.W. & Vale W.W., 1984: Corticotropin-releasing factor: co-expression within distinct subsets of oxytocin-, vasopressin-, and neurotensin-immunoreactive neurons in the hypothalamus of the male rat Data	Methods comparison

Physiological condition	Cell pool position in region	Hemisphere	Qualitative density of CRH in PVHmpd	Labeled cells count	Percentage labeled cells	Relative to basal	Annotation	Collator	
Chemical treatment: colchicine	everywhere	bilateral	not assigned	808	40.50	not measured	Collator note: see Figure 2 page 168. The percentage of labeled cells was calculated using the numbers provided in the legend of Figure 2 and represents the ratio between the labeled cells in the associated region and the total number of labeled cells in this experiment.	Mihail Bota	Metadata ✔
Structural manipulation: ablation Manipulated structure: Adrenal gland	not known	bilateral	exists	0	0.00	not measured	...90% of the brightly labeled cells were found in the... medial part of the parvocellular division. Collator note: see Figure 1b page 167. We assigned the CRH label as significantly higher than the normal state according to Swanson 1991 in Progress in Brain Research.	Mihail Bota	Metadata

immunohistochemistry data

Figure 34. Users can view detailed reports about the presence of a molecule in a particular CNS region. Experimental data is grouped in four categories, which depend on the physiological state of the animal, and coexpression data. Records verified by original authors are indicated with a green checkmark.

Records associated with the molecule of interest are grouped in four categories (molecule presence in normal and manipulated physiological state, and coexpression of other molecules in normal and manipulated state; *see* Fig. 34, by experimental condition, and by coexpression of other molecules in the same CNS region). The system first retrieves references corresponding to each category. Every reference is associated with a “Data” link that retrieves corresponding experimental records. If at least two experiments from different references are retrieved in the same category and have metadata associated with them, a new link called “Methods comparison” becomes available. Users can therefore compare methods used in all experiments associated with metadata retrieved in one of the four categories. An example of methods comparison is shown in Fig. 35.

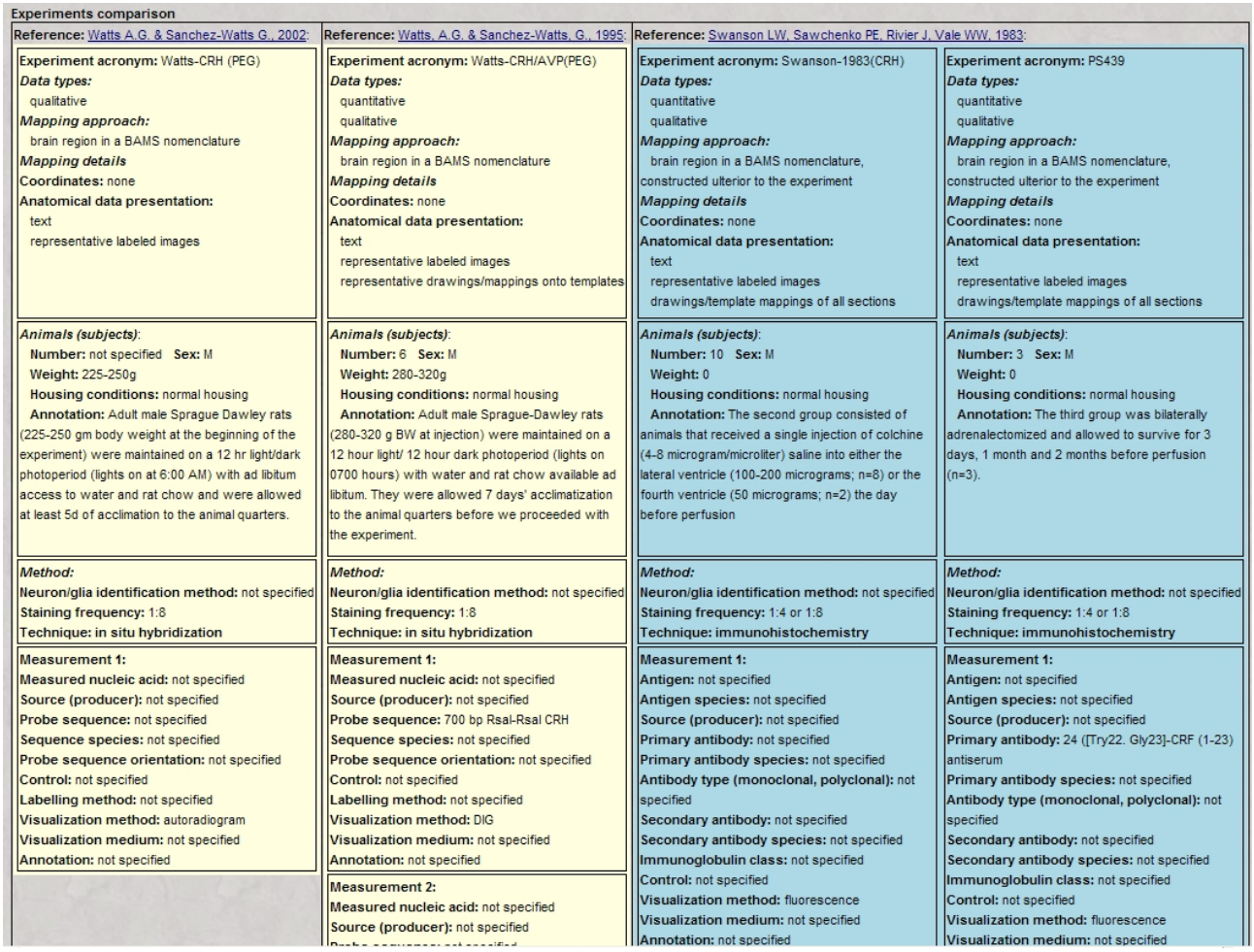


Figure 35. Users may compare metadata associated with experimental data and experiments for the presence of a molecule in a CNS region of interest.

BAMS's *Molecules* module includes an inference engine for reconstructing the chemoarchitectonic profile of a CNS region from the molecular data associated with its substructure. This engine can be accessed from the page describing CNS parts in BAMS, shown in Figs. 6 and 13. It is similar to the projections profile inference engine described above (section 3.3) and in Bota et al. (2005), and it displays gene expression data as a function of experimental conditions (normal and manipulated states). An example of chemoarchitectonic profile reconstruction of the rat PVH is shown in Fig. 36.

Inferred chemoarchitecture pattern of the Paraventricular nucleus of the hypothalamus (PVH)

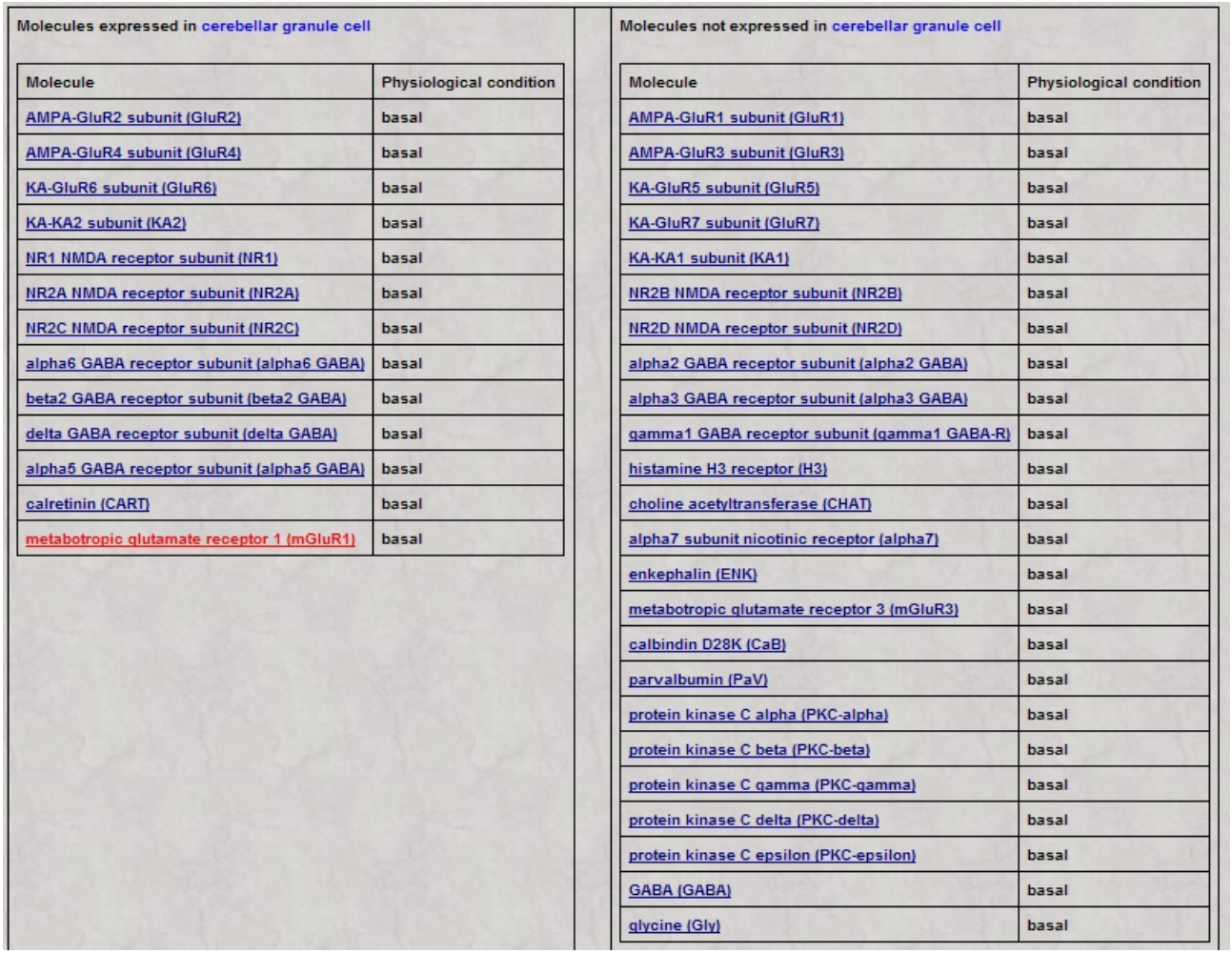
Click on symbols to access detailed reports

	PVHp	PVHm	PVHd	PVHpv	PVHmpd	PVHap	PVHpm	PVHmm	PVHam	PVHf	PVHlp	PVHdp	PVHmpv	PVHpml	PVHpmm
beta2 nAChR	+	+	+												
CRH		+		+	+ +	+	+	+	+	+	+	+	+		
alpha4-2 nAChR	−	+	+												
alpha4-1 nAChR	−	−	+												
Oxy				+ +	+ +	+ +	+ +	+ +	+ +	+ +		+			
VAS				+	+ +	+ +	+ +	+	+ +	+		+	+		
SS				+	+	+	+	+		+		+			
met-ENK				+	+	+	+	+	+	+		+			
leu-ENK				+	+	+	+	+		+					
QSOX				+	+	+			+	+	+	+	+	+	+
ENK					+ +										
NT				+	+	+									
MCH					+										
H/O					+						+				

+ molecule present in basal physiological state
+ molecule present in manipulated physiological state
− molecule absent in normal physiological state

Figure 36. The result of a BAMS gene expression pattern reconstruction dealing with the various subdivisions of the rat paraventricular nucleus of the hypothalamus (PVH). The reconstructed chemoarchitecture profile is similar with the matrix displayed in Fig. 29, and includes presence or absence of molecules in both normal and manipulated experimental conditions. Users can view details of the associated reports by clicking on the symbols in each cell.

Molecules reports inserted in BAMS are also associated with neuron types, if those were experimentally identified and recorded in the system. Therefore, BAMS also reconstructs the chemical phenotypes of neurons, in either of the physiological states. Thus, the neuron types records are associated in BAMS with reports of molecules presence or absence, and these are further dissociated by the physiological state. An example of the chemical phenotype reconstruction of a neuron type is shown in Figure 37. For details of the *Cells* module, *see* the next section of the manual.



Molecules expressed in cerebellar granule cell

Molecule	Physiological condition
AMPA-GluR2 subunit (GluR2)	basal
AMPA-GluR4 subunit (GluR4)	basal
KA-GluR6 subunit (GluR6)	basal
KA-KA2 subunit (KA2)	basal
NR1 NMDA receptor subunit (NR1)	basal
NR2A NMDA receptor subunit (NR2A)	basal
NR2C NMDA receptor subunit (NR2C)	basal
alpha6 GABA receptor subunit (alpha6 GABA)	basal
beta2 GABA receptor subunit (beta2 GABA)	basal
delta GABA receptor subunit (delta GABA)	basal
alpha5 GABA receptor subunit (alpha5 GABA)	basal
calretinin (CART)	basal
metabotropic glutamate receptor 1 (mGluR1)	basal

Molecules not expressed in cerebellar granule cell

Molecule	Physiological condition
AMPA-GluR1 subunit (GluR1)	basal
AMPA-GluR3 subunit (GluR3)	basal
KA-GluR5 subunit (GluR5)	basal
KA-GluR7 subunit (GluR7)	basal
KA-KA1 subunit (KA1)	basal
NR2B NMDA receptor subunit (NR2B)	basal
NR2D NMDA receptor subunit (NR2D)	basal
alpha2 GABA receptor subunit (alpha2 GABA)	basal
alpha3 GABA receptor subunit (alpha3 GABA)	basal
gamma1 GABA receptor subunit (gamma1 GABA-R)	basal
histamine H3 receptor (H3)	basal
choline acetyltransferase (CHAT)	basal
alpha7 subunit nicotinic receptor (alpha7)	basal
enkephalin (ENK)	basal
metabotropic glutamate receptor 3 (mGluR3)	basal
calbindin D28K (CaB)	basal
parvalbumin (PaV)	basal
protein kinase C alpha (PKC-alpha)	basal
protein kinase C beta (PKC-beta)	basal
protein kinase C gamma (PKC-gamma)	basal
protein kinase C delta (PKC-delta)	basal
protein kinase C epsilon (PKC-epsilon)	basal
GABA (GABA)	basal
glycine (Gly)	basal

Figure 37. BAMS's web interface reconstructs automatically the chemical phenotype of recorded neuron types. Users can also access details about each of the expressed molecules, as well as those that are not expressed, in the corresponding physiological state.

3.6 Searching for neurons in BAMS

The menu for searching neurons in BAMS can be found following the path: Menu→Cells. The webpage that includes three ways of searching neurons and neuron populations identified in different brain regions is shown in Fig. 38. The first two options of search are complementary, therefore, they will described together.

As with brain nomenclatures, neurons are grouped in BAMS in neuron nomenclatures. Neuron nomenclatures are internally consistent sets of terms that describe different neuron populations (neuron types and classes) in a specific part of the CNS. Neuron nomenclatures are defined by an author or group of authors, and are associated with a set of references in the literature. Since the populations that make up a specific part of the CNS can be named differently by different authors, those nomenclatures that are the most complete to our knowledge are called "BAMS reference" and used to construct BAMS ontology (Bota &

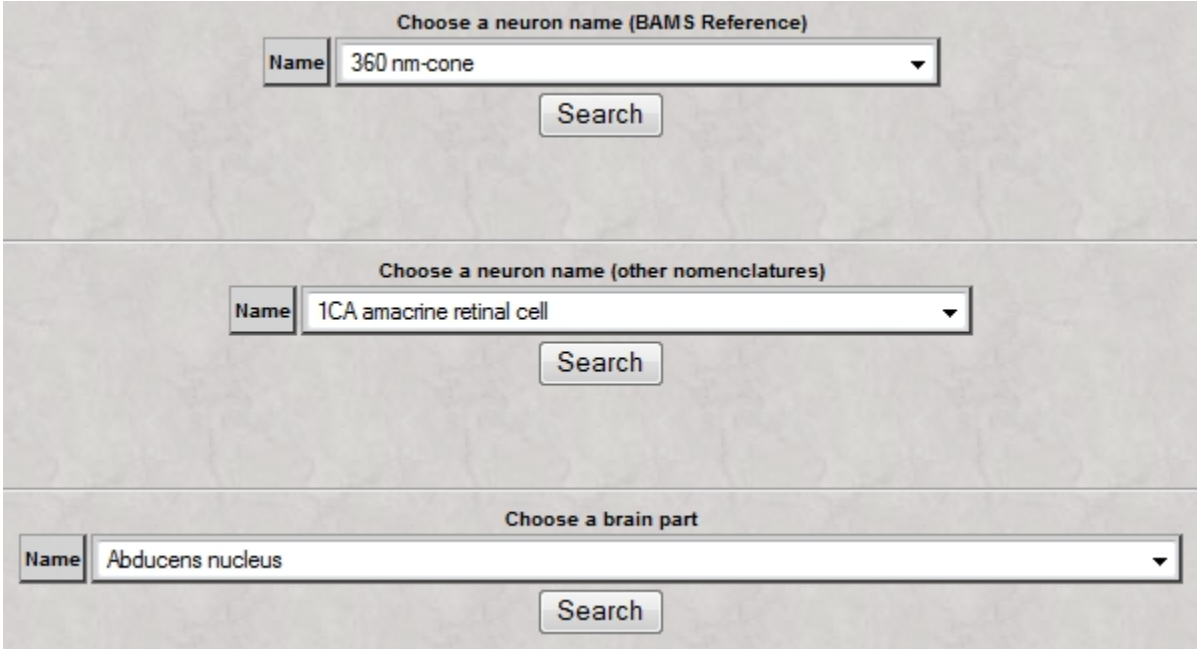
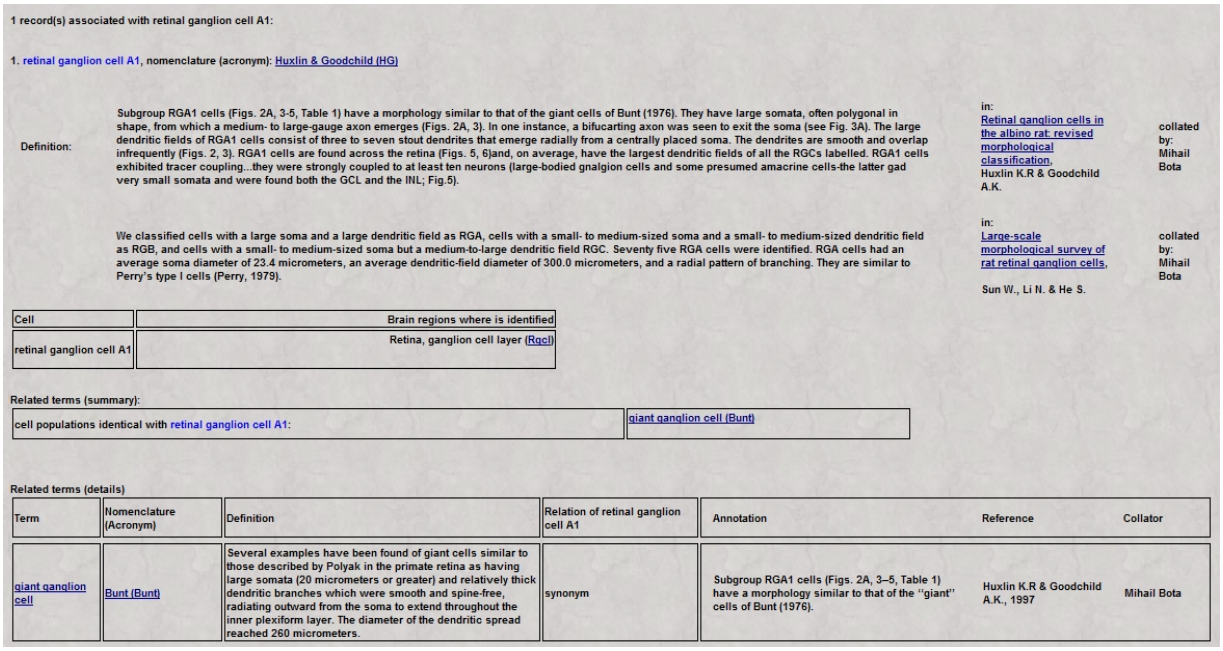


Figure 38. The search options of the *Cell* module interface of BAMS.

Swanson, 2008). Details about the criteria for constructing a "BAMS Reference" nomenclature can be found in Bota & Swanson 2007, and 2008.

Users can choose either the "BAMS Reference" or "Other nomenclature" drop-down lists to look for a neuron name. This action will return details about that neuron type or class, which include its definition, subclasses, CNS regions where it was identified, and terms defined in other nomenclatures and related to it. An example is shown in Fig. 39.



1 record(s) associated with retinal ganglion cell A1:

1. retinal ganglion cell A1, nomenclature (acronym): Huxlin & Goodchild (HG)

Definition:	Subgroup RGA1 cells (Figs. 2A, 3-5, Table 1) have a morphology similar to that of the giant cells of Bunt (1976). They have large somata, often polygonal in shape, from which a medium- to large-gauge axon emerges (Figs. 2A, 3). In one instance, a bifucarting axon was seen to exit the soma (see Fig. 3A). The large dendritic fields of RGA1 cells consist of three to seven stout dendrites that emerge radially from a centrally placed soma. The dendrites are smooth and overlap infrequently (Figs. 2, 3). RGA1 cells are found across the retina (Figs. 5, 6)and, on average, have the largest dendritic fields of all the RGCs labelled. RGA1 cells exhibited tracer coupling...they were strongly coupled to at least ten neurons (large-bodied gnalgion cells and some presumed amacrine cells-the latter gad very small somata and were found both the GCL and the INL; Fig.5).	in: Retinal ganglion cells in the albino rat: revised morphological classification, Huxlin K.R & Goodchild A.K.	collated by: Mihail Bota
	We classified cells with a large soma and a large dendritic field as RGA, cells with a small- to medium-sized soma and a small- to medium-sized dendritic field as RGB, and cells with a small- to medium-sized soma but a medium-to-large dendritic field RGC. Seventy five RGA cells were identified. RGA cells had an average soma diameter of 23.4 micrometers, an average dendritic-field diameter of 300.0 micrometers, and a radial pattern of branching. They are similar to Perry's type I cells (Perry, 1979).	in: Large-scale morphological survey of rat retinal ganglion cells, Sun W., Li N. & He S.	collated by: Mihail Bota

Cell	Brain regions where is identified
retinal ganglion cell A1	Retina, ganglion cell layer (Rgcl)

Related terms (summary):

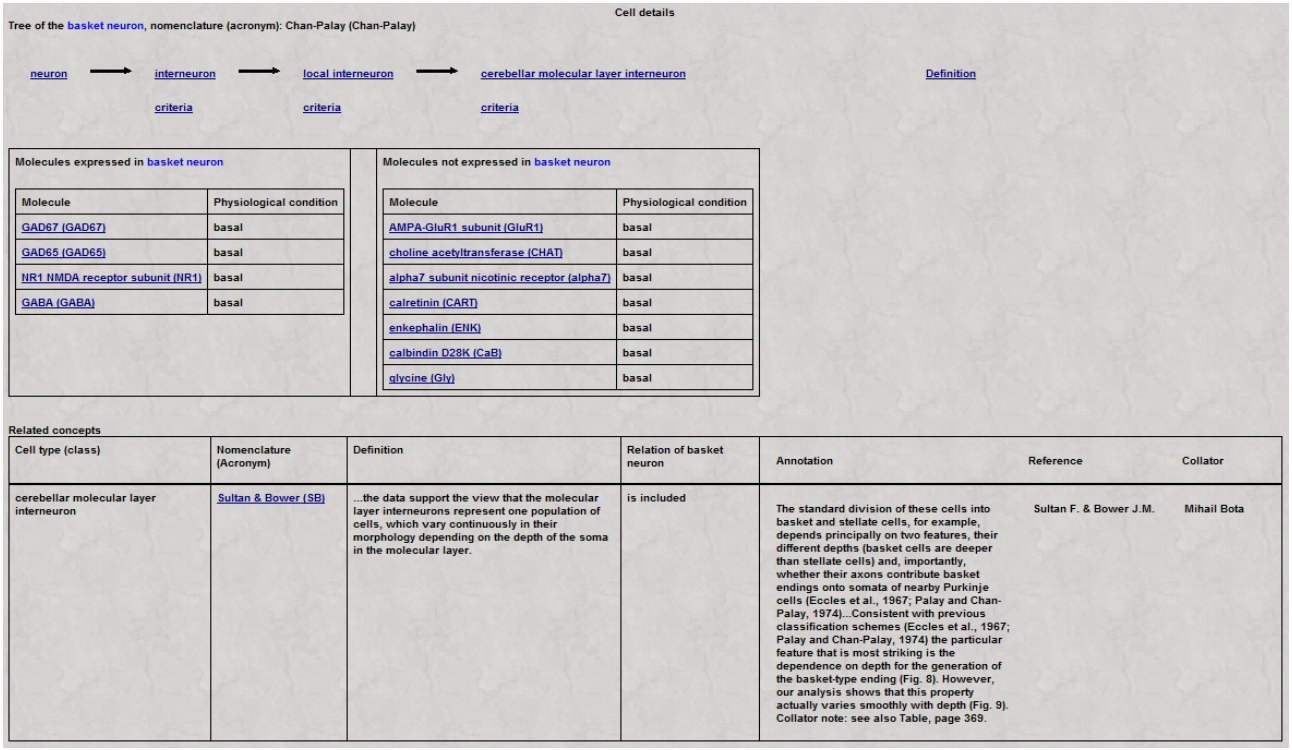
cell populations identical with retinal ganglion cell A1:	giant ganglion cell (Bunt)

Related terms (details)

Term	Nomenclature (Acronym)	Definition	Relation of retinal ganglion cell A1	Annotation	Reference	Collator
giant ganglion cell	Bunt (Bunt)	Several examples have been found of giant cells similar to those described by Polyak in the primate retina as having large somata (20 micrometers or greater) and relatively thick dendritic branches which were smooth and spine-free, radiating outward from the soma to extend throughout the inner plexiform layer. The diameter of the dendritic spread reached 260 micrometers.	synonym	Subgroup RGA1 cells (Figs. 2A, 3–5, Table 1) have a morphology similar to that of the "giant" cells of Bunt (1976).	Huxlin K.R & Goodchild A.K., 1997	Mihail Bota

Figure 39. The details about the neuron term of interest, which include its definition, the associated reference, collators, brain regions where it was identified, terms defined in other neuron nomenclatures and related to it, the semantical relations, and associated annotations.

Additional details about a "BAMS Reference" neuron type or class can be accessed from the page that provides the summary information about a CNS region (Figs.6, 13, and 33). Whenever a CNS region is associated with neuron types or classes, these will be listed in a tabular format in the summary web page. Clicking on links associated with the retrieved neuron names will retrieve the chemical phenotypes, distributions in the CNS region, and related terms. If the neuron type of interest is captured in the BAMS ontology, thus in the "is a" hierarchy, the classification criteria and its parents will also be displayed. The example of the cerebellar basket neuron is shown in Figure 40.



Cell details

Tree of the basket neuron, nomenclature (acronym): Chan-Palay (Chan-Palay)

neuron → interneuron → local interneuron → cerebellar molecular layer interneuron

Definition

criteria | criteria | criteria

Molecules expressed in basket neuron

Molecule	Physiological condition
GAD67 (GAD67)	basal
GAD65 (GAD65)	basal
NR1 NMDA receptor subunit (NR1)	basal
GABA (GABA)	basal

Molecules not expressed in basket neuron

Molecule	Physiological condition
AMPA-GluR1 subunit (GluR1)	basal
choline acetyltransferase (CHAT)	basal
alpha7 subunit nicotinic receptor (alpha7)	basal
calretinin (CART)	basal
enkephalin (ENK)	basal
calbindin D28K (CaB)	basal
glycine (Gly)	basal

Related concepts

Cell type (class)	Nomenclature (Acronym)	Definition	Relation of basket neuron	Annotation	Reference	Collator
cerebellar molecular layer interneuron	Sultan & Bower (SB)	...the data support the view that the molecular layer interneurons represent one population of cells, which vary continuously in their morphology depending on the depth of the soma in the molecular layer.	is included	The standard division of these cells into basket and stellate cells, for example, depends principally on two features, their different depths (basket cells are deeper than stellate cells) and, importantly, whether their axons contribute basket endings onto somata of nearby Purkinje cells (Eccles et al., 1967; Palay and Chan-Palay, 1974)...Consistent with previous classification schemes (Eccles et al., 1967; Palay and Chan-Palay, 1974) the particular feature that is most striking is the dependence on depth for the generation of the basket-type ending (Fig. 8). However, our analysis shows that this property actually varies smoothly with depth (Fig. 9). Collator note: see also Table, page 369.	Sultan F. & Bower J.M.	Mihail Bota

Figure 40. Information that can be retrieved in BAMS and is related neuron concepts include to the chemical phenotype, related terms, their semantic relations, annotations, references and collators, as well as the set of parents with links to the associated classification criteria

Any parent-child relationship between “BAMS Reference” terms can be associated in BAMS *Cell* module with criteria for classification that are collated from associated references. These are the major criteria used by various authors to classify neurons: morphology, specialized parts, input and output regions or neurons types, regions where the neurons were identified, expressed molecules, and physiology. The database classification criteria schema was constructed to comply with measurements performed by a broad range of research groups, and with the most recent efforts to create a unified terminology of neuron types. All variables included in the classification criteria are in text format, and are associated with annotations and references. Details about the database schema implemented in BAMS can be found in Bota and Swanson 2007, and 2008.

Thus, if a “BAMS Reference” term is associated with classification criteria, these can be viewed by clicking on the “criteria” links shown in Fig. 40. The page that will be returned will display the classification criteria used with all the intermediary classes, up to the class of interest. An example is shown in Fig. 41: the criteria used to classify the retinal ganglion cell A2 inner as a projection interneuron will displayed step-wise, passing through all intermediary classes.

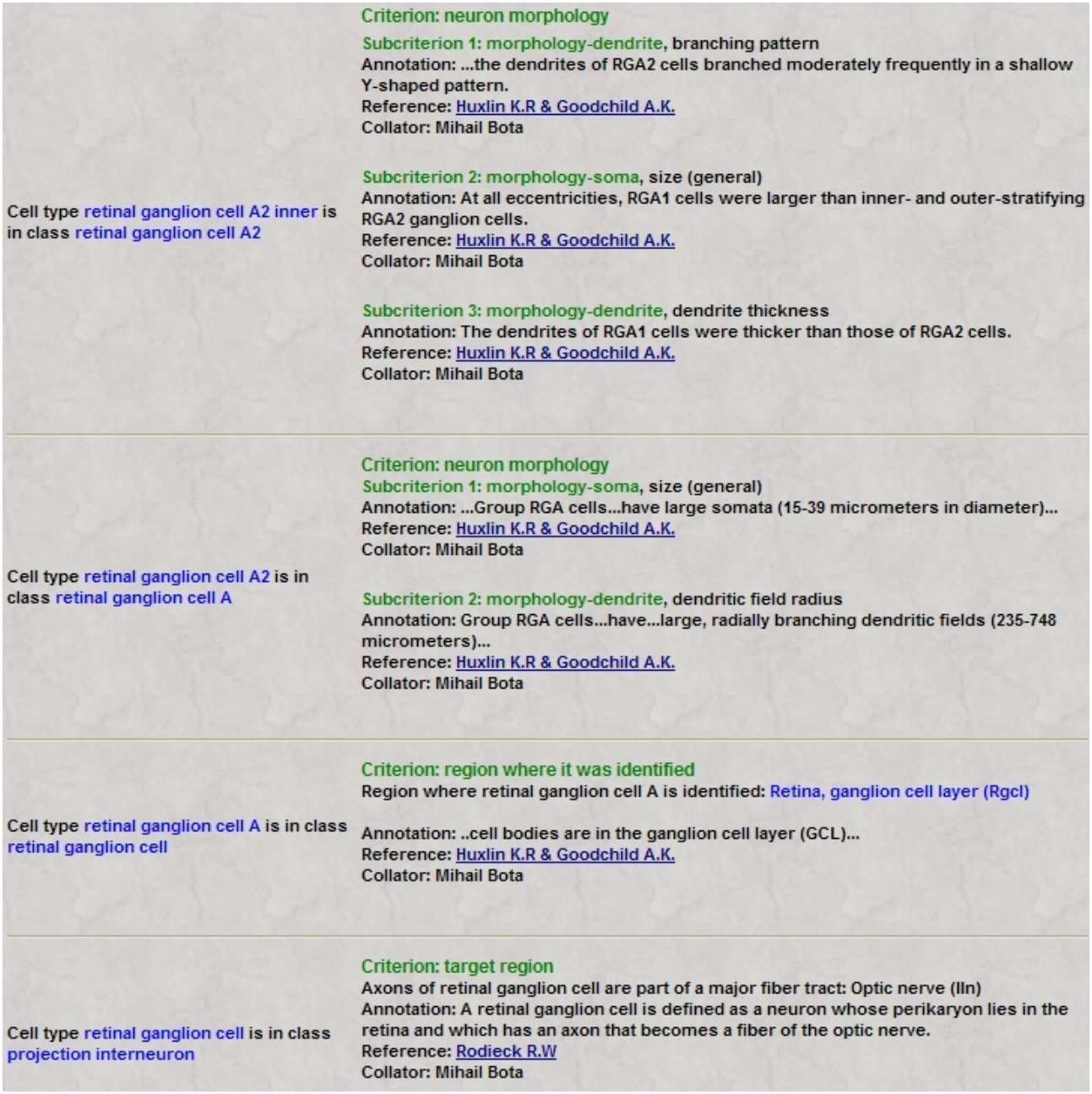


Figure 41. Users can access classification criteria associated with each “is a” relationship. Retrieved criteria are organized as ordered lists of variables used to define and classify the neuron concepts. Associated information includes textual annotations, references, and collator names. The list of variables shown in this Figure is used to classify rat retinal ganglion cells A2 inner as projection interneurons, passing through the intermediary classes.

Clicking on the classes displayed in Figure 40 will return the subclasses of each of them displayed in a tree like format. Thus, the tree of the class “interneuron” will be more general than that of the “local interneuron” and it will include it. Users can therefore access other neuron classes through this dynamically created tree. An example of such tree is shown in Fig. 42.

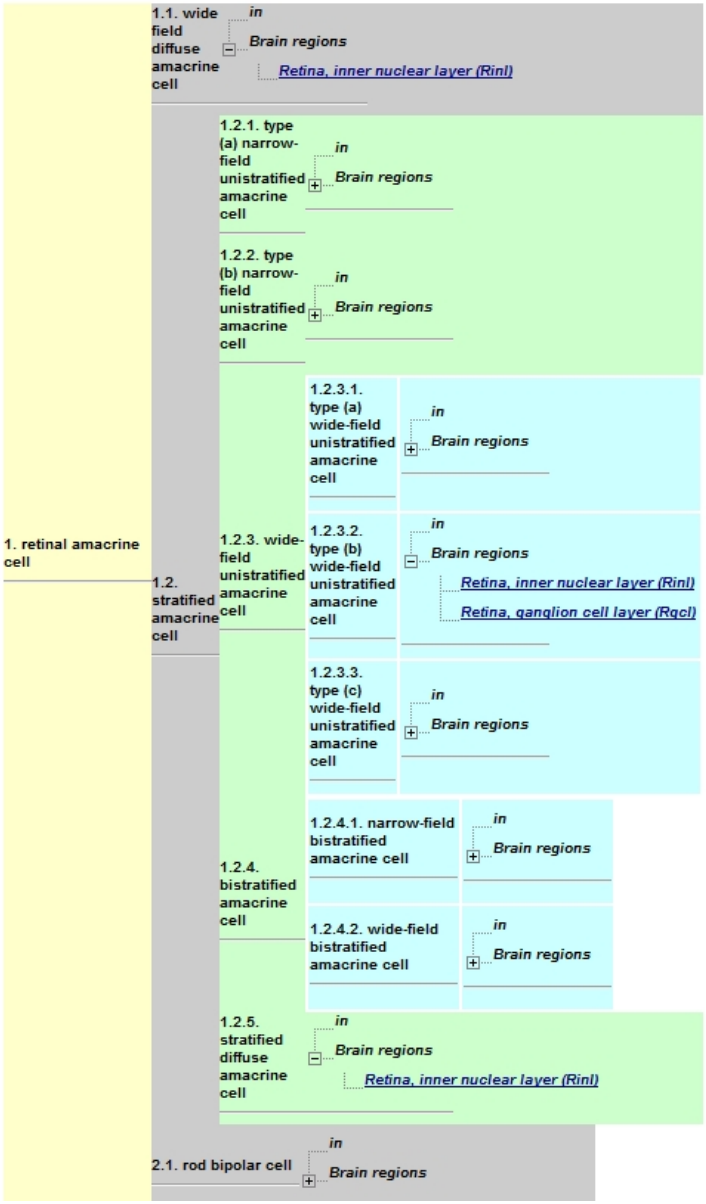


Figure 42. A “is a” hierarchical tree dynamically reconstructed in BAMS. Users can easily navigate across cell classes and types, and from here to the brain regions that contain those.

3.7 Searching for references in BAMS

Searching for information by reference (path: Menu→References) can be performed using any combination of three attributes: author, book or journal, and year of publication. The screen that allows users to search by authors, journal and year is shown in Figure 43. The database schema for handling reference information is described in detail in Bota et al. 2005.

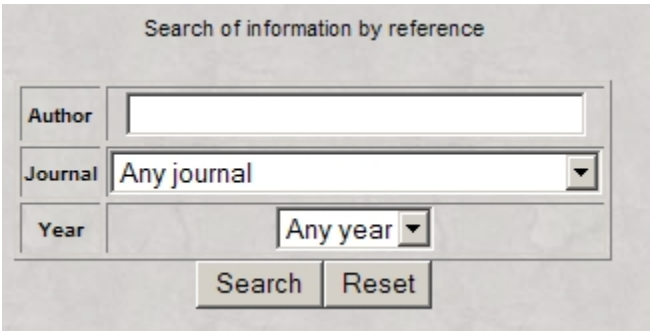


Figure 43. The interface for searching references in BAMS. Users can choose any combination of the three fields: author, journal, and year.

If users would like to see the entire set of publications of a certain author, then the journal and year fields of the form shown in Fig. 43 should be left blank. In this case, the system will return all references published by the author of interest, organized in several categories: books, book chapters, published articles, theses, etc. An example of such search is shown in Figure 44.

This type of search retrieves not only details about references recorded in BAMS but also details about what kinds of neurobiological information can be found in each of them (e.g., brain part definitions, fiber pathway reports). If a search by author retrieves references associated with information of the type "fiber tract," then users can view reconstructed connectivity matrices from the related references. The representation of connection matrices based on data collated from individual references is similar to that described for the reconstruction of connectivity data for a region from information associated with the set of its substructures. Users can organize connectivity data in two additional ways: they can view the connection matrix as reported in a given reference in terms of connection existence or absence, or in terms of maximum qualitative strength.

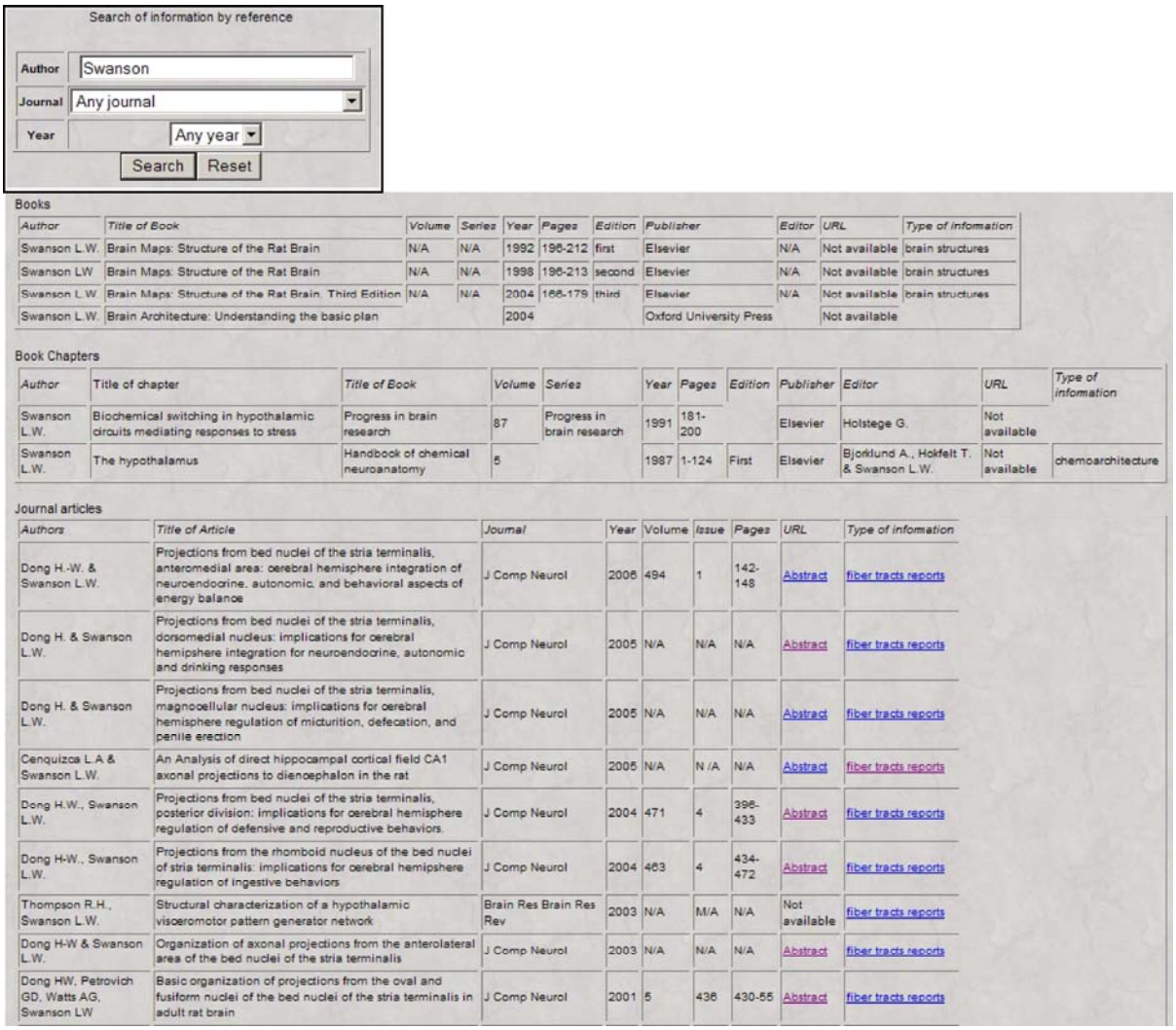


Fig 44. The output of a search for references, by author (*see* inset) in BAMS. Users can inspect details of each retrieved reference, and the types of neurobiological information found in it are also listed.

The interface that allows representation in tabular format of neuroanatomical connections reported in an individual reference is not restricted to the construction of matrices based on combined results. Instead, it also allows the display of data from individual experiments. Reconstruction of connectivity matrices from individual references has an additional feature: the ability to create a composite profile of all experiments reported in that reference. In the example shown in Fig. 45, the retrieved reference (Dong and Swanson, 2003) is associated with the reconstructed matrix of projections, and with tract tracing data for each of four individual experiments. Additionally the interface allows combination of all experiments in a single composite table (the link "Cases, composite" in Fig. 45).

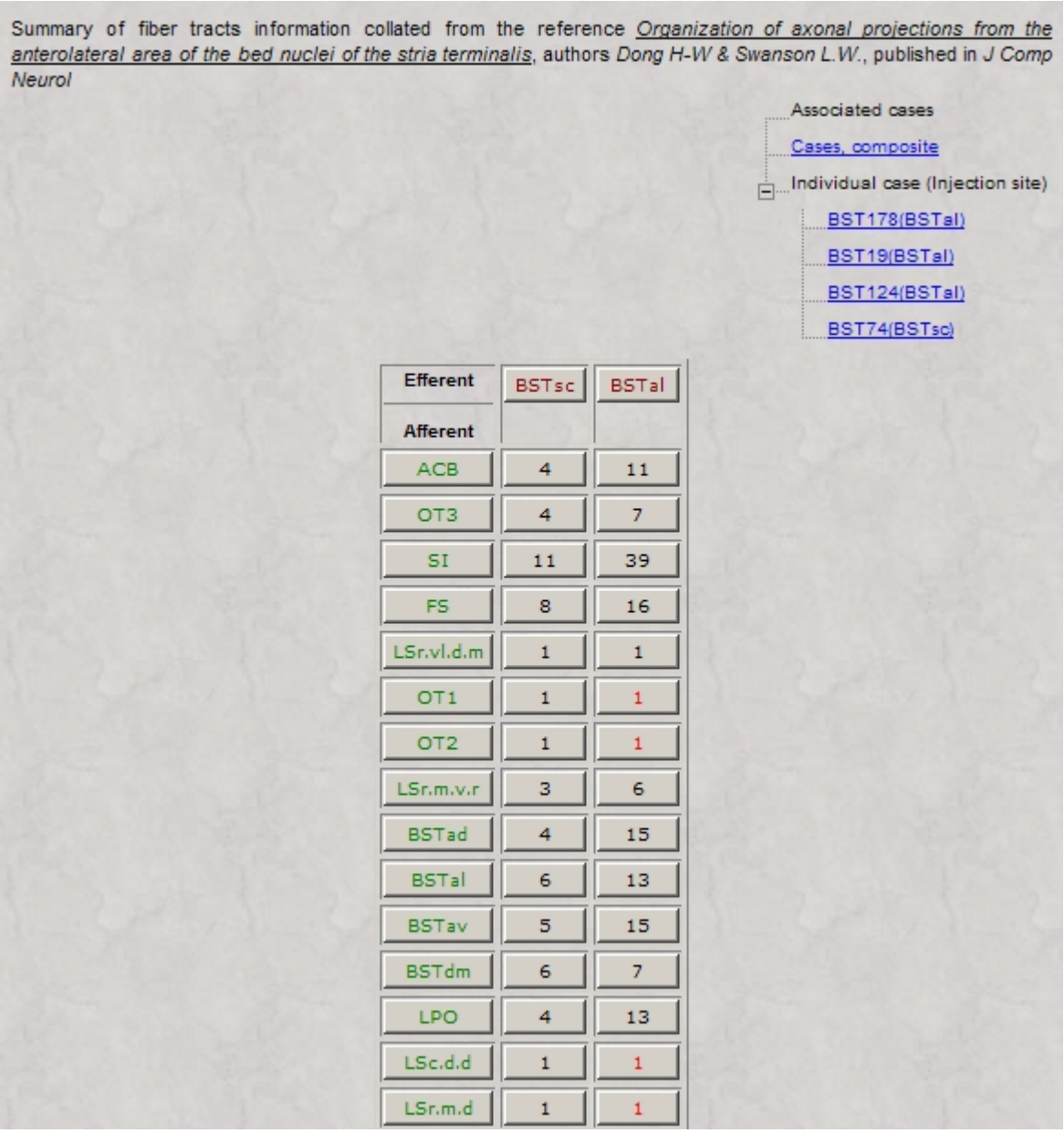


Figure 45. Users can reconstruct matrices of neuroanatomical connections as reported in individual references. If a reference is associated in BAMS with connectivity data for individual experiments, this information also becomes available to users. This connectivity matrix was obtained by search for information by author and accessing the associated “fiber tract reports” link as shown in Fig. 44.

4. Saving queries results in the Personal Workspace

The functionality of BAMS’s web interface has with two additional features: registered users may now add comments to data reports, and they can also save their activity in a personal workspace. Registered users are allowed to attach comments to brain region, projection, and molecule reports inserted in the public part of BAMS. These comments may be accessed and viewed at any time by the registered user who inserted them.

The BAMS Personal Workspace becomes the place where registered users can save and view reports of interest concerning CNS regions, their input and output axonal connections, customized connection matrices, molecules, and groups of gene expression pattern experiments. The number of reports and matrices that can be used by registered users is unlimited.

The process of registration in BAMS is very simple: just click on the link "Register" (path: Menu→Register) and the form with the first name, last name, and email address. The username of the newly registered user is his or her last name and the email address becomes the password.

Once the registration is completed, users can start using the workspace (path: Menu→Workspace). The system will display login interface, as shown in Fig. 46.

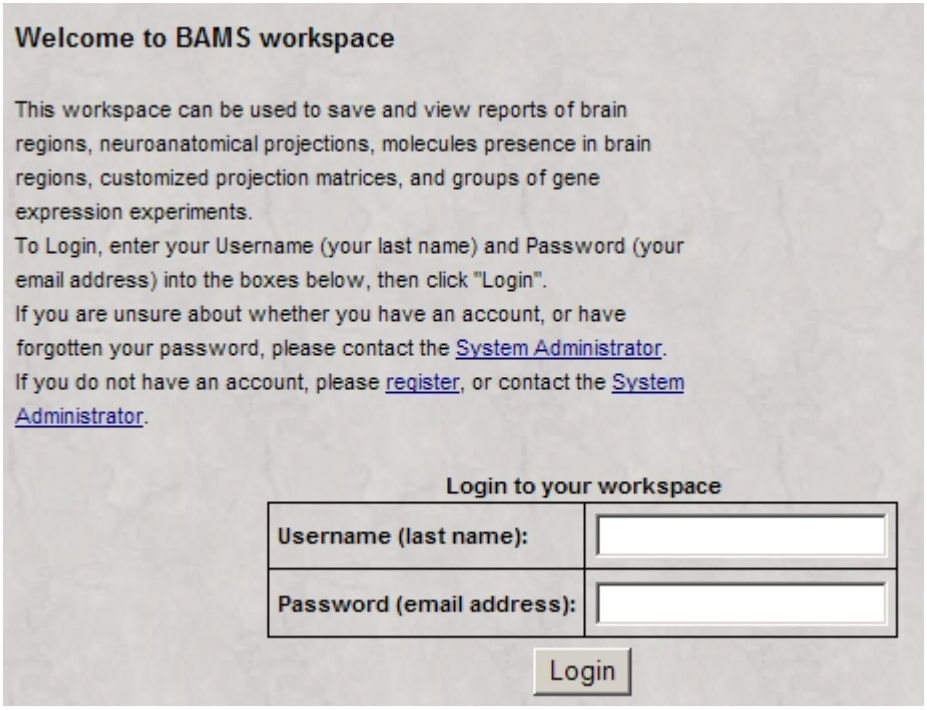


Figure 46. The login interface to the BAMS Personal Workspace.

Once users are logged to the Personal Workspace, they can use BAMS as before. The differences that will appear are related to the possibility of associating personal notes to results of queries, and saving these in the workspace. An example is shown in Figure 47: the summary page of the rat PVHmpd is almost identical with Figure 6, except the link that allows users to associate annotations with this region, and the link necessary to save it in the personal workspace.

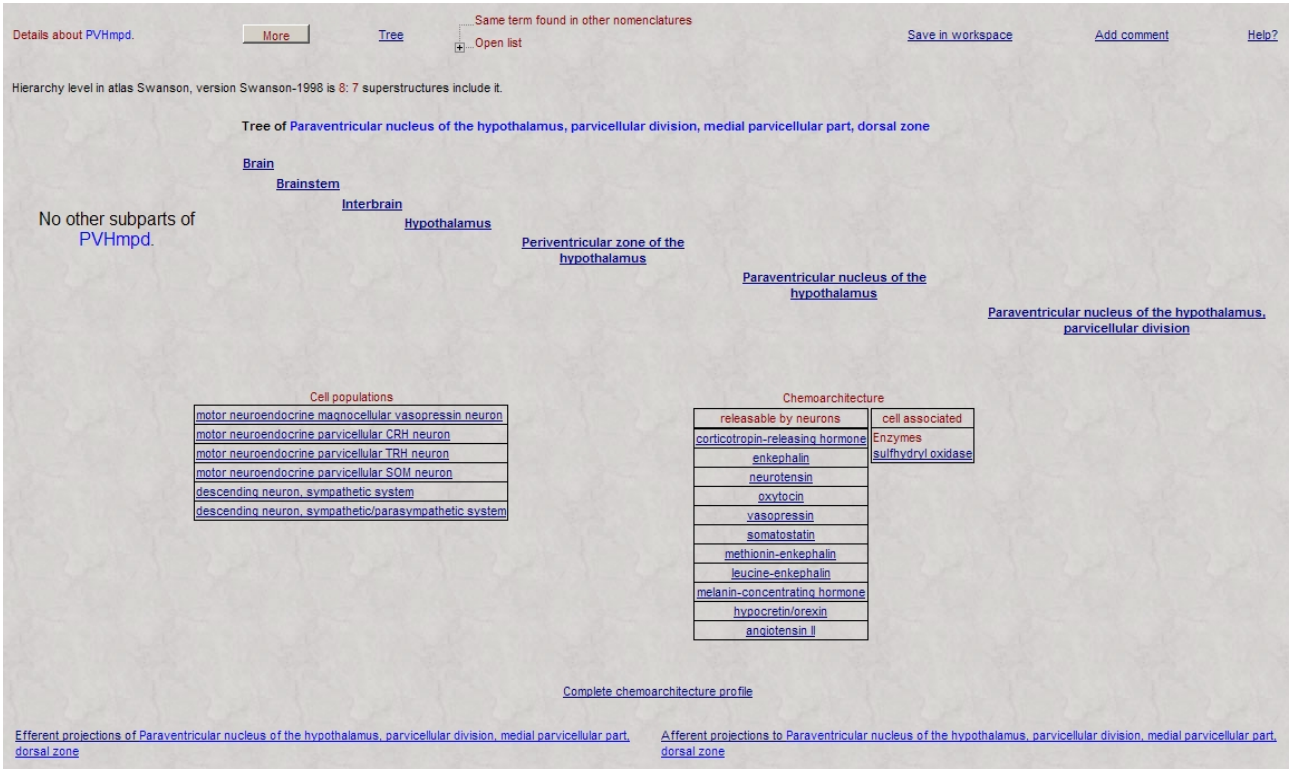


Figure 47. The summary page of the rat PVHmpd in BAMS, for a registered user who logged to the Personal Workspace. This page includes two additional links: “Save in workspace” that allows users to save this region, and “Add comment”, which users to associate any number of text annotations.

This approach was also implemented in the other modules of the BAMS web interface. Therefore, users can save CNS parts reports, projections patterns (both inputs and outputs), and molecules presence/absence reports, and gene expression experiments. A typical Personal Workspace, with several queries saved from each category is shown in Figure 48.

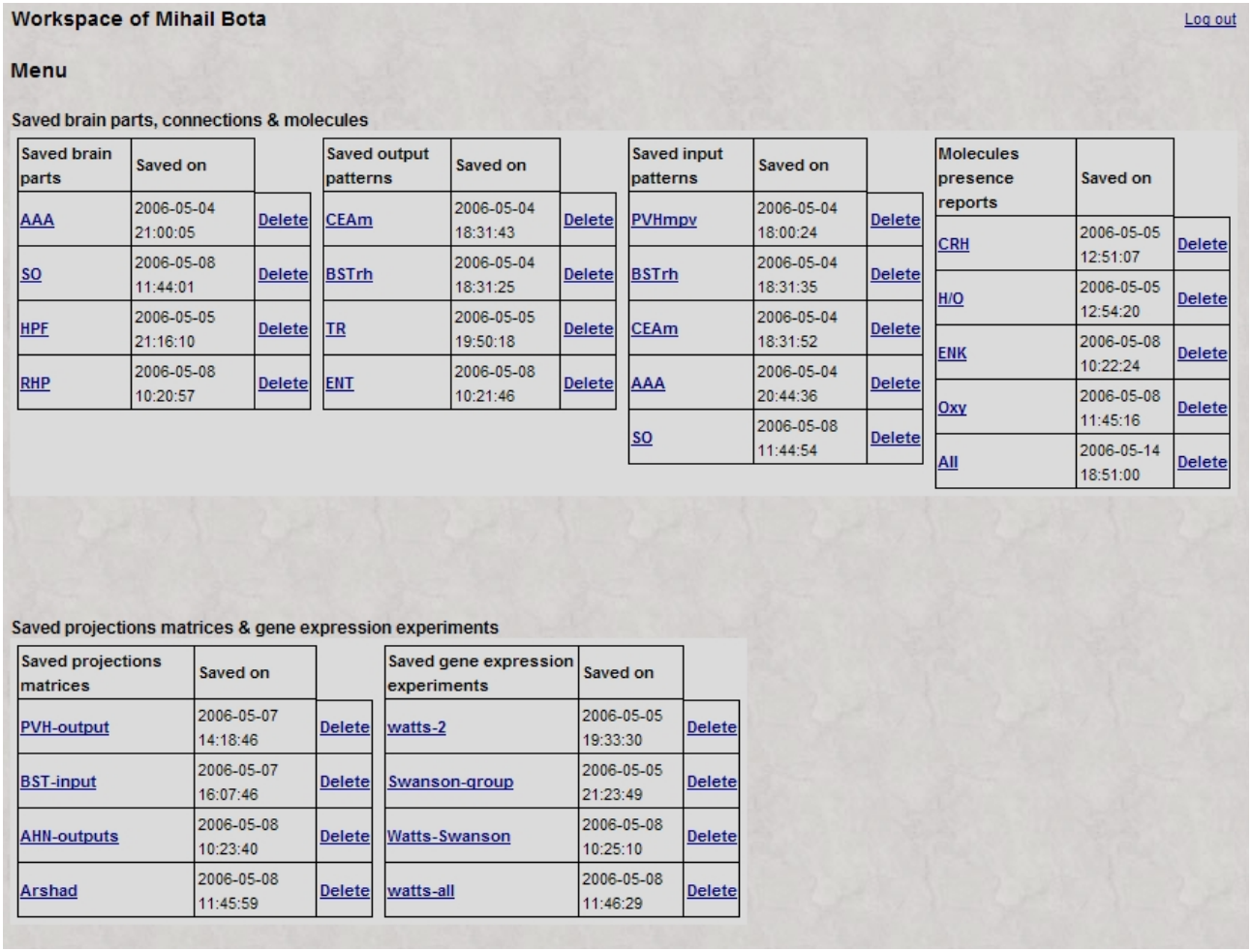


Figure 48. BAMS Personal Workspace allows registered users to store and view reports of interest concerning CNS parts and cell types, input and output axonal connections, and a wide variety of molecules—as well as complex, axonal connection matrices and groups of gene expression patterns. The number of saved reports in any category is unlimited.

5. Web services and downloadable forms.

Besides having a complex web interface and being open to the neuroscience community, BAMS is also is a data and knowledge provider. This is accomplished in several ways, which include backend MySql connections with other neuroinformatics groups (Senselab; http://senselab.med.yale.edu; LONI; http://www.loni.ucla.edu, etc.), and XML pages with the data and the metadata stored in BAMS. The access to the page that includes the XML pages is via the path: Menu→XML. Here, users will find XML pages organized by brain nomenclatures. The general structure of any XML page is exemplified by the snippet below:

<part id="**p524**" name="**Abducens nucleus**" abbreviation="**VI**" is_part_of_idrefs="**p519**" url_base_ref="**u1**" url_param="**aidi=524**">
<sources>
<source id="**s835**" name="**Flocculus**" abbreviation="**FL**" url_base_ref="**u2**" url_param="**eff=835&aff=524**" />
</sources>
<molecules_in_region>
<molecule_in_region id="**m17**" name="**beta2 subunit nicotinic receptor**" abbreviation="**beta2 nAChR**" url_base_ref="**u3**" url_param="**aidi=524&chem=17&type=1&what=0**" />
<molecule_in_region id="**m15**" name="**alpha4-1 subunit nicotinic receptor**" abbreviation="**alpha4-1 nAChR**" url_base_ref="**u3**" url_param="**aidi=524&chem=15&type=1&what=0**" />
<molecule_in_region id="**m16**" name="**alpha4-2 subunit nicotinic receptor**" abbreviation="**alpha4-2 nAChR**" url_base_ref="**u3**" url_param="**aidi=524&chem=16&type=1&what=0**" />
<molecule_in_region id="**m19**" name="**sulfhydryl oxidase**" abbreviation="**QSOX**" url_base_ref="**u3**" url_param="**aidi=524&chem=19&type=1&what=0**" />
</molecules_in_region>
<cells>
<cell id="**c241**" name="**motor neuron, extraocular muscles**" url_base_ref="**u4**" url_param="**aidi=524&id2=241**" />
</cells>
</part>

Since XML pages tend to become large, the loading time may become a problem, especially to those that use Internet Explorer. In this situation, we encourage the users to contact us, to either send the XML pages by email, or create custom (and smaller) XML scripts.

Any XML page can be saved in users' computers and later used as base for searching BAMS for additional information, or run different inference engines.

BAMS interface also includes a growing set of downloadable forms, written in Excel, which can be used to either construct "in house" small databases, or populate it. These forms can be found under the "Forms" category of the Menu (path: Menu→ Forms). So far, this category has only one downloadable Excel form, for populating the *Connections* module of the system. Here, we will add Excel forms for molecules and neuron types records.

Acknowledgements

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