The Brain Operation Database (BODB): Introduction and Tutorial

James J. Bonaiuto and Michael A. Arbib

Table of Contents

Introducing BODB

BODB, the Brain Operation Database, is a unique resource for keeping track of how models of neural processing, and other models of brain function, relate to empirical data, brain structures and general Brain Operating Principles (BOPs). Basically, the empirical data relevant to a model are structured as Summaries of Empirical Data (SEDs) that enter into either the design or testing of the model. Documenting a model requires showing what SEDs ground specific features of the module's design; while testing calibrates Summaries of Simulation Results (SSRs) against others SEDs, providing an explicit evaluation of the extent to which the model either explains the data or is contradicted by them. Models can be retrieved on the basis of the extent to which they share SEDs, model the same brain regions or exemplify the same BOPs. BODB then provides explicit means of comparing retrieved models that share various properties.

Why Using BODB is a Good Thing

In general, journal articles describing computational brain models are highly inhomogeneous. While efforts have been made to standardize the descriptions of models in terms of their equations and parameters (Gleeson et al. 2010, Nordlie, Gewaltig, & Plesser 2009), little work has been done in the way of standardizing the relations between models and experimental data. By linking descriptions of the model structure and simulation results with the experimental data used to build and test the model, documenting a

model in BODB makes these relations explicit in ways that can be obscured by the format of a typical journal article.

The chapters in the book have corresponding BODB entries for one or more models in the chapter. These allow students to complement the text in several ways. The experimental data used to build or test the model can be examined in more detail, and students can search for summaries of experimental data that confirm or contradict predictions made by the model. For many entries there are links to federated databases which contain more information on the dataset. Related models can be found that explain or use these data summaries in different ways, and can be compared to those described in the chapter.

A valuable exercise for students to expand their understanding of a chapter is to identify a new model related to that chapter and enter it into BODB, paying special attention to coding of SEDs in ways maximally similar to those of SEDs already in the system. This will help students think much more deeply about the relation between a general description of data, or copious details of a dataset, and the actual form of the dataset that is truly used in model design or testing.

The search and model benchmarking features in BODB let students explore to what extent similar models to the one they are studying are already documented in BODB. In addition to features that allow users to search for a specific model by keyword, title, or author name, BODB also allows models to be searched by the experimental data or BOPs related to them. Students can thus search for models that address the same or similar datasets, or are based on the same operating principles as the one they are studying. BODB includes a tag cloud that displays the keywords used to describe all the models in the system, with the font size of the tag proportional to the number of models including it. This allows users to quickly look for related models at a high level of abstraction. BODB's model benchmarking feature lets users compare two or more models in terms of the experimental data used to build them or are explained by or contradict their simulation results.

In addition to providing resources for documenting existing models, BODB can be used as a model development environment. Before beginning any programming, users can search for relevant summaries of experimental data to inform the design of the model. The key to the usefulness of SEDs for model building is that they are *summaries* of experimental data at a level of abstraction useful for modelers. Certain datatypes such as neuroimaging or connectivity SEDs are linked to federated databases which then provide more information on the dataset. For example, users wishing to build a model in which region A connects to region B can search the connectivity SEDs in BODB for such a connection. If it does exist, this reference can be used to support this model design decision. Connectivity SEDs link to corresponding entries in CoCoMac (http://www.cocomac.org), a neuroinformatics resource for detailed information on macaque tract-tracing experiments. Users wishing to create more detailed models can make use of the information in these links to include data on projection strength, for example. While building the model, the hierarchical description in BODB of its submodules, inputs, outputs, and states provides a high-level reference documentation. Simulation results and the experimental data that they relate to can be organized as SSRs

and related SEDs while the model is being analyzed. When the model is completed, an exported copy of its BODB entry should provide a ready-made skeleton for a journal article.

Structure and Function

BODB is centered on the idea that a brain model should be characterized not only by a structural ontology (the brain regions or finer structures to which it corresponds) but also by a functional ontology (the Brain Operating Principles, BOPs, which it exemplifies). Within neuroscience, the best known ontologies focus on the hierarchical nesting of brain regions in the mammalian brain (and this varies from species to species), while some effort has been devoted to ontologies for classes of neurons (Bota & Swanson 2007), and ontologies for neurological diseases (Gupta, Ludäscher et al. 2003). With the exception of the latter, these are structural ontologies. Our work in BODB will also make use of the structural ontologies of nested brain regions. However, our contribution to neuroinformatics ontology is to introduce the complementary *functional* ontology of Brain Operating Principles (BOPs), setting forth functional principles that can structure both models and observed neural function.

A *brain operating principle (BOP)* as a snapshot of knowledge about brain operation is more general than either empirical data or simulation results, being independent of an experimental protocol or simulation parameters. An example is the Winner-Take-All BOP, which postulates that a neural network converts a pattern of activation on its input surface to a peak of excitation on its output surface that corresponds to the locus of maximal excitation on the input surface. This has been postulated to apply to diverse brain regions (including frog tectum and monkey superior colliculus) as well as more abstract systems, in the service of diverse functions from prey selection to planning. A given BOP may be supported or weakened by diverse summary data, and be implemented in a whole range of models. Since BOPs influence the functional ontology utilized by BODB, the administrators of BODB curate the entries before making them public. The BOPs currently in BODB are grouped into several themes (Table 1).

Table 1: Brain Operating Principles (BOPs) grouped by Categories

Learning	**Sensory/Perceptual Processing**	**Motor Control (Continued**
Reinforcement Learning	Sensor Fusion	Feedback and Feedforward
Conditioning – Classical and Operant	Cross-Body Mirroring	Motor equivalence
	Perceptual Priming	Sensorimotor Coupling
Habituation	Recognition by Components	**Excitation & Inhibition**
Hebbian Learning	Saliency Map	Lateral Inhibition
Competitive Hebbian Learning	Gestalt Rule	Recurrent Excitation
Pavlovian Learning	Perceptual Grouping	Disinhibition
Self Organization	Binding Problem	Tonic Anticipatory Activity
Supervised Learning	Event Assignment	Gain Modulation
Eligibility Traces	Base grouping	Gating
Memory	Incremental grouping	**Processing Principles**
Memory	**Maps & Frames**	Temporal Pattern Processing
Working Memory	Topographical Mapping	Competitive Queuing
Consolidation	Reference frame interaction	Dynamic Remapping
Declarative Memory	Top-Down/Bottom-Up Hybridization	Local Association Field
Episodic Memory		Chunking

Procedural Memory **Decision Making** Winner-Take-All (WTA) Winner-Lose-All (WLA) k-Winners-Take-All (k-WTA) Loser-Take-All (LTA) Hysteresis	Action-oriented perception Cognitive Map **Motor Control** Corollary Discharge Efference Copy Optimality Principles in Motor Control Internal Models	Attention Extraction of Abstract Structure Noisy Exploration **Coding** Localist Coding Population Coding Pattern Separation Rank Order Coding

How to Use BODB

A Tour of the Tutorial

After introducing the BODB homepage and how to register for an account so that you may log in thereafter, we proceed as follows:

BOPs and Brain Regions: Brain operating principles (BOPs) provide the functional ontology for models (how they operate) while brain regions provide a structural ontology for models (making explicit what brain systems they model). For the moment, BOPs and brain regions are fixed elements of the BODB environment to which other entries may be linked as appropriate.

Entering experimental data: At present, most summaries of experimental data (SEDs) are free form text entries, as we describe in the section *Generic SEDs*. BODB currently supports two additional specialized formats, both described below, one for *Connectivity SEDs* and the other for *Brain Imaging SEDs*. For the former, we show how to use BODB to generate navigable network connectivity graphs, and for the latter, we introduce our BrainSurfer software for viewing anatomically structured data. However, as more groups of people who link models to similar data sets are formed, we expect an increasing number of SED formats to be created which allow ease of comparison of related data for, e.g., single-cell neurophysiology or event-related potentials.

Entering a Model: The first requirement is to outline relevant facts about the model and then, by providing suitable diagrams with accompanying narrative and a specification of the inputs and outputs of various modules, make the model architecture explicit. This stage of model entry can include links to relevant BOPs and brain regions. The next stage (though, in fact, the order of these steps can be varied as you explore the key features of the model) is to link the relevant SEDs to the model. In some cases, you can find the SEDs you need by searching BODB, in other cases you will need to enter needed SEDs – but in either case note that SEDs summarize *model-independent* empirical data, and are thus entered separately from any model that applies to them, with links, rather than the SEDs themselves, within the model entry. By contrast, summaries of simulation results (SSRs) are specific to the model and must thus be documented within the model entry. SEDs are then shown to be relevant either to building or testing the model – and in the latter case will be linked to the appropriate SSRs.

The BODB homepage

The BODB homepage provides limited functionality for searching for and viewing models, BOPs, and SEDs (Figure 1). The top right corner contains links to Login or Register for an account and for the Help

system. The toolbar below that contains links to Search entries, use the BrainSurfer Visualization tool (described below), or visit the BODB About page. The panel on the left contains tag clouds for Model, BOPs, SEDs, and SSRs. Tag clouds show the keywords used to describe each type of entry, with the relative size of the tag based on the number of entries of that type with that keyword (also shown in parenthesis after the tag). Click on a tag to view entries associated with it. The right panel contains links to view recently added models, BOPs, SEDs, and SSRs.

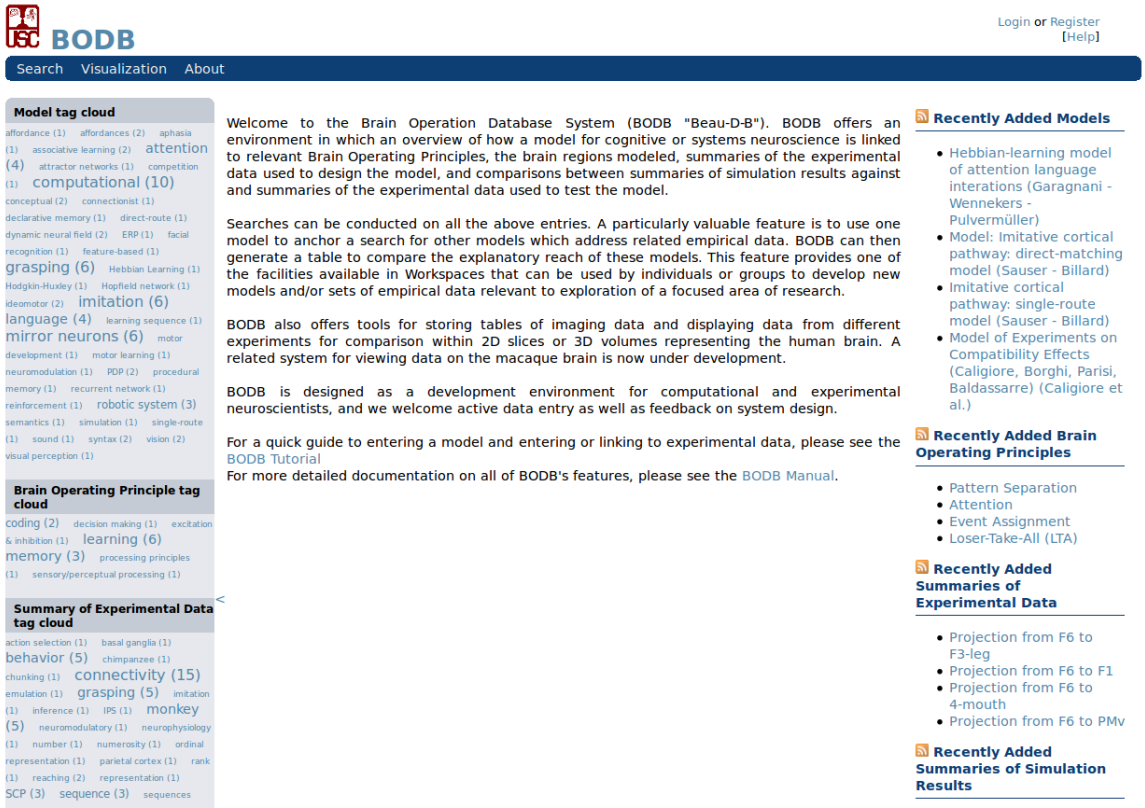


Figure 1: The BODB homepage before logging in.

After logging in, more options will appear in the toolbar (Figure 2). Click on the *Insert* link to add new entries.

Figure 2: The toolbar options after logging in. The *Admin* link will only appear for administrators.

The Insert page gives access to four types of insertion (Figure 3):

Literature: Literature (Journal Article, Book, Chapter, Conference, Thesis, Unpublished Information

Brain Operating Principle: Brain Operating Principle (BOP, e.g. Winner-Take-All)

Model: Structured description of a model with links to related entities. (e.g. FARS Model))

Summary of Experimental Data: A generic summary of experimental data, a summary of brain imaging data, or a summary of evoked response potential (this is still preliminary).

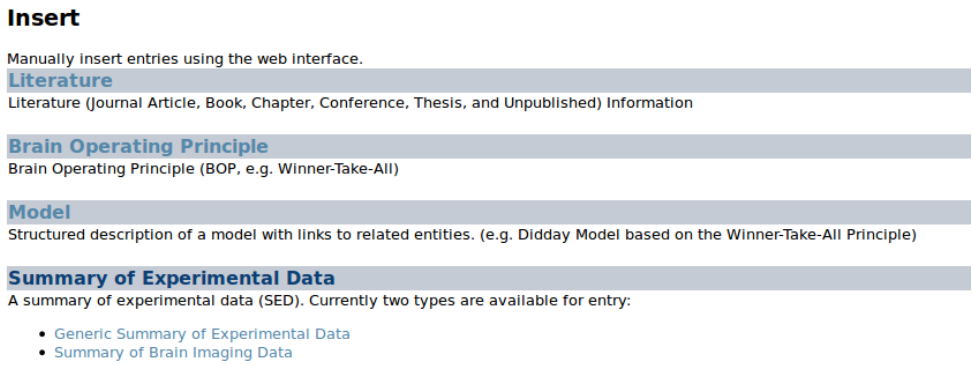


Figure 3: The Insert page

Starting from the Insert page, you can choose any one of these possibilities. At the top right of the page that opens, you will find a link to [Help] that will tell you more about the type of insertion. In this Tutorial, we will discuss entering experimental data and model entry at some length.

Registering for an Account

To register for an account on BODB, click on the *Register* link at the top-right corner of the screen. On the registration page (Figure 4), enter your desired username, email address, desired password (twice for verification), first and last names, and affiliation. After clicking the Register button, a confirmation email will be sent to the email address you provided. Click on the link in this email to complete the registration process.

Figure 4: The Registration page.

Of course, once you are registered you can use your Username and Password to log in as you would for any other Website.

BOPs and Brain Regions

Brain operating principles (BOPs) provide the functional ontology for models (how they operate) while brain regions provide a structural ontology for models (making explicit what brain systems they model). For the moment, BOPs and brain regions are fixed elements of the BODB environment to which other entries may be linked as appropriate. Each *brain operating principle* entry consists of a title, brief description, related entries, relevant brain regions, and full description or narrative and references (Figure 5). The BOP entries allow specification of related SEDs, Models, and other BOPs, which thus allows cross-linkages to develop within the system.

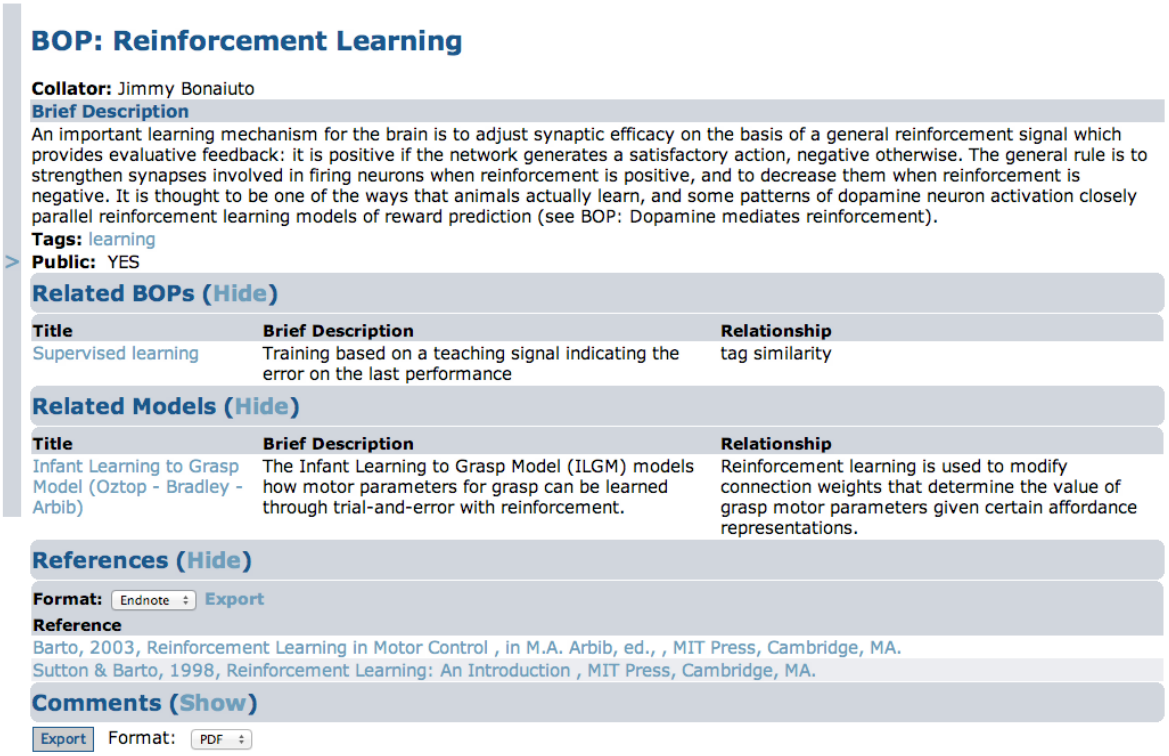


Figure 5: An example BOP entry. The entry panel lists the hyperlinks of other relevant BOPs and Models that are previously defined by collators, allowing one to readily navigate associated entries. In addition, the panel allows the collator and other users to add comments to the entry, in order to facilitate collaborative refinement of the BOP.

BODB maintains a simple structural ontology for brain regions centered around nomenclatures, with extensions to coordinate spaces and brain atlases for use with BrainSurfer (see section below). Each

nomenclature is linked to the literature reference it is defined in, as well a list of the brain regions defined in that region. Translation between nomenclatures is not currently addressed by BODB. These brain regions can be linked to models and their submodules that simulate their functionality, SEDs that describe results from experiments involving the region, and BOPs that the region is thought to implement.

Citing References

Models, SEDs, SSRs, and BOPs can all be linked to related references. These entries all have a References section in the edit and view pages. BODB allows users to search for reference entries already in its database, import reference information from PubMed, and enter new entries when these methods fail. On edit pages, the References section provides links to *Search* for existing references or *Add a New* reference (Figure 6).

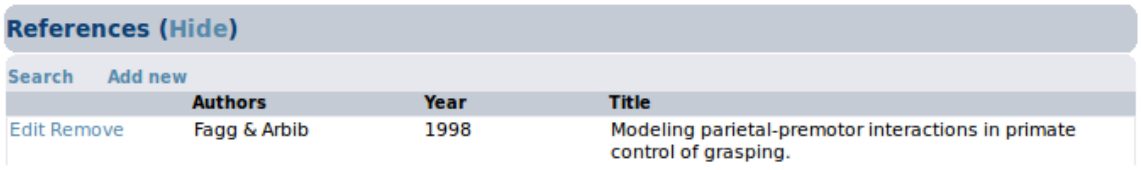


Figure 6: The References section of a Model entry

To search for existing BODB literature entries, click the *Search* link above the References section. Click on the *Show* link next to the Advanced Options section to show additional search options (Figure 7). When the search button is clicked, literature records matching the entered criteria will be displayed in the Results section. Clicking on the reference will bring up the Literature View page for that reference. Clicking on the *Select* link next to an entry will link it to the Model, BOP, SED, or SSR you initiated the search from.

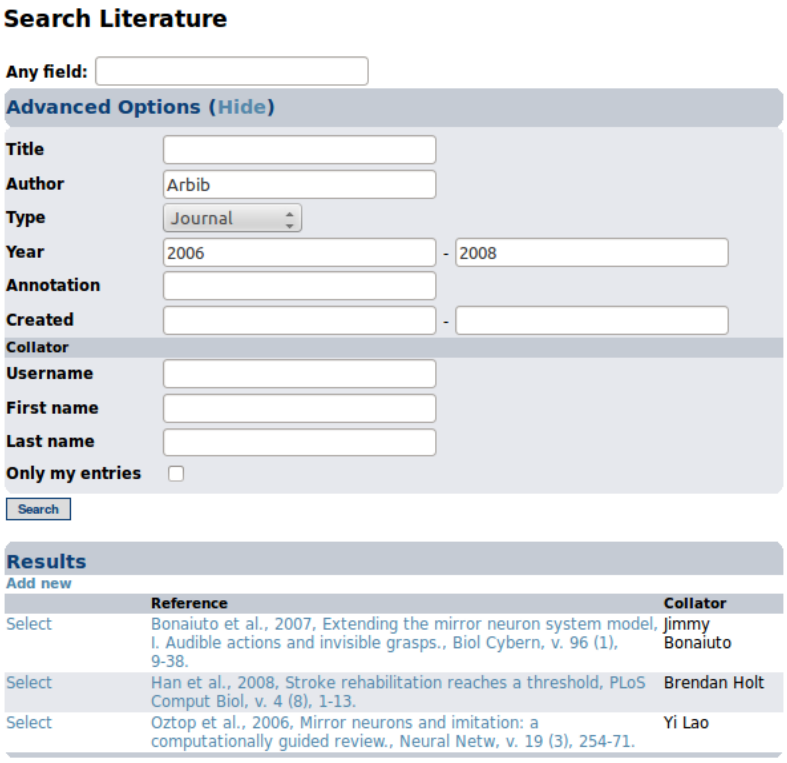


Figure 7: The Literature Search page after search for journal articles by Arbib published between 2006 and 2008. Search results are shown in the lower section.

If BODB does not contain the reference you are searching for, click on the *Add new* link in the References section of your entry to display a window containing the Literature Insert page (Figure 8). Before filling out this form, however, click on the **Search PubMed** button to try to import the reference information from PubMed.

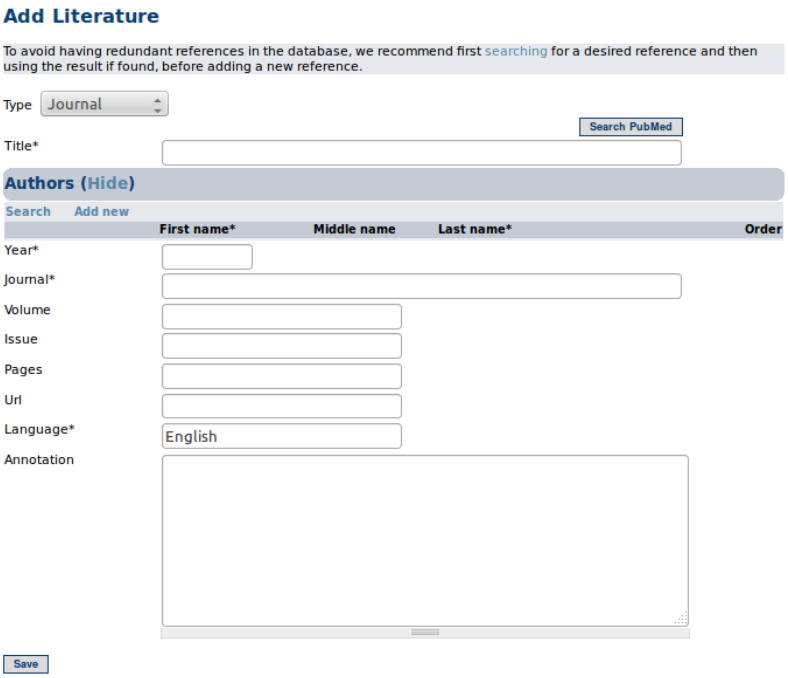


Figure 8: The Literature Insert page. Selecting the type of reference (Journal, Book, Book Chapter, Conference, Thesis, or Unpublished) will change the fields available.

The Search PubMed window allows users to search for PubMed entries based on keywords and year ranges (Figure 9). After clicking Submit, search results will be shown in the section below. Click the *Import* link next to an entry to import it to BODB. This will fill in the fields of the Literature Insert page and you can then click Save to save the reference entry. If the *Import* link is inactive, this means that an entry already exists in BODB for that reference and can be found with the Literature Search functionality described above. If the reference you are looking for cannot be found in BODB or in PubMed, you may manually fill in the fields of the Literature Insert page and click Save to insert the reference.

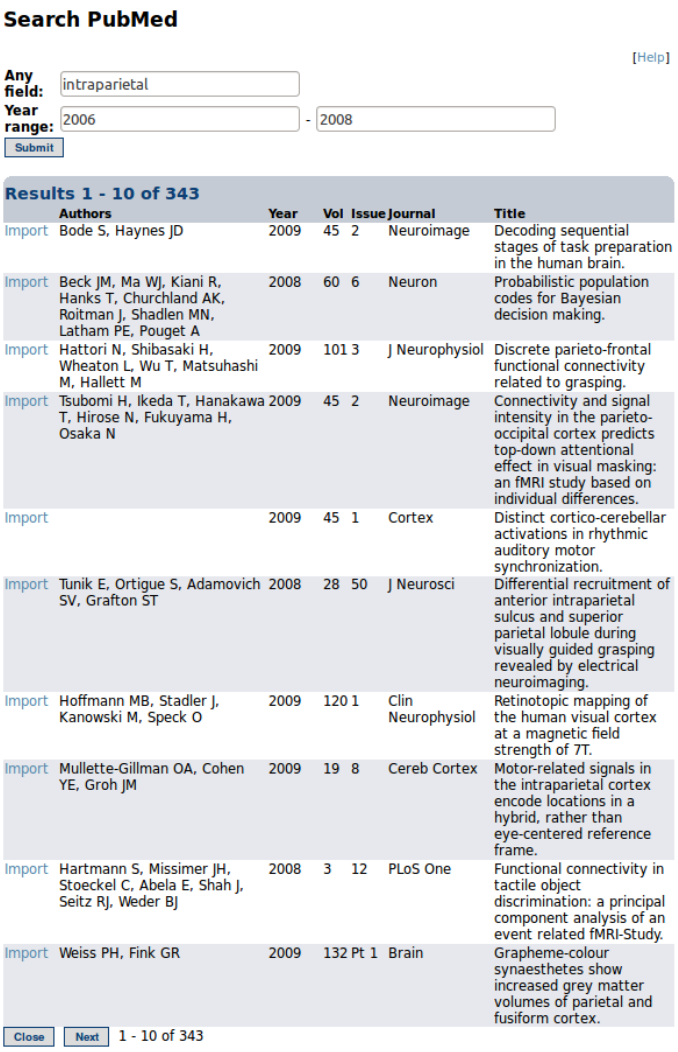


Figure 9: The PubMed search and import page.

Entering experimental data

For an experimentalist, recording your data in a database shared by your part of the neuroscience community has value that has been well attested. However, BODB emphasizes *summaries* of empirical data (SEDs) that can be shared with both your peers and the community of model builders, ensuring that your scientific results will be easily accessible for those interested in building computational or conceptual models. At present, most SEDs in BODB are free form text entries, as we describe but BODB already supports two specific formats, one for *Connectivity SEDs* and the other for *Brain Imaging SEDs*. However, as more groups of people who link models to similar data sets are formed, we expect an increasing number of SED formats to be created which allow ease of comparison of related data for, e.g., single-cell neurophysiology or event-related potentials.

Our motivation here is that other databases can act as repositories for the full details of experiments which can only be sampled in the figures and tables of a journal publication. However, in systems and cognitive neuroscience, we rarely want to model the fine details, of, e.g., the firing of a specific neuron of a specific monkey during a specific protocol. But we might want to explain general properties of how neurons of a particular class behave during that protocol. An SED would thus present these general properties in the form that you would want the modeler to explain. Similarly, to ground the model, you might structure data on synapses at just the right level to generate an SED which would constrain the way connections are specified in setting up a model.

Of course, this requires that experimentalists gain some feel for what current models do and do not explain, and this would help set the granularity of SEDs that would adequately enter into the design and testing of models. To date, many SEDs entered in BODB are too qualitative, thus yielding rather weak constraints on modeling. Thus we hope to develop patterns of collaboration between modelers and experimentalists to better specify SEDs at the right granularity to both assist and challenge modeling.

In this way, empirical studies could see their impact improved by providing both a background for future models, paving the way toward areas unexplored or unexplained by current models, but also by reinforcing or contradicting existing models. BODB offers the possibility to benchmark models based on their capacity to explain empirical data, and any new experimental entry, once linked to models as supporting or contradicting it, will instantaneously be part of the tests that compared models have to take.

In its current version, BODB offers the possibility to enter either an imaging SED or an unstructured SED. Connectivity SEDs exist in the database and are derived from federation with the CoCoMac database (http://www.cocomac.org), but new ones cannot be entered by users. The unstructured SED simply requires you to provide a narrative for the experimental summary. On the other hand, the imaging SED, which in its current form encompasses PET and fMRI, offers you the possibility to enter a detailed record of imaging data. While imaging SEDs can be entered by users, there exist some that are derived from federation with the Brede database (http://neuro.imm.dtu.dk/services/jerne/brede/).

On the Insert page you will find links to both

- Generic Summary of Experimental Data
- Summary of Brain Imaging Data

If the proper format for your data is not yet available in BODB, please share your ideas on the type of format that would best suit the description of your experiment.

Generic SEDs

Clicking on the *Generic Summary of Experimental Data* link from the Insert page will lead to the Add SED page (Figure 10). This page contains fields for the title, a brief description, narrative, and tags. Enter a short, but descriptive title, and a description brief enough so that the gist of the SED can be understood given that field in the search results. The narrative can expand upon this description and should refer to associated figures. Figures can be uploaded by clicking on the *Add new* link in the **Figures** section, or

existing figures in the system can be linked to the entry by clicking on the *Search* link in the same section. Brain regions that the SED pertains to should be linked to by clicking on the *Search* link in the **Related Brain Regions** section. Some SEDs will be collated from a single reference, while others will generalize across the results in several articles. References associated with the SED should be added or linked to in the **References** section.

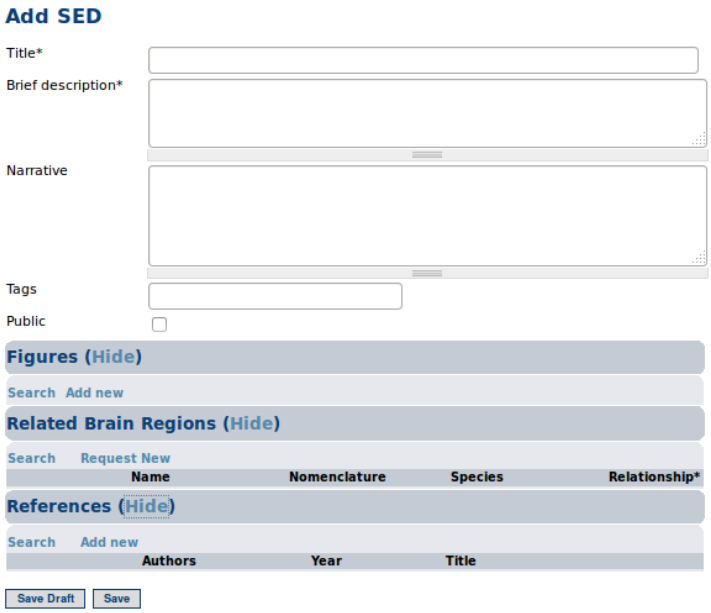


Figure 10: The Generic SED Insert page.

Connectivity SEDs

Connectivity SEDs represent anatomical projections from one region to another based on the results of tract tracing studies. These SEDs cannot be entered by the user, but there exist a great number of them based on federation with CoCoMac. To search for connectivity SEDs, first click on the *Search* link in the toolbar, then select the *Summary of Experimental Data* tab (Figure 11). Click on the *Show* link in the **Advanced Options** section. In the new fields that appear, select connectivity from the *Type* dropdown box. This will make more search fields specific to connectivity SEDs appear: Source Region, Source Region Nomenclature, Target Region, Target Region Nomenclature, Source or Target Region, and Source or Target Region Nomenclature. These fields are described in detail in the manual, but for now enter the name of a region such as “F5” in the Target Region field and click the *Search* button.

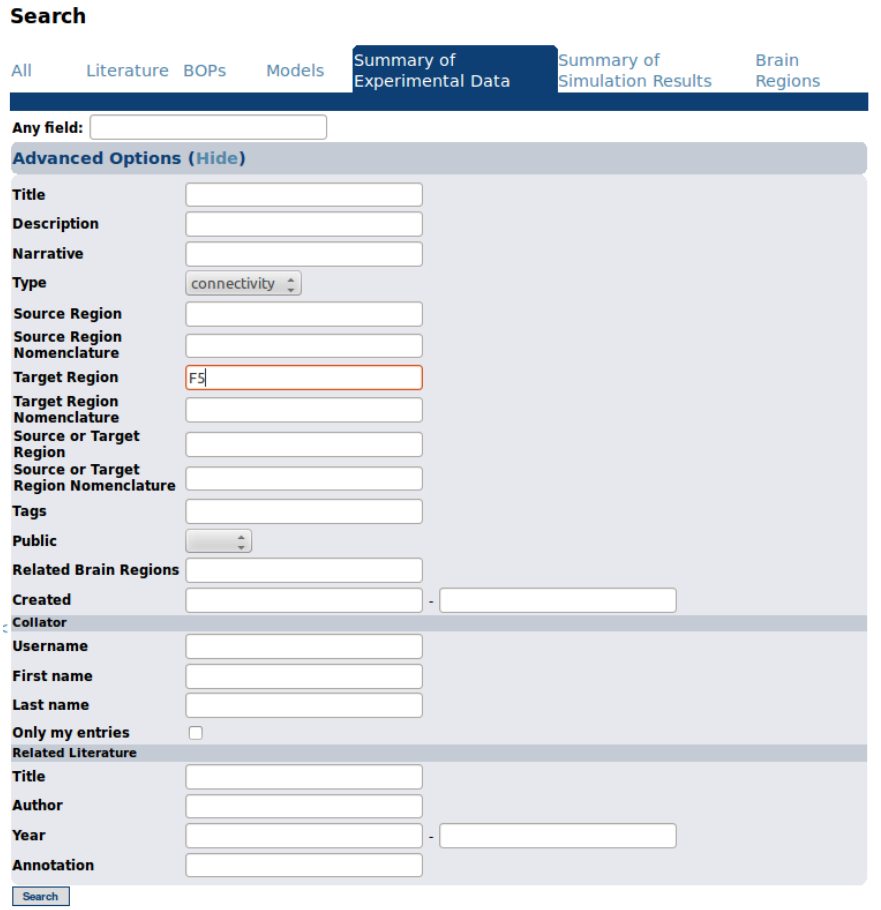


Figure 11: The Search page after selecting the *Summary of Experimental Data* tab and selecting connectivity for the Type field.

The Search Results page will display a list of all connectivity SEDs which describe a projection from region F5 to other brain regions (Figure 12). To view detailed information for any projection, click on the *View in CoCoMac* link in the appropriate row.

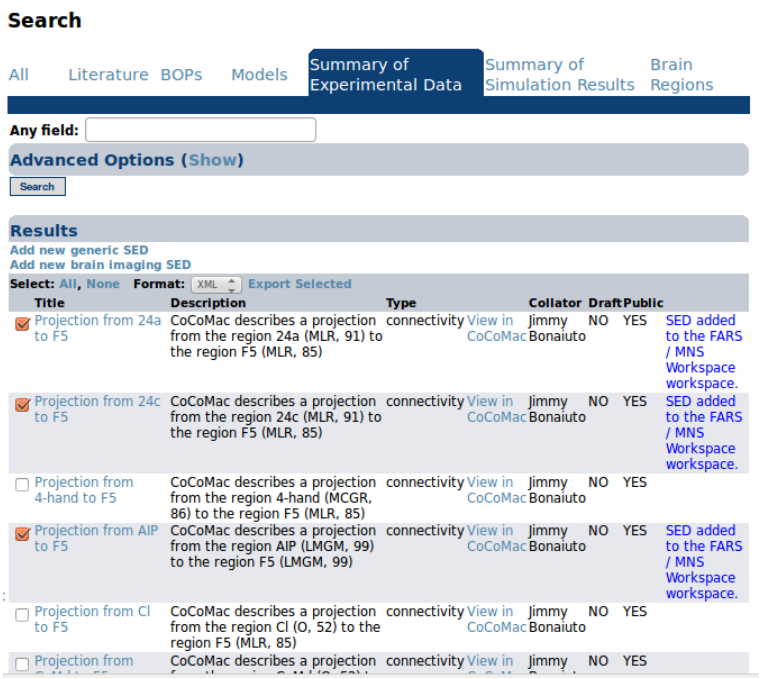


Figure 12: The Search results page after searching for connectivity SEDs describing projections to region F5.

BODB's workspace is described in more detail in the manual, but here we will describe workspace functionality that allows users to dynamically generate directed graphs which represent the network instantiated by selected connectivity SEDs. To select projections to include in the graph, click on the checkbox to the left of the desired SEDs in the search results. These selections persist in the workspace, so multiple searches can be performed to select the desired connections. Once the desired connections are selected, click on the *[Active Workspace]* link at the top-right corner of the screen and select the *SEDs* tab on the resulting View Workspace page. The **Connectivity SEDs** section will display a list of the connectivity SEDs previously selected. To unselect a previously selected projection, uncheck the checkbox to the left of it. To generate the graph, click on the *Generate Connectivity Graph* link at the bottom of the section. The generated graph will appear below (Figure 13). Each node represents a brain region and each edge represents a projection with the arrows indicating the direction of the projection. Clicking on nodes will display the corresponding page for that region listing all of its projections and related models, BOPs, SEDs, and SSRs. Clicking on edges will display the corresponding connectivity SED page for that projection.

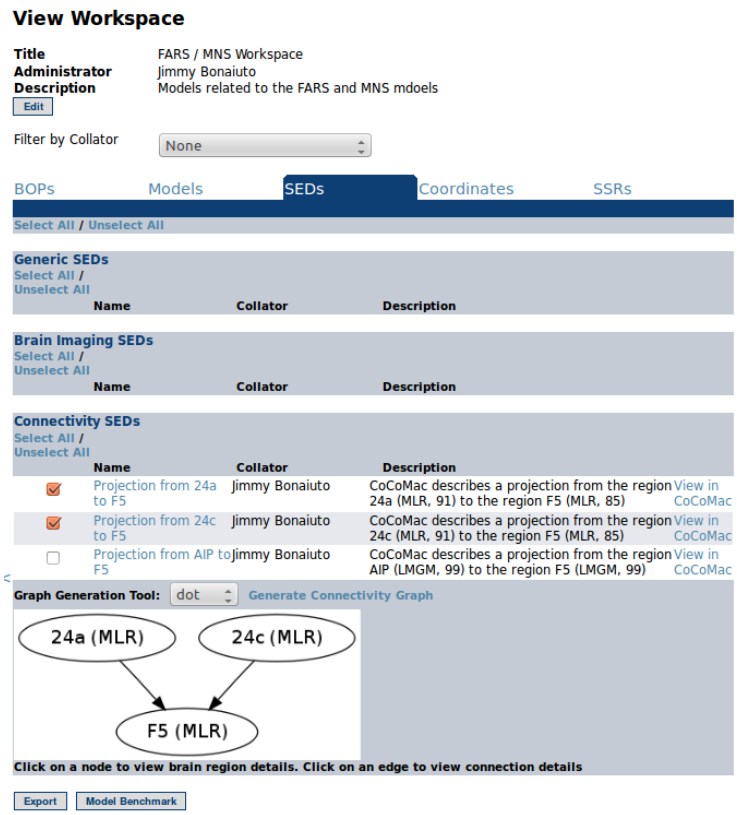


Figure 13: Viewing connectivity SEDs in the Workspace.

Brain Imaging SEDs

Although brain imaging data are often supplied in table format, different articles may differ in the number, labeling and layout of columns, and differ in the freeform description of the experimental conditions of that table. In order to have an optimal impact on the modeling community, the recorded empirical result needs to offer to the modeler details that are relevant to the current state of the art in his field while omitting those that are still far out of reach of the explanatory power of existing modeling endeavors, and do so in a way that encourages comparison and integration across multiple studies.

A difficulty when attempting to register contrast fMRI data into a standard format stems from the variety of forms the reported results can take. Most of the time, the findings are shaped into a table, but as Tables 2 & 3 show, this format is not standardized.

Table 1. Stereotactic Coordinates (x, y, z) for Significant Clusters (Random Effects, $p < .001$, Uncorrected, or $p < .005$, Uncorrected if Marked by an Asterisk) are Given in Millimeters Together with Effect Sizes (Z = Z Scores)

Brain Region	*x*	*y*	*z*	*Z*
(A) Action-related vs. Abstract (Irrespective of Body Part)				
L IFG (PO)	−52	10	16	4.91
(B) Mouth vs. Abstract (Masked Exclusive for Hand vs. Abstract and Leg vs. Abstract)				
L IFG (PO)	−56	12	12	5.01
	−44	2	24	3.63
L IFG (PT)	−40	30	16	4.20
L IPL	−60	−34	32	3.09*
L MTG	−58	−62	0	3.16*
(C) Hand vs. Abstract (Masked Exclusive for Mouth vs. Abstract and Leg vs. Abstract)				
L precentral gyrus	−30	−2	56	3.81
L insula	−36	0	4	4.35
L IPL	−62	−26	36	3.36*
L anterior IPS	−46	−38	44	3.54*
L posterior IPS	−28	−68	48	3.20
L posterior ITG	−50	−58	−16	4.17
L MTG	−40	−58	4	4.11*
R MTG	40	−62	20	4.19
(D) Leg vs. Abstract (Masked Exclusive for Mouth vs. Abstract and Hand vs. Abstract)				
L SFS	−26	4	64	3.70
L IPL	−64	−32	28	3.89
L anterior IPS	−38	−50	56	3.76*
L posterior IPS	−28	−72	48	3.33*
L MTG	−58	−62	4	3.32*
(E) Abstract vs. Action-related				
R/L posterior CG	2	−56	28	5.26

L = left; R = right; IFG = inferior frontal gyrus; PO = pars opercularis; PT = pars triangularis; SFS = superior frontal sulcus; IPL = inferior parietal lobule; IPS = intraparietal sulcus; MTG = middle temporal gyrus; ITG = inferior temporal gyrus; CG = cingulate gyrus.

Table 2. from Tettamanti et al. 2005

Table I Anatomical regions, peak voxel coordinates, and *t*-values of detected activations

Anatomic region	BA	Voxels	MNI coordinates *x*	*y*	*z*	*t*-value
Presentation of particles						
Left inferior frontal gyrus	47	118	−38	24	−14	7.19
Left superior/middle temporal gyrus	39/22	151	−58	−54	2	5.28
Left angular gyrus	39	97	−40	−64	24	5.04
Presentation of verbs						
Right globus pallidus		81	12	−2	2	6.48
Left dorsal prefrontal cortex	9/8/45	336	−50	12	42	5.60
Left inferior frontal gyrus	47/45	191	−32	22	−2	5.43
Medial superior frontal gyrus	6	114	−2	10	62	4.98

BA, Brodmann area; MNI, Montreal Neurological Institute.
Greater activations in syntactic judgment compared with phonological judgment in experiment I ($P < 0.05$ corrected for the cluster level).

Table 3. from Ogawa et al. 2007

BODB therefore offers a tool to enter fMRI tables which is flexible enough to encompass most of the table's formats found in the literature while maintaining an output which is standard for all SED. Our solution for importing the table is to provide a structured input form for pasting the table's description and data, and specifying metadata.

Both Table 2 and 3 contain results for a variety of contrast conditions. The first step in entering an fMRI SED is to select the contrast of interest. The table has to be broken down into sub-tables, each one describing a single contrast. For example, in Table 2, one could choose to focus on the contrast noted (B),

while in Table 3 one could choose the contrast describing the processing or particles in language comprehension (first part of the table).

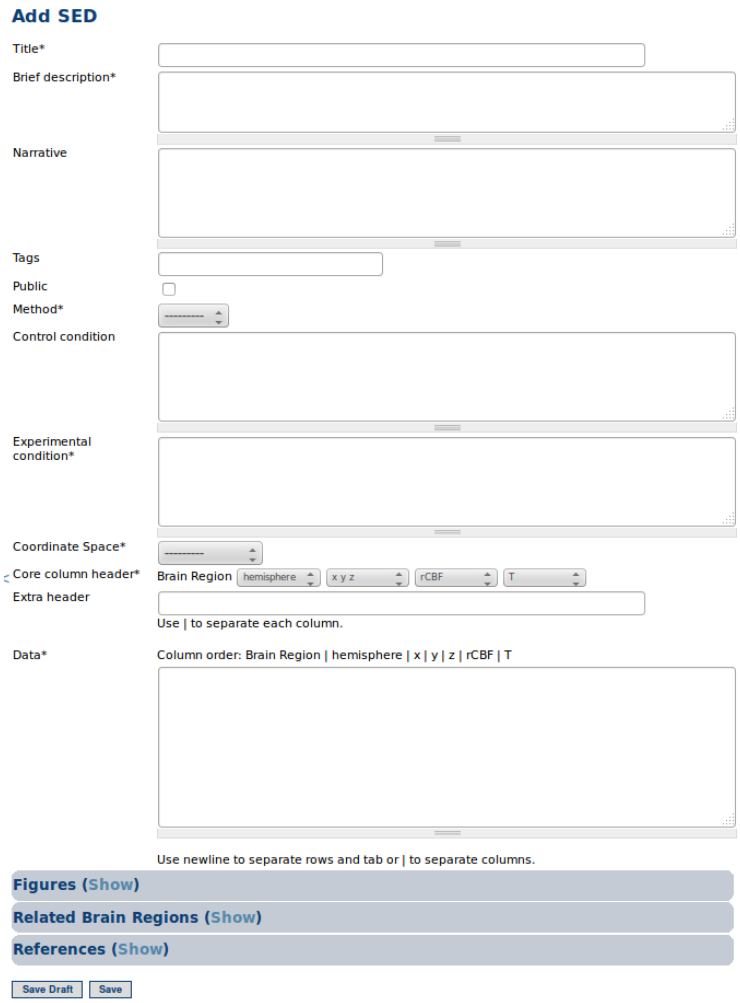


Figure 14: The Brain Imaging SED Insert page

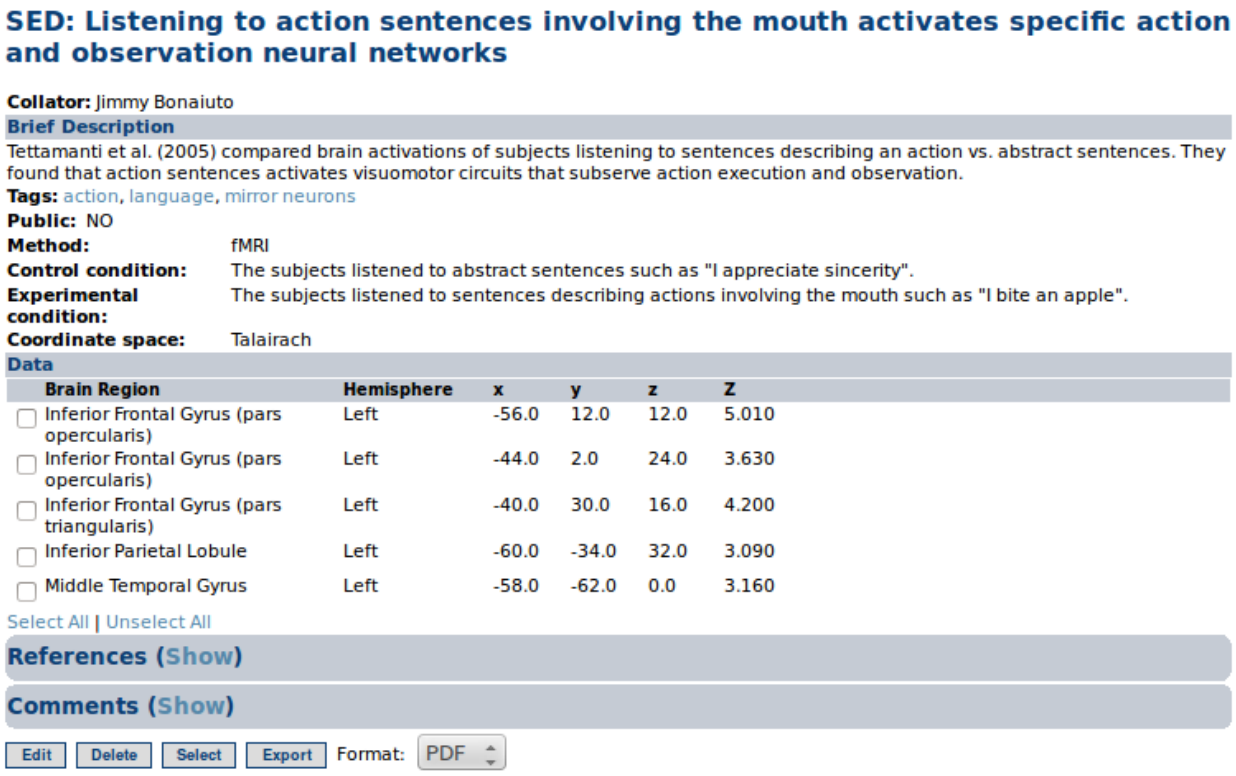
To insert an imaging SED click on the *Summary of Brain Imaging Data* link on the Insert page. This will display the Brain Imaging SED Insert page (Figure 14). The first step in entering an imaging SED consists in providing a title, brief description of the study as well as tag words. This SED type is used for fMRI and PET studies, so select the type of imaging technique in the Method field.

In a contrast study, there is always a control and an experimental condition. The contrast results from the subtraction of the activity during the control condition from the activity during the experimental condition. A description of both conditions is therefore required in the Control condition and Experimental condition fields.

Once this is done, the data itself needs to be entered. As exemplified by the two example tables, MNI or Talairach coordinates can be used (Table 2 uses Talairach coordinates). BODB offers the possibility to choose between the two types of coordinates and ensure the reciprocal conversion between them. Select the appropriate coordinate space from the Coordinate Space field.

Columns type can also vary between table, the user has the choice to define the name of the columns by using both pre-defined column type such as brain region, x, y, x, hemisphere, Z score, t-value, Brodmann Area (BA), or by entering their own column names. Note that Table 2 uses Z score while Table 3 uses t-values and that the order of columns differs. BODB possesses its own ontology for brain regions and it will therefore check with you to ensure that the region's name you entered fits the one he detected based on the coordinate you entered.

Below, we show entries corresponding respectively to Table 2 and 3 (Figures Figure 15 and Figure 16, respectively). Both tables have been summarized into their features most relevant for the work the user is focusing on. They are now standardized and can be added to a workspace, linked to a model or visualized using BrainSurfer (see below).



SED: Listening to action sentences involving the mouth activates specific action and observation neural networks

Collator: Jimmy Bonaiuto

Brief Description

Tettamanti et al. (2005) compared brain activations of subjects listening to sentences describing an action vs. abstract sentences. They found that action sentences activates visuomotor circuits that subserve action execution and observation.

Tags: action, language, mirror neurons

Public: NO

Method: fMRI

Control condition: The subjects listened to abstract sentences such as "I appreciate sincerity".

Experimental condition: The subjects listened to sentences describing actions involving the mouth such as "I bite an apple".

Coordinate space: Talairach

Data

Brain Region	Hemisphere	x	y	z	Z
Inferior Frontal Gyrus (pars opercularis)	Left	-56.0	12.0	12.0	5.010
Inferior Frontal Gyrus (pars opercularis)	Left	-44.0	2.0	24.0	3.630
Inferior Frontal Gyrus (pars triangularis)	Left	-40.0	30.0	16.0	4.200
Inferior Parietal Lobule	Left	-60.0	-34.0	32.0	3.090
Middle Temporal Gyrus	Left	-58.0	-62.0	0.0	3.160

Select All | Unselect All

References (Show)

Comments (Show)

Edit Delete Select Export Format: PDF

Figure 15: The Brain Imaging SED entry for contrast B from Table 2.

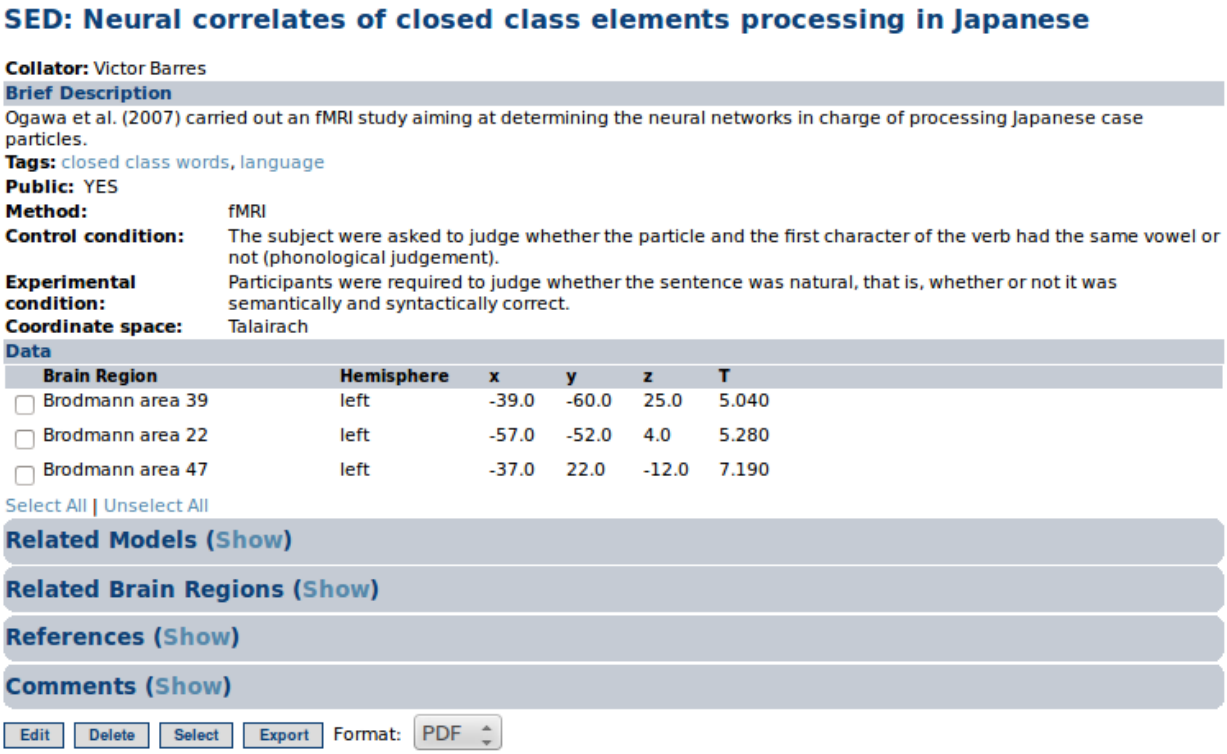


Figure 16: The Brain Imaging SED entry for the Presentation of particles contrast from Table 3.

BODB is coupled with a 3D brain visualization tool called BrainSurfer. BrainSurfer allows users to navigate brains from multiple species (currently macaque and human), coordinate spaces and nomenclatures (currently Paxinos-Watson for macaque, and MNI or Talairach for humans). When launched from BODB, users can visualize the location of selected coordinates from brain imaging SEDs. To search for brain imaging SEDs, first click on the *Search* link in the toolbar, then select the *Summary of Experimental Data* tab (Figure 17). Click on the *Show* link in the **Advanced Options** section. In the new fields that appear, select imaging from the *Type* dropdown box. This will make more search fields specific to brain imaging SEDs appear: Control Condition, Experimental Condition, Method, Coordinate Brain Region, and Coordinate Range. After entering the search criteria, click the *Search* button.

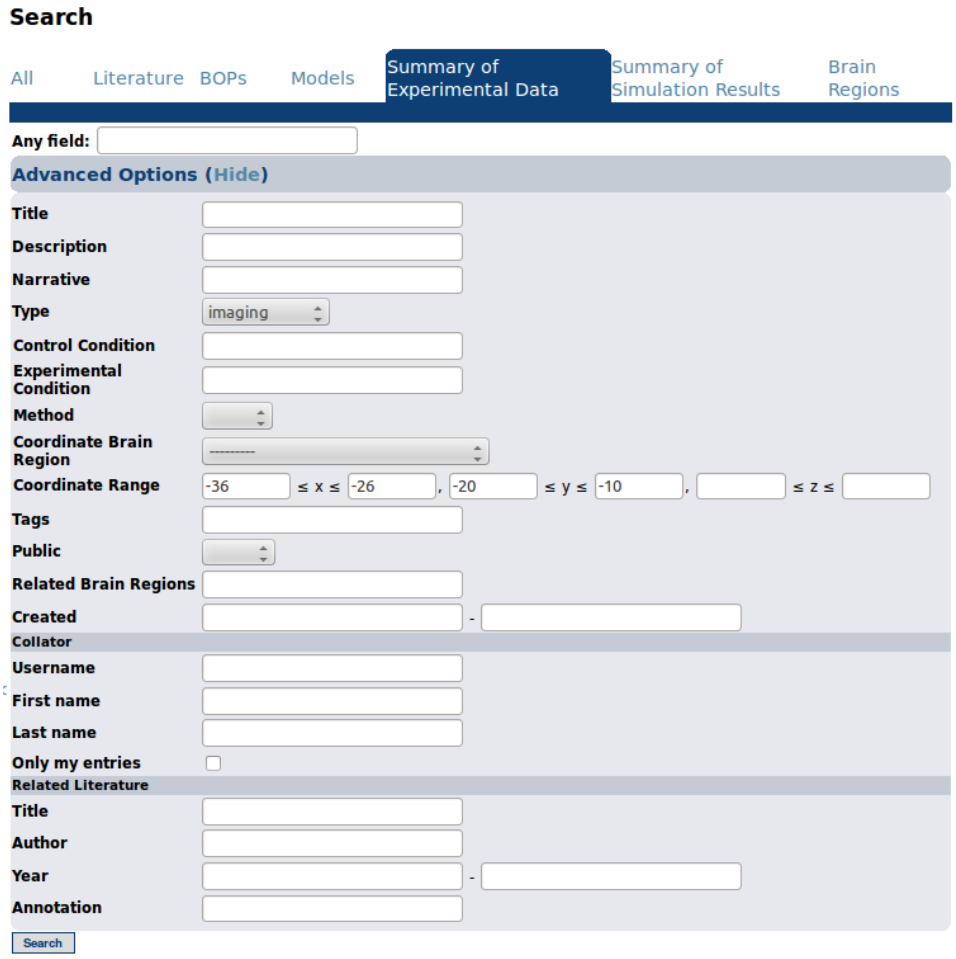


Figure 17: The Search page after selecting the *Summary of Experimental Data* tab and selecting imaging for the Type field.

The Search Results page will display a list of all imaging SEDs which match the criteria you entered (Figure 18). Imaging SEDs derived through federation with Brede will have a *View in Brede* link next to them. Click this link to view more information on this dataset in the Brede database. To select a coordinate for visualization in BrainSurfer, click on the checkbox next to it. To view all the coordinates in an imaging SED click on the *Select All* link below the list of that SED's coordinates.

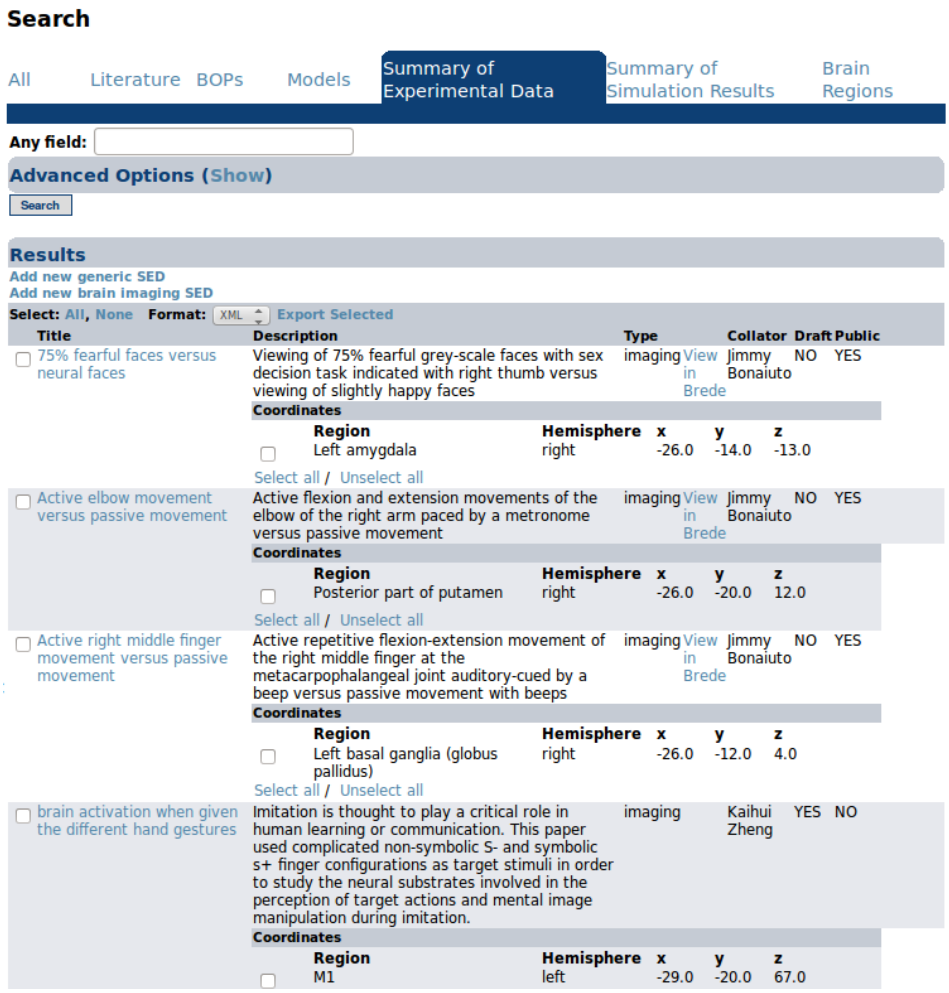


Figure 18: The Search results page after searching for imaging SEDs.

Imaging SED coordinate selections are persisted to the workspace, so multiple searches can be performed to select a set of coordinates for visualization. After selecting the desired coordinates, click on the *Visualization* link in the toolbar. If this is the first time you have run BrainSurfer, a warning box might pop-up (Figure 19). Click the checkbox next to “Always trust content from this publisher” and click the Run button. When BrainSurfer starts, it will load the human MNI atlas first – it may take a few minutes to load the atlas data if it is not already cached on your computer (Figure 20).

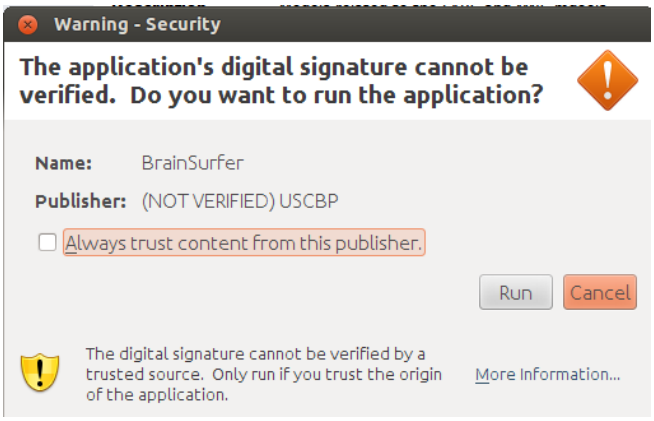


Figure 19: The warning pop-up shown the first time BrainSurfer is run on your computer.

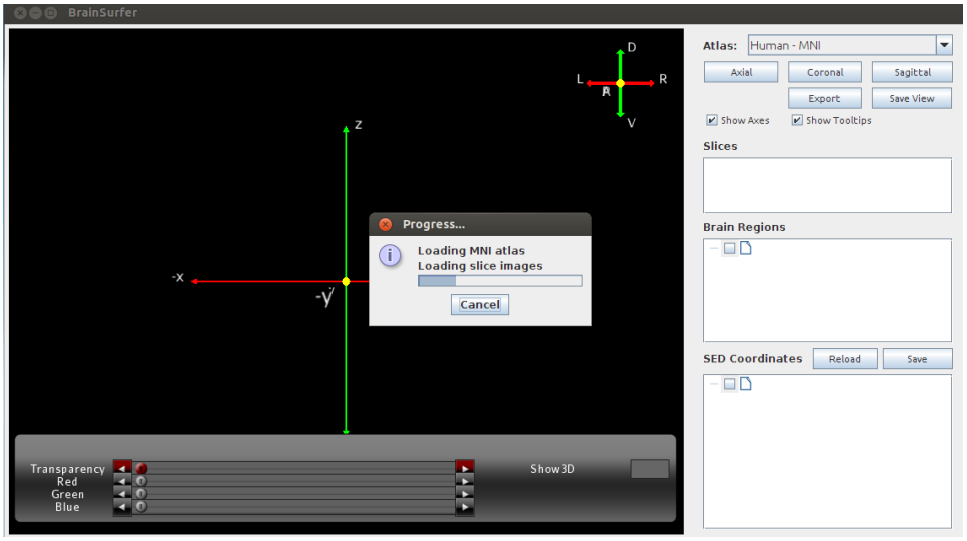


Figure 20: BrainSurfer loading the MNI atlas on startup.

The operation of BrainSurfer is described in detail in the manual, but the basic operations are described here (Figure 21). The atlas (species, nomenclature, coordinate space combination) can be selected from the Atlas dropdown box. The entire brain can be rotated by clicking-and-dragging on a location outside of the slices. The slices themselves can be moved by clicking-and-dragging, and this will update the image on the slice. Brain regions can be viewed as 3d shapes or as projections onto the slices by selecting them from the Brain Regions tree. Click the Export button to export an HTML report of the visualization including slice images, or the Save View button to save a snapshot of the current view.

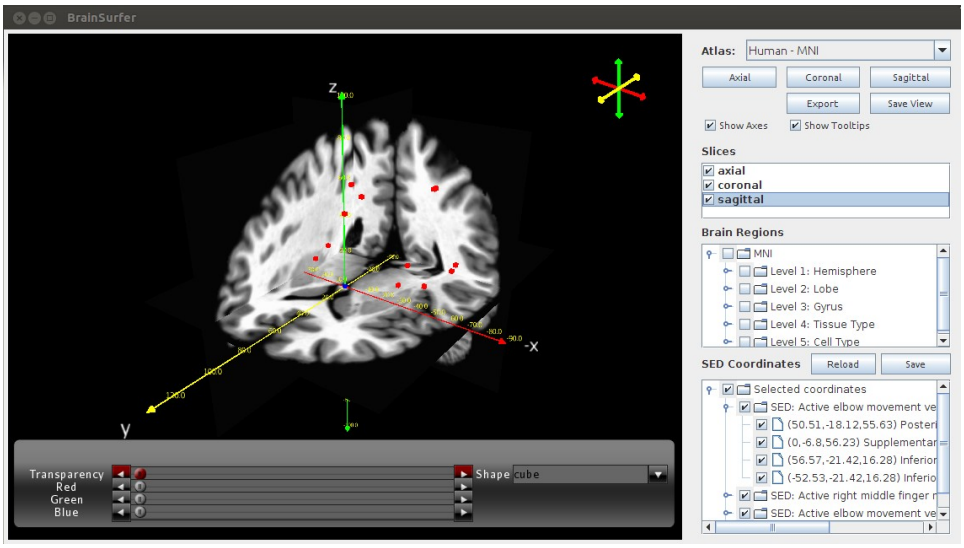


Figure 21: The BrainSurfer main screen.

Entering a Model

In general we view a model as comprising a single "Top level module" hierarchically decomposed into a number of interconnected submodules, which themselves may or may not be further decomposable. If a module is decomposable, we say this "parent module" is decomposed into submodules known as its "child modules". Otherwise, the module is a "leaf module". Figure 22 illustrates three example models. The example shows that models may be nested hierarchically, independent models can be reused as submodules by other models, and some subsystems of models can be further decomposed into new models.

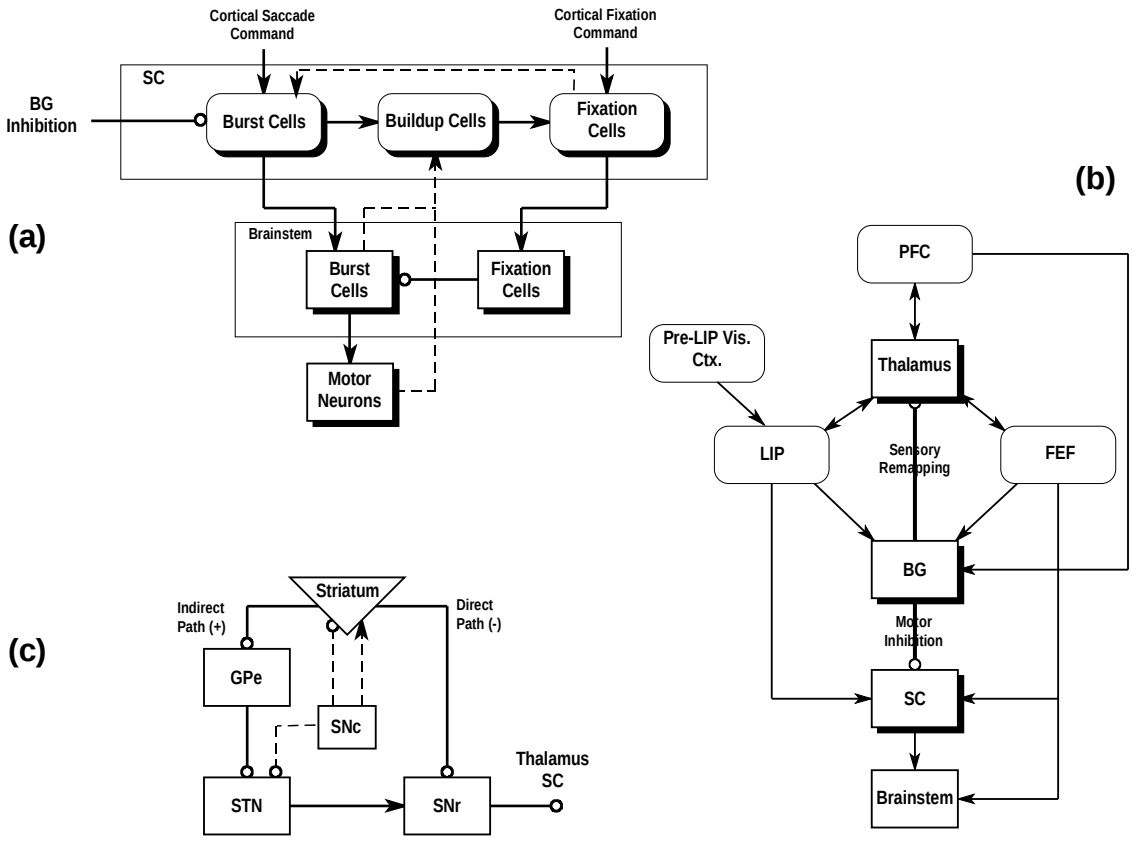


Figure 22: (a) A basic model of reflex control of saccades involves two main modules, one for superior colliculus (SC), and one for brainstem. Each of these is decomposed into submodules, with each submodule defining an array of physiologically defined neurons. (b) The model of (a) is embedded into a far larger model which embraces various regions of cerebral cortex (represented by the modules Pre-LIP Vis, Ctx., LIP, PFC, and FEF), thalamus, and basal ganglia. While the model may indeed be analyzed at this top level of modular decomposition, we need to further decompose BG, as shown in (c) if we are to tease apart the role of dopamine in differentially modulating (the 2 arrows shown arising from SNc) the direct and indirect pathways within the basal ganglia (Arbib 2001, based on the model of Crowley 1997).

Figure 22 illustrates modular design of a model by showing (a) a basic model of reflex control of saccades involving two main modules, each of which is decomposed into submodules, with each submodule defining an array of physiologically defined neurons; and (b) this model embedded as two modules within a far larger model which embraces various regions of cerebral cortex, thalamus, and basal ganglia. While the model may indeed be analyzed at this top level of modular decomposition, (c) shows how to further decompose basal ganglia to tease apart the role of dopamine in differentially modulating the direct and indirect pathways. This example introduces the case where the modules correspond to some

physical structure of the brain – whether a brain region, an array of neurons, a neuron, or some subcellular structure.

The hierarchical composition and modularity of models aids model development because one can easily reuse existing models as a part of a new model. One does not have to know the exact details underlying a module – only the *function* of such models is required (by function we mean a model behavior which maps a certain set of inputs – perhaps via dynamic internal states – to a certain set of outputs in a well-specified manner). This process is analogous to implementing a software system in an object-oriented programming manner, where we select relevant objects each with a set of inputs, outputs and its function, fitting them to the other peer modules in that system.

The model entry page allows users to insert many features of a model through the use of inline forms. However, it is typically easier to insert models through a staged process rather than all at once. The most efficient way to enter a model in BODB is in five steps:

1) Enter the model outline

2) Flesh out the model architecture

3) Enter or link to outlines of SEDs and SSRs

4) Finalize model entry

Enter the model outline

Click on the Insert link at the toolbar at the top of the page. Then click on the Model link from the Insert page, leading to the Model Insert page (Figure 23).

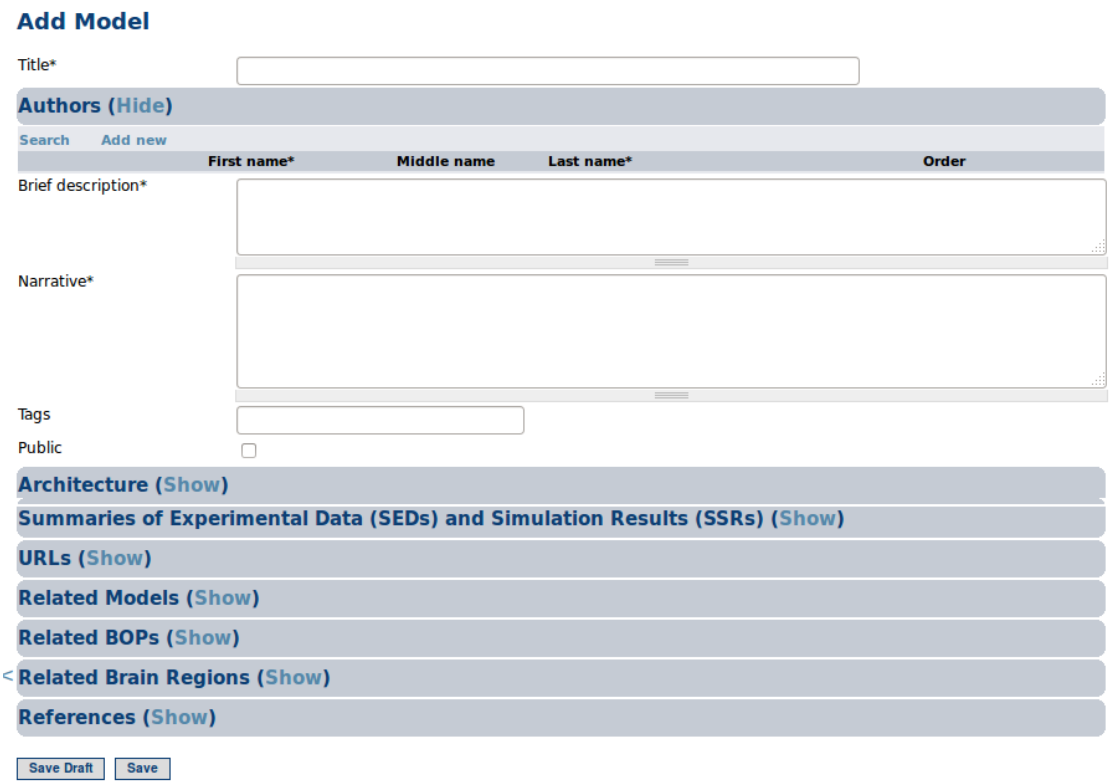


Figure 23: The Model Insert page.

First enter the title of the model entry in the *Title* field. If the model has a formal name such as FARS or MNS, enter the unabbreviated name followed by the abbreviation in parenthesis, if any. If the model does not have a formal name, it is acceptable to create one. Model names should not include the name of the author (it will be included in the next step).

Enter the names of the model authors (not necessarily you, the model entry author!). Click the "Search" link in the **Authors** section to first check if the authors already exist in the database. If not, click the "Add new" link and enter the author's name in the textboxes that appear. Multiple authors can be added, and their order can be adjusted by altering the value in the *Order* field that will appear next to each added author.

Enter a brief description of the model in the *Brief description* field. This should be descriptive enough so that another user can understand what the model addresses from the search results, but not an exhaustive exposition. This will come later when the *Narrative* field is filled in under step 5. This should not be the abstract of the key paper, but rather should summarize key points of the Narrative.

Insert keywords for the model in the *Tags* field. This should be a comma-delimited list with multi-word tags enclosed in quotes. Where possible, use existing tags from the **Model tag cloud** sidebar on the left.

Click on the “Show” link next to the **Architecture** section to expand it. Since the model may be hierarchical, there may be one or more diagrams. One will present the overall structure of the Model. In some cases, a diagram will explicitly show not only the immediate submodules but also the further decomposition of some of these. In other cases, a separate diagram will show how a module given as a unit of an earlier diagram is expanded to reveal the structure of its submodules. In the **Diagrams** subsection, upload system overview figures - figures that show the entire model (figures relating to a specific submodule or simulation results will be uploaded later), along with a descriptive caption. This should briefly mention all the modules seen in the diagram and how the interactions between them contribute to the function of the model. If a module is documented in a separate diagram within the current Model entry, we briefly describe its role in the present diagram, then add “See Diagram entry below for further details.”

The following (Inputs, Outputs, States, SubModules) table is to be repeated both for the overall diagram considered as a single module, and for each module that occurs within the diagram. In general, the state of a module comprises the state of all the submodules which comprise it. It is thus a matter of judgment by the collator whether the state of a module whose decomposition is presented should be described or left implicit. The idea is to describe these entities in terms that would make sense to an experimentalist, or someone trying to understand “how the model works”, omitting details that would be documented in the code for the model. In entering a model in BODB, it will be a matter of judgment to decide which data are essential to understanding the model and which can be left to the documentation (see the following comments under “Narrative”). In the **Inputs**, **Outputs**, and **States** subsections, enter the inputs and outputs of the entire model, and the top-level state variables, respectively. In the **Submodules** subsection enter the name and description of top-level submodules (those with no parent modules except the model itself). To search for an existing submodule (one that may be used in another model, for example), click on the “Search” link in the **Submodules** subsection, or click “Add new” to add a new submodule.

Click on the “Show” link next to the **References** section to expand it. Click the “Search” link to search for existing references in the database that describe the model. This is recommended since on the reference search page there is an option to search and import from Pubmed if the reference is not found in the BODB database. Otherwise click the “Add new” link to add a new reference.

Click the “Save Draft” button at the bottom of the Model Insert page to save the entry as a draft. The Model View page will now be shown with the information you just inserted.

<u>Flesh out the model architecture</u>

In step 1, you entered only the title and brief description of just the top-level submodules. Now we will recursively go through each submodule and flesh out its description and enter sub-submodules.

From the Model View page, click on each submodule in the **Submodules** subsection of the **Architecture** section. This will bring you to the Module View page for that submodule. From there, click

the “Edit” button to show the Module Edit page, which is similar to the Model Insert page encountered in step 1 (Figure 24).

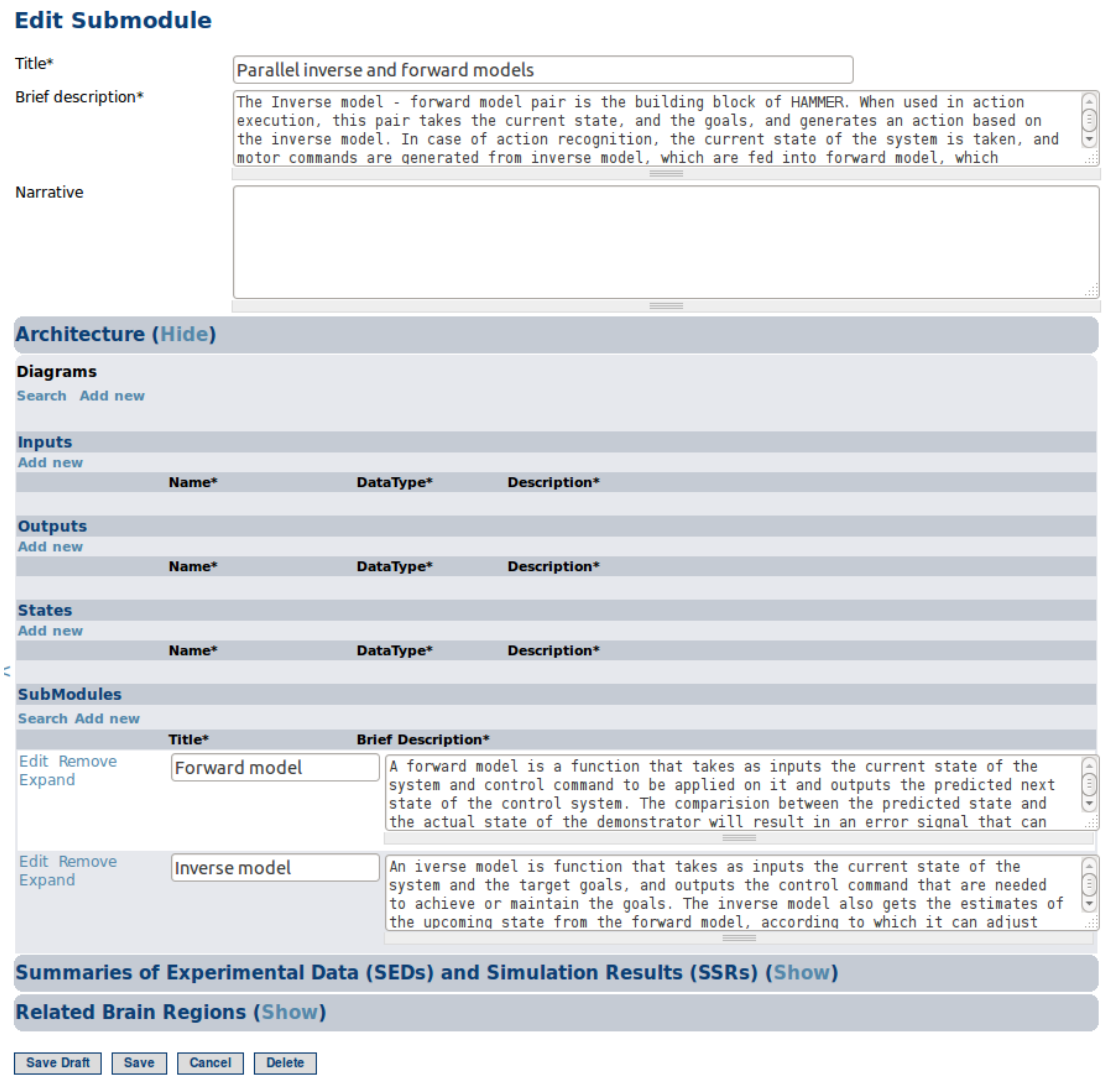


Figure 24: The Module Edit page.

Click on the “Show” link next to the **Architecture** section to expand it. In the **Diagrams** subsection, upload submodule-specific figures - figures that show zoom in on and show the operation of just this submodule, along with a descriptive caption. In the **Inputs**, **Outputs**, and **States** subsections, enter the inputs and outputs of this submodule, and its internal state variables, respectively. In the **Submodules** subsection enter the name and description of any sub-submodules. To search for an existing submodule (one that may be used in another model or module, for example), click on the “Search” link in the **Submodules** subsection, or click “Add new” to add a new submodule.

To add related BOPs and Brain Regions, click on the “Show” link next to the **Related Brain Regions** or **Related BOPs** sections to expand them (Figure 25). Click the “Search” link to search for and link to brain regions or BOPs that this submodule represents or simulates.

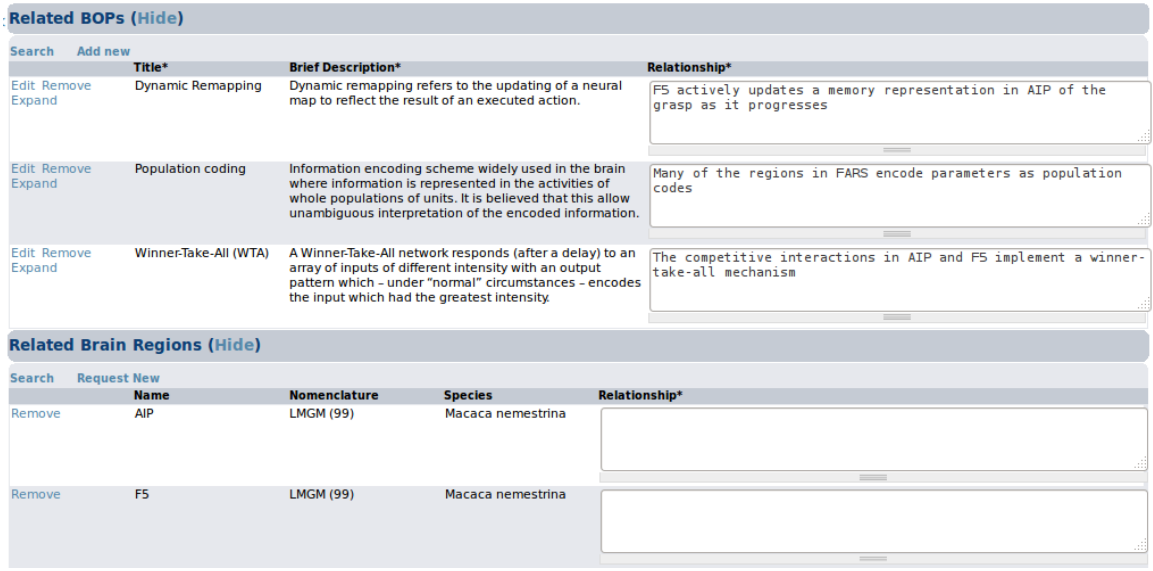


Figure 25: Related BOPs and Related Brain Regions sections on the Model Edit page

Click on the “Save” button at the bottom of the Module Edit page. Repeat this process recursively for any sub-submodules of this submodule.

Enter or link to SEDs and enter SSRs

This step involves entering new SEDs and SSRs for the model, or linking to existing ones. SEDs and SSRs should be linked to the lowest submodule in the hierarchy that encompasses them. So a SSR that only demonstrates the operation of a particular submodule should be linked to that submodule and not the model entry itself.

From the Model View or Module View page, click on the “Edit” button. From the Model Edit or Module Edit page that is then shown, click on the “Show” link next to the **Summaries of Experimental Data (SEDs) and Simulation Results (SSRs)** section (Figure 26).

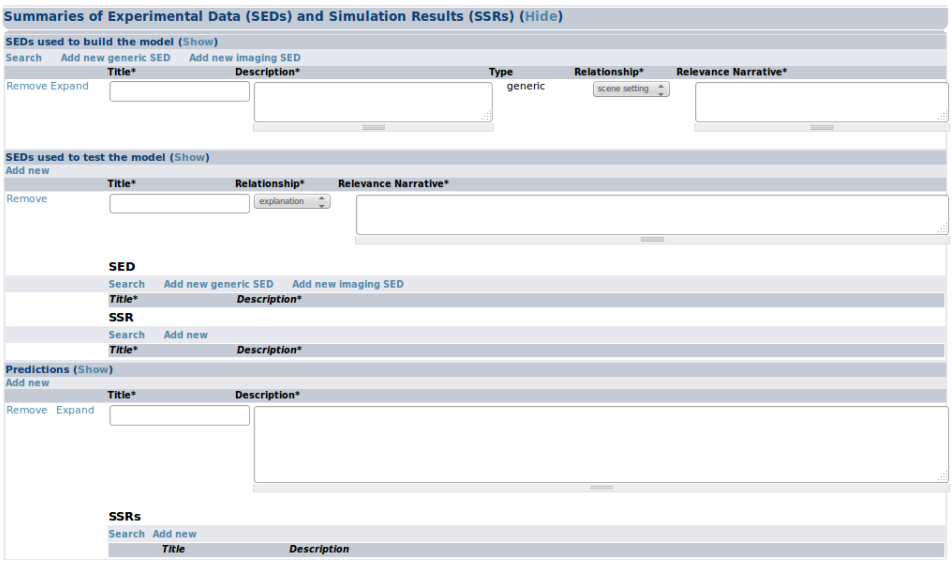


Figure 26: The SEDs and SSRs section of the Model Insert page.

SEDs for Model Building

Many SEDs are involved in thinking through the design of a Model, but only some – the "support" SEDs – enter into its actual design:

Scene setting: In the paper(s) describing a Model, there may be some empirical data that are cited but not actually used either in defining or testing the model. In very few cases, they may strengthen the Model Entry by setting the scene for the actual modeling but in most cases they can be omitted.

Support: SEDs that *support* some aspect of model design. The "Description" entry will link explicitly to part of the model description: e.g., an SED showing an inhibitory connection between 2 brain regions would support the decision to constrain the connection between Model modules representing those brain regions to be inhibitory. Note that documenting the relevance forces the collator to sharpen the presentation of the SED to ensure that it contains enough information to make clear how it constrains model design.

Each entry for such an SED will have three components: a Name, the Relationship to the model ("scene setting" or "support"), and a description that is detailed enough to show what the SED provides to the model.

In the **Building SEDs** subsection you can enter SEDs that enter set the scene for a model - i.e. were not directly used in its construction but are relevant, or support the model - where directly used in its construction.

Click on the "Search" link to search for and link to existing SEDs in the database. Once linked, select the type in the *Relationship* field (scene setting or support) and enter a description of how the SED relates to the model or module in the *Relevance Narrative* field.

Click on the "Add new generic SED" link to add a new generic SED entry. This will create a row of fields in the **Building SEDs** subsection to be filled out. Enter the title and brief description of the new SED

in the appropriate fields, select the type in the *Relationship* field (scene setting or support) and enter a description of how the SED relates to the model or module in the *Relevance Narrative* field. The other details of the SED will be fleshed out in step 4.

Click on the "Add new imaging SED" link to add a new neuroimaging SED entry. See the BODB reference manual, section x.x for instructions.

SEDs and SSRs for Model Testing

Other SEDs are *explained* by or *contradict* one or more SSRs of the model. As with the other entries here, this is *not* the SED entry *per se* – it is a linkage entry that documents the relevance of the SED to the model.

Explanation: SEDs that are *explained* by one or more SSRs of the model. The "Description" entry will link to specific model SSRs: e.g., an SSR showing that the firing of a certain group of neurons during a certain experimental protocol is matched by runs of the model. The entry needs to make clear at what level the SSR and SED match. Does the SSR yield a qualitative or quantitative fit for the data? Again, documenting the relevance forces the collator to sharpen the presentation of the SED (in its own, *separate* entry) to ensure that, e.g., it makes the qualitative results or quantitative results explicit to ground the SSR comparison.

Contradiction: the case where SSRs *contradict* the SED. This situation is subtle in 3 ways: (a) It is easy to set parameters in the model so that the simulations do not match the SED. So to document a contradiction something more is required. For example, it is a problem if the parameter settings used to claim success in explaining other SEDs do not explain this SED. Another case is where an SED shows the network settles into a limit cycle, but the model can be proved not to exhibit limit cycles. (b) However, note that the range of any model is limited – so one may decide that an apparently relevant SED does not in fact fall within the scope of the Model. (c) However, if one does conclude that there is a genuine contradiction, one should not only explain the contradiction, but also make clear what it implies for the future of the model – e.g., "this is a crucial flaw that invalidates the modeling;" versus "overall the model remains useful; however, the present contradiction poses several challenges for further development of the model, namely zzz, yyy, etc."

In the **Testing SEDs** subsection you can enter SEDs that are used to test the operation of the model, and the SSRs that they are compared to. The SSR can either explain or contradict the SED.

Click on the "Add new" link in the **Testing SEDs** subsection to add a new Testing SED entry. This will create a new sub-subsection for the entry. Enter the name of the SED in the *Title* field, select the type in the *Relationship* field (explanation or contradiction), and enter a description of how the SED relates to the SSR in the *Relevance Narrative* field.

Now an SED and SSR entry needs to be linked to the Testing SED.

SED

Click on the “Search” link in the **SED** sub-subsection to search for and link to existing SEDs in the database. Click on the “Add new generic SED” link in the **SED** sub-subsection to add a new generic SED entry. Enter the title and brief description of the new SED in the appropriate fields. The other details of the SED will be fleshed out in step 4.

Click on the “Add new imaging SED” link in the **SED** sub-subsection to add a new neuroimaging SED entry. See the section Brain Imaging SEDs, above, for instructions.

SSR

Click on the “Search” link in the **SSR** sub-subsection to search for and link to existing SSRs in the database. Click on the “Add new” link in the **SSR** sub-subsection to add a new SSR entry. Enter the title and brief description of the new SSR in the appropriate fields. The other details of the SSR will be fleshed out in step 4.

Predictions

Some simulation results may not link to SEDs in the literature (it may take quite some search in Entrez PubMed to feel reasonably confident about this claim) yet be so interesting that is worthwhile to recast the result as an empirical Prediction in the hope of encouraging someone to conduct the necessary experiment. It looks very similar to a generic SED. In the **Predictions** subsection you can enter SSRs and more general predictions that the model makes which haven’t yet been evaluated.

Click on the “Add new” link in the **Predictions** subsection to add a new prediction. Enter the title and description of the prediction in the appropriate fields. The description should outline what experimental protocol would be used, and summarize the predictions of what would be found using this protocol. A prediction entry can link to one or more SSRs. To link to an existing SSR, click on the “Search” link in the **SSRs** sub-subsection. Click on the “Add new” link in the **SSR** sub-subsection to add a new SSR entry. Enter the title and brief description of the new SSR in the appropriate fields. The other details of the SSR will be fleshed out in step 4. Finally click on the Save Draft button at the bottom of the Model Edit or Module Edit page.

Now navigate through the architecture hierarchy of the model entry and click on the link of each SED or SSR that you would like to add more details (figures, narrative, etc) for. From the SED View or SSR View page, click the “Edit” button at the bottom of the page to go to the SED Edit or SSR Edit page.

SED

From the SED Edit page (Figure 27) you can change the title or description, add a narrative describing the SED, enter tags, upload figures, and link to related brain regions and references.

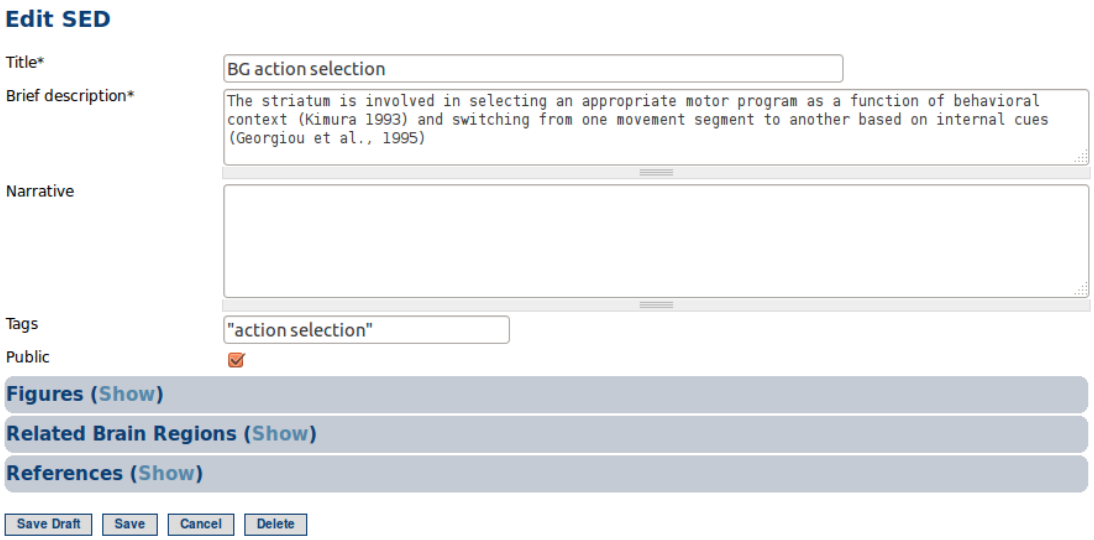


Figure 27: The Generic SED Edit page.

SSR

From the SSR Edit page (Figure 28) you can change the title or description, add a narrative describing the SSR, enter tags, upload figures, and link to references.

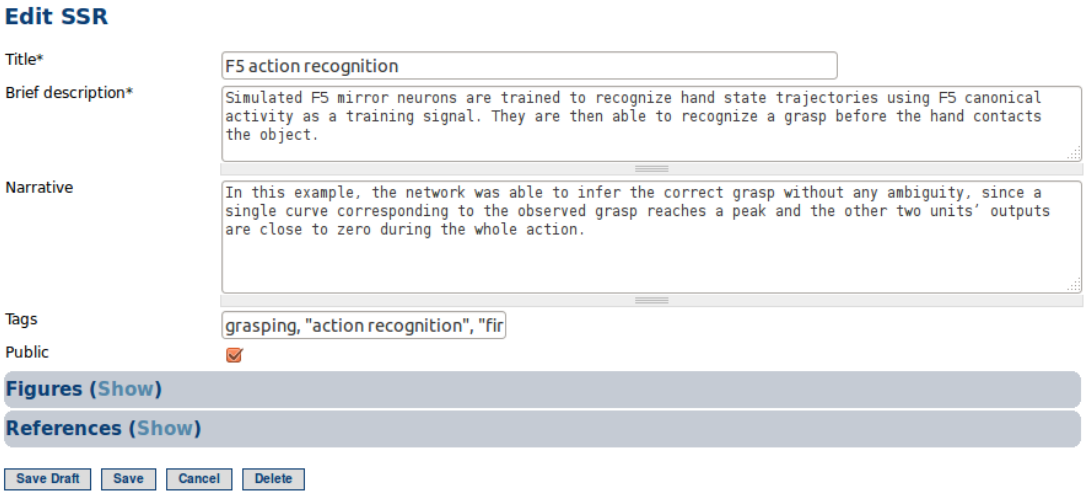


Figure 28: The SSR Edit page.

Finalize model entry

Enter a Narrative for the model describing the model architecture, operation, and brief overview of SEDs and SSRs. Enter narratives for submodules if desired. The Narrative reviews "how the model works" and "what the model does". It will thus refer *in summary fashion* to the diagrams, as well as the Summaries of Experimental Data (SEDs) and Simulation Results (SSRs) presented *and their relationships*.

The challenge here and in presenting the SEDs and SSRs is to be judicious in what you highlight and what you omit. The BODB entry is not meant to replace the article(s) which document the Model but rather to help the user assess the Model in relation to available empirical data and modeling goals.

Enter URLs for online resources such as model execution, documentation, description, and simulation results. (For example, this might tie into an entry in ModelDB.) The URLs to be added are:

- Description - The e-file for relevant papers or fuller description
- Implementation - A link to runnable code for the model for the model
- Documentation - Documentation of the code
- Simulation Results - Results linked to running the code

Add links to other models and BOPs in the **Related Models** and **Related BOPs** sections. Finally, click Save to finalize the entry.

Exporting BODB Entries

The bottom of Model, BOP, SED, and SSR View pages contains is a list of buttons (Figure 29). The **Edit** button will open the edit page for the entry, Delete will delete the entry, Select (or Unselect) will add or remove the entry to the workspace. Entries can be exported in PDF, RTF, or XML format. To export the entry, select the desired format, and click on the **Export** button.

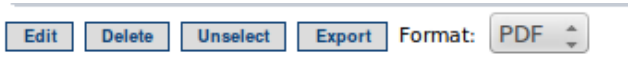


Figure 29: Buttons at the bottom of Model, BOP, SED, and SSR View pages.

References

Gleeson, P., Crook, S., Cannon, R. C., Hines, M. L., Billings, G. O., Farinella, M., Morse, T. M., Davison, A. P., Ray, S., Bhalla, U. S., Barnes, S. R., Dimitrova, Y. D. & Silver, R. A. (2010) NeuroML: a language for describing data driven models of neurons and networks with a high degree of biological detail. *PLoS Comput Biol 6*(6): e1000815.

Nordlie, E., Gewaltig, M. O. & Plesser, H. E. (2009) Towards reproducible descriptions of neuronal network models. *PLoS Comput Biol 5*(8): e1000456.