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The Brain Analysis Library of Spatial maps and Atlases (BALSA) Database

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Abstract

We report on a new neuroimaging database, BALSA, that is a repository for extensively analyzed neuroimaging datasets from humans and nonhuman primates. BALSA is organized into two distinct sections. BALSA Reference is a curated repository of reference data accurately mapped to brain atlas surfaces and volumes, including various types of anatomically and functionally derived spatial maps as well as brain connectivity. BALSA Studies is a repository of extensively analyzed neuroimaging and neuroanatomical datasets associated with specific published studies, as voluntarily submitted by authors. It is particularly well suited for sharing of neuroimaging data as displayed in published figures. Uploading and downloading of data to BALSA involves ‘scene’ files that replicate how datasets appear in Connectome Workbench visualization software. Altogether, BALSA offers efficient access to richly informative datasets that are related to but transcend the images available in scientific publications.

Keywords

Neuroimaging; neuroanatomy; connectivity; human; nonhuman primate

BALSA (Brain Analysis Library of Spatial maps and Atlases) is a new database dedicated to hosting extensively analyzed neuroimaging and neuroanatomical datasets. BALSA (<http://balsa.wustl.edu>) serves dual purposes, complementary to one another and to what is provided by existing neuroimaging databases (see *Relationship to Other Resources*).

BALSA Reference is a curated repository of reference data accurately mapped to brain atlas surfaces and volumes. It includes various types of anatomically and functionally derived spatial maps, such as cortical and subcortical parcellations, myelin maps, and retinotopic maps. It also includes connectivity data derived from retrograde tracers (macaque), plus tractography (from diffusion imaging) and resting-state functional connectivity (human and macaque) in a well-defined spatial coordinate system for each species. **BALSA Studies** will enable sharing of extensively analyzed neuroimaging and neuroanatomical datasets associated with published studies, as voluntarily submitted by authors. It is particularly well

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suited for sharing of neuroimaging data as displayed in published figures but can include many ancillary files and data representations.

Human Connectome Project data

A major source of data for both *BALSA Reference* and *BALSA Studies* will come from the Human Connectome Project (HCP; <http://humanconnectome.org>; Van Essen et al. 2013). The HCP has acquired, analyzed, and shared high quality multimodal neuroimaging data from a large number of healthy young adults using cutting-edge preprocessing methods (Glasser et al., 2013a) that include improved intersubject alignment based on a new Multimodal Surface Matching registration method (Robinson et al., 2014; Glasser et al., in revision). A growing number of studies are analyzing HCP data using the Connectome Workbench software platform (<http://www.humanconnectome.org/software/connectome-workbench.html>), which includes many features that capitalize on key aspects of the HCP data. This includes CIFTI ‘grayordinate’ datasets, which efficiently represent cortical surface vertices and subcortical gray matter voxels in a standardized format. Much of the extensively analyzed HCP data emerging from such studies is well suited for *BALSA*, in contrast to the unprocessed and minimally preprocessed HCP data from 1200 individual subjects that are better handled by the ConnectomeDB database (<http://connectomedb.org>; Marcus et al., 2013; Hodge et al., 2015).

The HCP data in *BALSA Reference* will include extensive group average data, including cortical surfaces and structural MRI volumes; and maps of cortical thickness, myelin, folding, sulcal depth, task-fMRI activations, and fMRI-based resting state networks (RSNs). These are derived from the “S900” datasets released in December, 2015. Another major data component involves a 180-area per hemisphere group average cortical parcellation (Glasser et al., in revision), plus a variety of datasets mapped to this parcellation (e.g., parcellated myelin maps and task-fMRI maps). A third component will include maps of data from hundreds of individual HCP subjects contained in composite files, enabling efficient cross-subject comparisons of individual-subject parcellations, myelin maps, task-fMRI maps, etc.

HCP data to be included in *BALSA Studies* will include extensively analyzed data from individuals and group averages associated with specific publications, including the aforementioned cortical parcellation study (Glasser et al., in revision). This includes detailed evidence supporting the delineation of cortical areal boundaries using the multimodal HCP data.

Nonhuman primate data

BALSA Reference includes MRI-based group average atlases of macaque - the MY19 (MacaqueYerkes19) atlas (Donahue et al., in review) - and chimpanzee - the CY29 (ChimpYerkes29) atlas. Both were generated in the Van Essen lab using preprocessing pipelines similar to those implemented for the HCP (Glasser et al., 2013a,b). The MY19 and CY29 atlases include cortical myelin maps and thickness maps that provide useful architectonic landmarks for both species. The macaque atlas also includes a variety of cortical parcellations mapped from the F99 atlas previously used in the Van Essen lab (Van

Essen and Dierker, 2007), plus quantitative retrograde tracer connectivity data from the Kennedy lab (Markov et al., 2013). **BALSA Studies** will include tractography data from postmortem Old World monkey brains (Donahue et al., in review).

‘Scene files’ for data upload, preview, download, and visualization

Many of the data files available in BALSA Reference and BALSA Studies are maximally informative when displayed in appropriate combinations, such as a cortical area parcellation displayed on an appropriate cortical surface mesh and overlaid on complementary data types (e.g., myelin maps and task-fMRI maps). For many published figures this can involve complex, multilayered, and multipanel displays. For these and other reasons, BALSA is organized around ‘scene files’ that facilitate efficient data upload, previewing, download, and internal data management. A scene file contains any number of individual scenes; each scene enables exact replication of the spatial configuration and data overlays used in a given data display (e.g., zooming, labeling, thresholding, color palettes, etc.), whether it is simple or highly complex and whether it represents a reference dataset or a precise replication of a published figure.

Scene files were originally implemented for Caret software and are extensively used in the SumsDB database (<http://sumsdb.wustl.edu>) (Van Essen et al., 2001; Dickson et al., 2001). BALSA capitalizes on numerous improvements in scene file capabilities that have been implemented for Connectome Workbench (version 1.1 and higher) (<http://www.humanconnectome.org/software/connectome-workbench.html>), including text annotations and multi-panel displays such as that illustrated in Figure 1 for four human cortical parcellation schemes mapped to the same HCP atlas surface. Other scenes in the same scene file show left and right hemisphere views of the individual parcellations with each cortical area (or RSN) having an attached label (i.e., that rotates/pans/zooms along with the surface) to facilitate easy identification of areas.

Data modalities, formats, and availability

BALSA became publicly accessible in the spring of 2016. Early content for BALSA Reference includes group average volume and surface data from the aforementioned MRI-based atlases of macaque, chimpanzee, and human brains. For BALSA Studies, early content will include studies from the Van Essen lab comparing tractography to tracers in the macaque (Donahue et al., in review) and the aforementioned human cortical parcellation based on HCP data (Glasser et al., in revision).

Imaging modalities supported by BALSA (i.e., with relevant metadata extracted as described below) include structural MRI (T1w, T2w scans), task-fMRI, resting-state fMRI, and diffusion imaging. Many derived data types will also be supported, including cortical surfaces, myelin maps and thickness maps, resting-state networks, and tractography results. In addition, the macaque datasets include quantitative retrograde tracer data at an area-to-area granularity.

Although BALSa is designed to store and manage neuroimaging data, extensive individual-subject behavioral and demographic data for all of the HCP datasets is available in the ConnectomeDB database (<https://db.humanconnectome.org/>).

Standard and nonstandard neuroimaging data formats

BALSa can handle a variety of standard neuroimaging data formats, including NIFTI volume data, GIFTI surface data, and CIFTI ‘grayordinate’ data (surface vertices plus volume voxels, Glasser et al., 2013a). BALSa also supports other Workbench file formats that have proven useful. Besides the aforementioned scene files, there are ‘border’ files, ‘foci’ files, and several tractography-related files that are not currently standardized across neuroimaging platforms.

File identifiers and citable URLs

Every dataset, scene, and individual data file uploaded to BALSa will be assigned a unique, permanent BALSa identifier (an “OID”) and a related unique URL. For example, each scene has a URL ([http://balsa.wustl.edu/\[OID\]](http://balsa.wustl.edu/[OID])), allowing it to be accessed directly (e.g., by including the URL in a publication, as in Fig. 1 above). In the converse direction, each scene in a scene file, and its corresponding webpage in BALSa, can include a PMID and/or doi that links it directly to a relevant publication. These bidirectional linkages emulate features previously introduced in SumsDB (e.g., Van Essen et al., 2012a,b).

Each file is also associated with file metadata that includes a “file path” (filename along with the directory structure used when the scene was uploaded) along with selected metadata extracted from the file contents (including provenance metadata that Connectome Workbench adds to output files); this information is stored in a unique “file metadata ID”, distinct from the file OID. When a file with exactly the same contents (based on hash comparisons) is uploaded as part of a different scene file, BALSa will use the original OID and data file (thus avoiding inefficient data storage and saving space) but will link to that file using the file’s file metadata ID associated with the new scene file.

Searchable metadata tags

Individual files in BALSa are associated with searchable metadata tags, in which each tag has a category and a value (as “category:value” pairs). Tags can be assigned automatically by a scanning process that uses “handles” (prespecified text strings) to scan the file name, file path, and within-file metadata whose fields are customized for each file type. Each scene aggregates the tags of all its supporting files, and each scene file aggregates the tags for its constituent scenes. Importantly, tags for both scenes and files can be edited (by curators or data providers), to handle cases where the scanning process erroneously assigned tags or failed to assign appropriate tags. Currently implemented categories include: species, modality, stereotaxic space (based on the atlas template), volume registration method, surface geographic convention (e.g., HCP’s Conte69_fs_LR, FreeSurfer’s fsaverage, or macaque MY19 or F99), surface resolution (e.g., HCP’s 164k or 32k meshes), parcellation

(e.g., HCP_MMP1.0); we anticipate incorporating additional categories as the diversity of uploaded datasets grows and user feedback is obtained regarding what is most useful.

Data Curation

The BALSAs upload process requires that each data submitter set up an account and provide contact information as well as essential information about the uploaded dataset. This includes specifying any constraints on data sharing (e.g., HCP Open or Restricted Access Data Use Terms) and also providing an assurance that any protected health information (PHI) has been redacted from any human data. Once an archive is uploaded and processed in BALSAs, an automatic notification will be sent to the BALSAs curation team in the Van Essen lab. Curation of submitted archives will include technical checks to ensure that uploaded files are in the accepted formats and that scenes can be properly displayed, are associated with studies that the submitter reports to be under review or published, and are compatible with the stipulated data sharing constraints. BALSAs curators will contact the data provider and resolve issues as needed to address issues or concerns. Uploaded archives will be kept private pending curation, publication of the associated manuscript, and author permission.

Navigating the BALSAs website

The BALSAs website includes several features for easy navigation. The home page (Fig. 2) includes a large section showing previews of currently available scene files. Each preview displays one scene within the scene file; datasets containing multiple scenes can be quickly previewed using a carousel option (arrows in each preview). Checkboxes enable rapid selection of Reference, Studies, or both data types. The “Add Filter” button enables filtering by tags or handles within each of the available metadata tag categories (see above). (BALSAs does not currently include an API that would enable machine-based queries (e.g., REST calls), but this may be incorporated in the future.)

Each preview includes the scene name immediately below the image, the scene file immediately above, and the dataset name immediately above that. Each of these names provides active links to extensive additional information. For example, clicking on the scene name brings up a window with additional information (e.g., the scene ‘description’ plus the associated tags). The scene file and its contents can be immediately downloaded using the Download button (or “Login to Download” button when Data Use Terms apply – see below).

Clicking on the “Supporting Files” button in a scene description page lists all of the files contained in that scene. Selecting a file from that list displays a page containing file-specific information and an option to download just that file. The “see all scenes using this file” displays previews of all scenes that contain (but don’t necessarily display) the selected file (based on the BALSAs file OID, not just the name of the file).

Data access and security

BALSAs is accessible without restriction for previewing of scene thumbnail images and browsing of the data files that are publicly released. For some studies (e.g., some macaque and chimpanzee datasets), there will be no additional constraints on data access (though

anyone who downloads such data will be encouraged to obtain a BALSAs user account, which will provide the option of being notified of updates to datasets the user chooses). Most HCP neuroimaging data will be accessible using the Open Access Data Use terms that can be read by pressing the Data Use Terms button. Investigators who have already agreed to HCP Data Use Terms will not need to reapply. For published studies that involve HCP Restricted Data Elements (e.g., family structure, handedness), users will need approved HCP Restricted Access (<http://humanconnectome.org/data/data-use-terms/restricted-access.html>). For other datasets, data submitters will be able to stipulate project-specific data use terms.

For datasets associated with data use terms, the Download button is replaced by a “Login to Download” button, which opens the login/register form appropriate for that dataset. If the user has not agreed to the relevant Data Use Terms, an option to initiate that process will be provided.

Version control

We plan to implement a process to allow problematic data files in BALSAs to be removed and replaced (for example, if the file is corrupted). A file marked as “removed” will still exist in the database, but will be ignored by standard searches, queries, and downloads, and it will be identified as “removed” in the list of supporting files for each scene that contained it). If a removed file is replaced with a different version (e.g., to correct an error), the new version will be assigned a new OID. However, if the path (including the file name) is unchanged, the scenes in which it was displayed will be updated. File owners will be able to initiate a request for file removal/replacement, but final action will require approval by a BALSAs curator to ensure that it is not disruptive for other scenes and datasets that use the file in question. If an uploaded file is discovered to inadvertently contain PHI (Protected Health Information), curators will immediately place the file and associated scenes in a quarantine (non-downloadable) state until the situation is resolved. We plan to introduce a history page for handling reference and study datasets that will be accessible to owners and curators, and will provide direct links to removed files, information on when they were removed or replaced, and the option to reverse the removal of a file.

For datasets in which data is withdrawn, revised or added to, we plan to alert investigators who have downloaded the data and have a BALSAs user account. This information will also be shared on a BALSAs wiki page. We plan to establish a BALSAs mailing list that provides an electronic general forum for addressing practical issues relating to BALSAs datasets.

Tracking data downloads

For each data download, we will track which archives were downloaded, along with the date/time, IP address, and username (if logged in), similar to what was previously implemented for SumsDB. This detailed information will only be available to BALSAs administrators, and will provide useful statistics and information that may help improve database design and performance. We also plan to make anonymized summary statistics of downloads publicly available and may also share (on request) more specific usage information to data providers concerning the data they uploaded.

Data download and local storage

Users browsing BALSA will be able to browse and select specific datasets for download, or to download an entire BALSA Reference dataset for each species of interest, along with automatic notification of atlas updates to those having accounts. Future plans call for BALSA access through Connectome Workbench to cache any used files so that they can be accessed repeatedly without downloading again, with this cache referred to as BALSA Local. If the user is offline, they will still be able to explore the files and scenes in BALSA Local with Connectome Workbench, with some functionality similar to online BALSA available.

Contributing data to BALSA

Investigators are welcome to contribute new data to BALSA Studies, subject to several constraints. (1) In the current instantiation, data must be uploaded to BALSA by way of scene files that can be read by Connectome Workbench, as this is central to the data upload, download, and curation mechanisms. Importantly, this does not require that the primary data analyses have been carried out in Workbench. For example, analyses carried out using other widely used platforms (e.g., FreeSurfer, AFNI/SUMA, FSL) and saved in NIFTI/GIFTI/CIFTI format can be viewed in Workbench, saved as appropriate scene files, and then uploaded to BALSA. (2) Investigators will be strongly encouraged to provide data in a standard surface and volume based atlas framework that maximizes compatibility with BALSA Reference datasets and other BALSA Studies datasets. A future version of the Connectome Workbench 'wb_view' user interface will provide an option to directly upload scene files to BALSA, in order to facilitate uploading of datasets once they are finalized.

We hope that BALSA will become an attractive repository not only for HCP-derived datasets, but for other projects as well, particularly from a growing number of non-HCP neuroimaging projects that will use "HCP-style" data acquisition and analysis approaches. This applies to investigator-initiated projects in individual laboratories as well as large-scale endeavors such as the HCP Lifespan projects and the Connectomes Related to Human Disease program. Users who carry out advanced analyses using Connectome Workbench should find it easy to generate scene files that are uploaded to BALSA. Those who carry out analyses on other platforms will need to carry out final stages of scene generation in Connectome Workbench.

For inclusion in BALSA Reference, each dataset should meet reasonable criteria for being generally useful reference data (e.g., parcellations or population-average maps of task activations). We will lean on the side of openness and will consult with an established BALSA Advisory Committee (see below) in the event of difficult judgment calls. Another consideration will be consistent alignment with other BALSA Reference atlas datasets, given the importance of hosting datasets that are maximally comparable to one another (e.g., comparing parcellation schemes). For datasets analyzed by registration to a different atlas template (e.g., FreeSurfer's fsaverage instead of an HCP MSM template), guidance will be provided on achieving alignment (e.g., by using standardized registered spheres using command-line tools in Connectome Workbench).

BALSA Advisory Committee

A group of external advisors has agreed to provide feedback and guidance, and to help set policies for data submission and curation that best serve the scientific community. This committee will have a virtual (online) meeting at least twice per year (starting in the spring of 2016), plus email exchanges as needed. This committee includes representation by developers of major brain-mapping platforms (e.g., FreeSurfer and FSL).

Relationship to other resources

A growing number of databases have emerged in recent years relating to different types and stages of neuroimaging data analysis. Most of them have little or no overlap in functionality with BALSA. Some, including the aforementioned ConnectomeDB, focus on unprocessed or minimally processed data rather than extensively processed spatial maps. Others focus on even more highly redacted data than BALSA, such as 3D stereotaxic coordinates (e.g., the BrainMap and Anima database; Fox et al., 2014; Reid et al., 2016).

Perhaps the closest in spirit to BALSA is Neurovault (Gorgolewski et al., 2016; <http://neurovault.org>), a repository where researchers can publicly store and share unthresholded statistical maps, parcellations, and atlases generated by MRI and PET studies. Neurovault currently displays only volumetric data, not surface or CIFTI data and hence is largely complementary to BALSA. If investigators submit data from the same study to BALSA and to Neurovault (or another analogous repository) it should be relatively straightforward to incorporate links that make such ‘multiple listings’ evident to those querying either resource.

At a broader level, neuroimaging is a relative newcomer in the realm of large-scale databases. There is much to learn about the design, management, and federation of database and related resources from the many successes in other fields of biology (https://en.wikipedia.org/wiki/List_of_biological_databases) and even in nonbiological realms such as earth sciences (<http://www.pangaea.de>) and astronomy (https://en.wikipedia.org/wiki/Category:Astronomical_databases).

Long-term plans

The BALSA database is hosted on servers managed by the Neuroinformatics Research Group headed by Dan Marcus at Washington University and will be on the same network as HCP’s ConnectomeDB. BALSA is currently supported by an NIMH grant to the Van Essen lab through 2019. We plan to generate a tutorial that guides users through various aspects of BALSA usage and will also update the current Connectome Workbench tutorial documentation to reflect its closer integration with BALSA.

In summary, recent years have seen dramatic advances in the neuroinformatics infrastructure that supports large scale neuroimaging projects that share unprocessed and/or moderately processed data. Resources that enable investigators to readily share their extensively processed data associated with published studies have been lacking. BALSA aims to fill an important niche in this arena.

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Highlights

- BALSAs is a new database for sharing extensively analyzed neuroimaging data.
- BALSAs Reference includes data mapped to human and nonhuman primate atlases.
- BALSAs Studies includes datasets associated with specific published studies.
- BALSAs offers efficient access to richly informative neuroimaging data.

Figure 1.

Example scene generated and saved in Connectome Workbench, showing four published human cortical parcellation schemes mapped to the fs_LR atlas mesh and displayed on the HCP S900 group average inflated atlas surface. Note that the text annotations are incorporated into the scene file itself (i.e., a separate application was not needed for annotation). Connectome Workbench version 1.1 or higher is needed to view scene annotations in the downloaded data. [Scene file available at [http://balsa.wustl.edu/\[OID\]](http://balsa.wustl.edu/[OID]) *ADD SceneID*]

Figure 2. Balsa home page (March, 2015), including descriptive text, options for search and filtering of available files, and previews of available scene files meeting search criteria.