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EBRAINS Data Descriptor

TITLE*

Selected 1 micron scans of BigBrain histological sections (v1.0)

AUTHORS*

Christian Schiffer^{1,2}, Claude Lepage³, Mona Omidyeganeh^{3,4}, Hartmut Mohlberg¹, Andrea Brandstetter¹, Sebastian Bludau¹, Katja Heuer⁵, Paule-Joanne Toussaint³, Susanne Wenzel^{1,2}, Timo Dickscheid^{1,2,6}, Alan C Evans³, and Katrin Amunts^{1,7}

AFFILIATIONS*

1. Institute of Neuroscience and Medicine (INM-1), Forschungszentrum Jülich, Germany
2. Helmholtz AI, Forschungszentrum Jülich, Germany
3. McGill Centre for Integrative Neuroscience (MCIN), McGill University
4. Digital Technologies at National Research Council Canada (NRC), Canada
5. Institut Pasteur, Paris, France
6. Institute of Computer Science, Heinrich-Heine-University Düsseldorf, Germany
7. Cécile and Oscar Vogt Institute for Brain Research, University Hospital Düsseldorf, Heinrich-Heine University, Düsseldorf, Germany

corresponding author(s): Christian Schiffer (c.schiffer@fz-juelich.de)

ABSTRACT*

This dataset contains selected microscopic scans of tissue sections at 1 micron in-plane resolution from the BigBrain, a whole brain 3D reconstruction of a human postmortem brain. Each image is provided both in its original histological space, as well as aligned to the corresponding coronal section of the 3D-reconstructed BigBrain space. The images were acquired by rescanning the original histological sections of the BigBrain model at an in-plane resolution of 1 μ m. The sections were aligned to their corresponding coronal planes in the 20 μ m 3D-reconstructed BigBrain space using 2D non-linear transformations, and allow to identify microscopic features at the cellular level due to their increased resolution.

Version Specification:

This dataset contains 145 microscopic scans at 1 micron in-plane resolution of tissue sections from the BigBrain.

The aligned images can also be viewed in the [siibra-explorer](#) (currently) using a plugin: Please go to the [siibra-explorer \(space: BigBrain, parcellation maps: Isocortex\)](#), click the menu icon on top right and select '1 μ m viewer'. A new window appears, where available sections can be selected. The according 1 micron section is displayed in coronal view on top left. You can navigate through the section by moving the image with your mouse. Do not move horizontal or sagittal views, you would leave the coronal view of the 1micron section. You can zoom in with your mouse wheel. The slider in the plugin window allows to change opacity of the 1 micron section to overlay the 1 micron with the according 20 micron section. The plugin will be added as core functionality to the siibra-explorer soon.

BACKGROUND & SUMMARY

Analysing the human brain based on digitized series of histological sections is considered the gold standard for mapping cytoarchitectonic brain areas, which are important indicators for functional modules. The first 3D reconstruction of an entire human brain from histology was generated at 20 μ m isotropic resolution and shared as 'BigBrain' (Amunts *et al.*, 2013). This dataset was created through rescanning of the original histological sections of the BigBrain model at an in-plane resolution of 1 μ m and subsequent alignment to the 20 μ m 3D BigBrain space and with this provides now an even higher resolution offering new opportunities to locate and characterise individual neurons as well as to map their distribution across cortical layers, areas and subcortical nuclei.

METHODS*

Data acquisition

Cell-body stained histological sections (20 μ m thickness) of the original BigBrain were re-scanned with a whole slide scanner (Tissue Scope, Huron Technologies, Inc.) at an in-plane resolution of 1 μ m. As described in detail in Amunts *et al.* (2013), sections were embedded in paraffin and stained using a modified silver staining. Consequently, the images show cell bodies with a strong dark contrast.

As the sections were rescanned more than 10 years after their histological preparations, only a subset is still of sufficient quality, e.g., free of crystallisation artifacts. Therefore, the sections were visually inspected using the Web tool MicroDraw (<https://microdraw.pasteur.fr>), and 145 sections with high quality were selected, evenly distributed at distances of about 1 mm in coronal direction, to be released in this dataset.

Non-linear registration of 1 μ m Histology Sections into 3D 20 μ m BigBrain Space

For each selected section, a transformation (affine + non-linear) was computed from the 1 μ m section, resampled at 20 μ m, to the 20 μ m unaligned repaired section of the original BigBrain, then concatenated to the known non-linear deformation field from the repaired 20 μ m section to its final position in the reconstructed 3D volume. The application of the global transformation at 1 μ m is made possible by breaking up the input image into small tiles of manageable size to avoid computational memory bottlenecks during resampling of the tiles. For efficiency, only tiles contained within the tissue mask are resampled. The final tiles are recombined into a single image after transformation (Omidyeganeh 2020). The operations are carried out using the *minctools* (<http://bic-mni.github.io/>). Finally, images were converted to the BigTiff image format.

The next version of this dataset will provide optical balanced images.

TECHNICAL VALIDATION*

The quality of selected sections was visually checked by trained neuroanatomists using MicroDraw, and verified using a 4-eyes principle.

USAGE NOTES*

The microscopic images of raw and aligned brain sections are provided as multipage BigTiff files. The pages of each file correspond to multiple resolutions (1 μ m, 4 μ m, 16 μ m, 64 μ m) of a specific image. Raw and aligned images are stored in folders "raw" and "aligned", respectively. The file format is identical for both raw and aligned images.

Images can be visualised with any image viewer that is compatible with the BigTiff image format, for example FIJI (<https://fiji.sc>). Sufficient computational resources (e.g., memory) are required to visualise images at full resolution. We recommend using the provided lower resolution images for easier visual inspection.

Images can be analysed programmatically using BigTiff-compatible software libraries, for example **pytiff** (<https://github.com/FZJ-INM1-BDA/pytiff>) or **libtiff** (<http://www.libtiff.org/>). Images are tiled with a square tile size of 256 pixels, enabling efficient extraction of rectangular chunks.

The aligned images can also be viewed in the [siibra-explorer](#).

SPATIAL ANCHORING:

The "metadata" folder contains affine transformation matrices describing the relationship between the pixel space of each aligned section and the 3D BigBrain template space. Affine matrices are provided as 4x4 transformation matrices. Given a pixel coordinate tuple **x** and **y** (column and row, starting at zero) defined on a section **s**, the corresponding location in the 3D BigBrain space can be obtained as demonstrated by the following python-like pseudo-code:

```
function pixel_to_bigbrain(x, y, s):
    # load transformation matrix for section.
    matrix = load_matrix(section=s)
    # create pixel position as homogeneous coordinate vector.
    # x and y specify a pixel coordinate on the image with section
    number s.
    # x is the column index, y is the row index, starting in the top
    left corner of the image.
    # indices start at zero.
    pixel_pos = (x, 0, y, 1)
    # apply transformation
    pixel_3d = matmul(matrix, pixel_pos)
    # return coordinate part
    return pixel_3d[:3]
```

DATA RECORDS*

In the repository the data are stored in the following structure

repository-root/

EBRAINS-DataDescriptor_BigBrain_1micron_sections.pdf [contains a short description of the dataset]

Licence-CC-BY-NC-SA.pdf

raw/

B20_XXXX.tif [original microscopic image of section XXXX before alignment in BigTiff format]

aligned/

B20_XXXX.tif [microscopic image of section XXXX aligned to BigBrain template space in BigTiff format]

B20_XXXX_affine.json [4x4 affine transformation matrices between pixel space of aligned images and BigBrain template space]

CODE AVAILABILITY*

The alignment of 1 μm sections to the 20 μm BigBrain space was performed using an in-house workflow which utilised the *minctools*. The workflow is still under development and will be released once it is ready for general usage.

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Pavel Chervakov and Xiao Gui (both INM-1) built and generally maintain the infrastructure to provide interactive online visualisation of the provided dataset.

Roberto Toro leads the development and maintenance of MicroDraw which provides a Web interface able to display and annotate data at the highest resolution.

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Author contributions

Christian Schiffer: Data anchoring, quality control and review

Dr. Claude Lepage: Methods development and performing the non-linear spatial alignment

Dr. Mona Omidyeganeh: Methods development non-linear spatial alignment

Hartmut Mohlberg: Data provision, quality control

Dr. Sebastian Bludau, Andrea Brandstetter: Quality control and review

Katja Heuer: Co-develops MicroDraw, quality control and review

Dr. Paule-Joanne Toussaint: Coordination, quality control and review

Dr. Susanne Wenzel: Coordination

Prof. Dr. Timo Dickscheid: Coordination and supervision
Prof. Dr. Alan C Evans: Funding and supervision
Prof. Dr. Katrin Amunts: Funding, data acquisition, and supervision

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