European Journal of Geography Volume 8, Number 1:6 - 31, February 2017

THE BRAIN AS A MULTI-LAYERED MAP. SCALES AND REFERENCE POINTS FOR PATTERN RECOGNITION IN NEUROIMAGING

Margarita Zaleshina
Moscow Institute of Physics and Technology, Moscow, Russia
zaleshina@gmail.com

Alexander Zaleshin
Moscow Institute of Physics and Technology, Moscow, Russia
terbiosorg@gmail.com

Abstract

In this paper, we provide an overview of brain mapping in neuroscience and describe the application of spatial data processing techniques to represent the brain as a multi-layered map.Anatomical reference points (landmarks) are determined from the topological properties of the brain, including the shapes of sulci, gyri, and fissures. Functional reference points are calculated by measured parameters of brain activity. Linking experimental results with spatial and temporal reference points is a necessary step for performing a comparative analysis of heterogeneous data regarding brain structures and activity. Using reference points helps define coordinate systems and scales, highlight points of interest and regions of interest, create templates, and classify data. The paper shows that spatial analysis is a convenient approach to pattern recognition in neuroimaging. We also discuss the role of extrinsic behavior landmark stimuli and intrinsic brain structural elements such as place cells and grid cells in navigation tasks.

Keywords*: Brain mapping, neuroimaging, pattern recognition, positioning systems in the brain.*

1. INTRODUCTION

The brain can be represented as a spatially distributed multi-scale and multi-level structure in which continuous dynamic processes occur.

Two main blocks of spatial data processing tasks in neuroscience are shown in Figure 1. Studies of brain mapping generally focus on addressing the question, “What is the space of the brain?” (Figure 1A). Thus, analyses of the brain’s structure at different levels – ranging from individual cells to the entire brain’s architecture – are practiced by scientific researchers as well as by specialists in the fields of medicine and neuroradiology.

On the other hand, studies of brain activity during orientation in space generally focus on addressing the question, “How does the brain navigate in space?” (Figure 1B). This block of study includes the investigation of spatial perception, navigation, and the brain’s positioning functions.

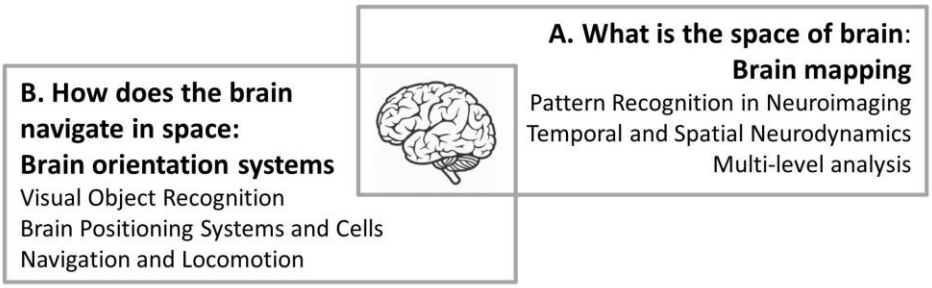

Figure 1. The two main blocks of spatial data processing tasks in neuroscience. Block A addresses the question, "What is the space of the brain?" Block B addresses the question, "How does the brain navigate in space?"

The remaining sections in this paper are organized as follows:

Section 2 provides a brief description of the subject areas and common interests between brain mapping and geomapping. Section 3 provides an overview of the techniques used in brain mapping. Section 4 describes how to use the scale and reference points for analyzing multi-level data in brain mapping. Section 5 contains the report about pattern recognition in neuroradiology with application of geographic information system technologies. Section 6 discusses the perception of spatial information and positioning systems in the brain. Finally, we provide conclusions in Section 7. Additional information about the standards and software, which typically applied in brain mapping, is contained in the Appendix.

2. COMPARISON OF SPATIAL DATA PROCESSING BETWEEN NEURO-INFORMATICS AND GEOINFORMATICS

Although geoinformatics and neuroinformatics deal with materially different objects, the tools for spatial data processing are based on certainly similar methods and are designed to solve similar problems.

Integrated vector-and-raster models, which are implemented in geographical information systems (GIS), provides a representation of the outer and inner surfaces of anatomical structures and enables the identification of anatomical structures and spatial analyses (Barbeito et al., 2015). Brain-mapping software and GIS technologies use a common set of instruments, including measure of distances and areas, coordinate representation system, multi-layer datasets, metadata storing, and metadata sharing.

GIS technologies can be valuable in brain mapping due to the processing of raster data and vector data. GIS technologies are also applied in the collection and analysis of heterogeneous spatial data, organization, and publication of maps. Moreover, GIS tools are applied for tasks that involve a large number of images. Suitable applications have already been developed in advanced geographic information systems, such as ArcGIS: (http://www.esri.com/software/arcgis) and QGIS (http://www.qgis.org).

Brain mapping techniques would help GIS cartographers analyze dynamic processes. Due to the relatively fast processes that occur in the brain, phenomena such as pacemakers and oscillations are often recorded and studied in neuroscience. However, similar phenomena can also be observed in the relatively slow dynamic processes that occur at the Earth's surface, for example in environmental studies. These similarities serve as an additional bridge between GIS and brain mapping. In both cases, the mapping techniques should be flexible with respect to the essential characteristics of the space, its connections, and its inherent dynamics.

To visualize similarities in mapping technologies, consider a typical brain map (an example of multi-layer dataset based on the Interactive Multiresolution Brain Atlas (Mikula

et al., 2007) is shown in Figure 2A), and compare this map with raster or vector map in a typical GIS (an example is shown in Figure 2B).

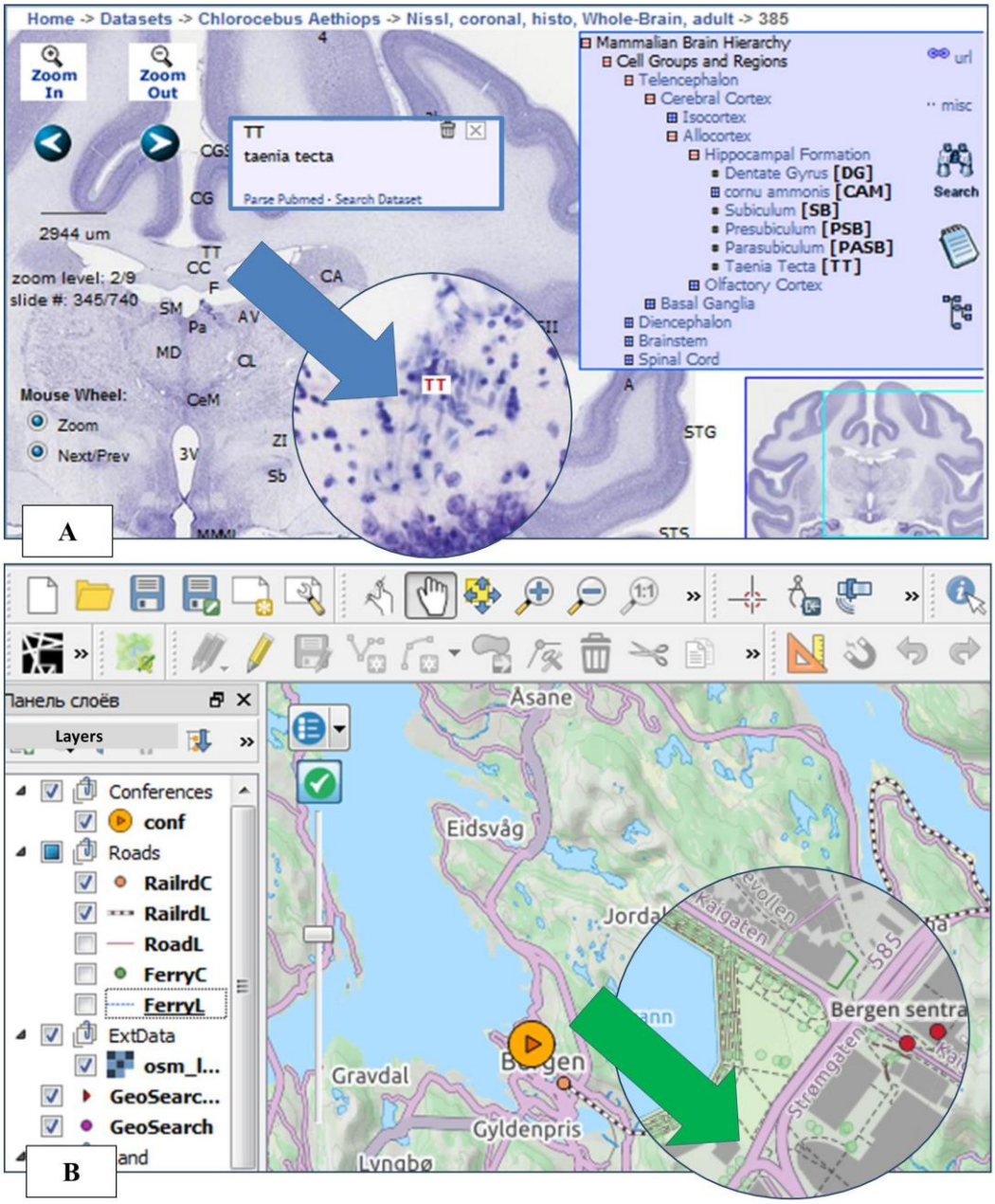

Figure 2. A. Multi-layered brain map of the grivet monkey *Chlorocebus aethiops*. Figure shows the map of brain slice at a wide scale, and zoomed part near the taenia tecta (TT) area. The individual layers are represented by functional brain units (reproduced from http://brainmaps.org). B. Multi-layered map in QGIS. Figure shows the terrain map at a wide scale, and zoomed part near the railway station.

Nowadays, location-specific geodata are provided in large quantities by both industrial equipment (for example, remote sensing devices) and personal media tools (for example, smartphones). Similar situation is occurring with respect to brain mapping, in which radiologists typically view hundreds – or even thousands – of images. For example, advanced multidetector computed tomography produces several thousand images during a single examination (Andriole et al., 2011).

Table **1** summarizes the similarities between brain mapping and GIS mapping.

Table 1. Comparison of subject areas between brain mapping and GIS mapping

Subject area	Brain mapping	GIS mapping
I. Primary data processing		
Selection of coordinate systems. Configuring sets of layers. Spatial measurements: calculation of geometrical parameters (length, area, volume). 2D/3D transformations. Vectorization. Spatial database. Data compression.	Primary data sources: Magnetic resonance imaging (MRI), functional magnetic resonance imaging (fMRI), single-photon emission computed tomography (SPECT/CT), electro-encephalography (EEG), magnetoencephalography (MEG), optogenetics.	Primary data sources: Remote sensing, land surveying.
II. Recognition and classification		
Finding of surface specific points and lines. Contouring. Generalization. Data classification.	Pattern recognition in neuroimaging.	Pattern recognition in geoimaging.
III. Multi-scale data integration		
Data standards.	Digital Imaging and Communications in Medicine (DICOM) standards (http://dicom.nema.org), DICOM Files, XML.	The Open Geospatial Consortium (OGC) standards (http://www.opengeospatial.org/standards), WMS, GML, KML, XML.
Combining data from different sources.	Brain atlases.	Geodata integration.
IV. Spatio-temporal processes and connectivity		
Dynamic processes and connectivity.	Area's connectivity. Brain activity.	Engineering communication. Urban planning. Ecology.
V. Positioning systems		
Orienteering by reference points. Wayfinding.	Place cells and grid cells. ROIs, POIs.	Natural or manmade landmarks. ROIs, POIs.
Navigation. Movement control.	Route selection. Visual object recognition. Locomotion.	Route selection. Logistics.

3. SPATIAL DATA PROCESSING IN BRAIN MAPPING

The basic mission in brain mapping can be summarized as follows (Frackowiak & Markram, 2015): the aim of cerebral cartography is to generate atlases that use anatomical frameworks to organize and convey spatially and temporally distributed functional information regarding the brain at all organizational levels ranging from genes to cognition and at all relevant spatial and temporal scales.

Thus, ideal brain atlas should provide a comprehensive multi-scale spatial representation of the brain at both the structural and functional levels.

3.1 Basic components and datasets

3.1.1 Neuroimaging data

Neuroimaging is used to collect and process images, thereby allowing researchers to visualize the structures and functional characteristics of the brain.

Tomography produces a series of brain images in the form of two-dimensional (2D) slices, allowing researchers to measure the brain's activity in response to external stimuli and to identify tumor-containing and/or diseased areas of the brain. Neuroradiologists obtain these original 2D slices, which are then could be converted into 3D data.

Digital Imaging and Communications in Medicine (DICOM, http://dicom.nema.org) is the current standard for handling, storing, printing, and transmitting medical imaging information.

MicroDicom (http://www.microdicom.com) is an application for the primary processing and preservation of medical images obtained in DICOM format. MicroDicom user interface is depicted in Figure 3.

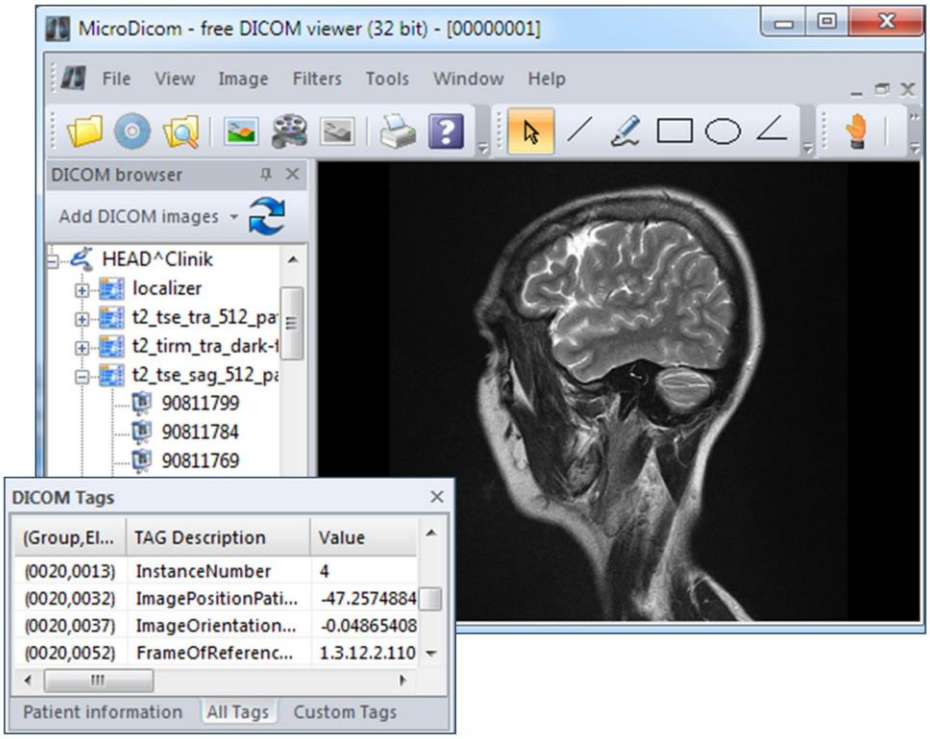

Figure 3. Data representation in MicroDicom.

3.1.2 Functional magnetic resonance imaging

Functional magnetic resonance imaging (fMRI) is a neuroimaging procedure using technology that measures brain activity by detecting changes associated with blood flow. FMRI provides information regarding the brain's functions with spatial reference for the brain's response.

Despite its advantages, fMRI has limited temporal resolution. Specifically, regions in which the blood oxygen level-dependent (BOLD) signals changes in fMRI may not necessarily correspond with regions of neural activity (Baillet et al., 2001).

3.1.3 Brain activity

Magnetoencephalography (MEG) and electroencephalography (EEG) provide a non-invasive measure of neural activity by measuring electromagnetic signals. In EEG, electrical potential differences are measured between pairs of "electrode – referent" placed on the scalp. The electrodes can be either glued directly to the skin at specific locations (for example, directly above cortical regions of interest) or they can be fitted in an elastic cap that can be placed easily over the top of the head, providing near-uniform coverage of the entire scalp. Because

the electrodes are placed on the surface of the head and not directly in the area being observed, the precise location of the source of activity should be determined by calculation.

Combining MEG and/or EEG with another methodologies allows researchers to better localize and separate various components in the brain's electrical responses (Baillet et al., 2001). Individual MEG and EEG source maps can be normalized to a common brain atlas, and statistical inference can be performed at the group level (Evans et al., 2012).

The recorded brain activity is typically characterized by distinct frequencies and spatial distributions, which depend on the various states of the brain (for example, sleep or wakefulness). The recorded signals are the result of superimposing the activity of large populations of neurons (neuronal ensembles). Because the number of signals per unit time is extremely large, EEG data is generally analyzed using established statistical methods.

A spatial-temporal representation of activity of neuronal ensemble can be described by oscillatory dynamics. Thus, oscillatory brain activity can be displayed as a map of wave distribution.

3.2 Data structures in brain mapping

3.2.1 Layered structures

Radiologists typically work with sets of images (two-dimensional slices) taken at intervals of few millimetres.

Subsequently, the sets of 2D projections can be arranged in a 3D representation. This is very similar to the construction of three-dimensional terrain model based on satellite imagery data (Figure 4).

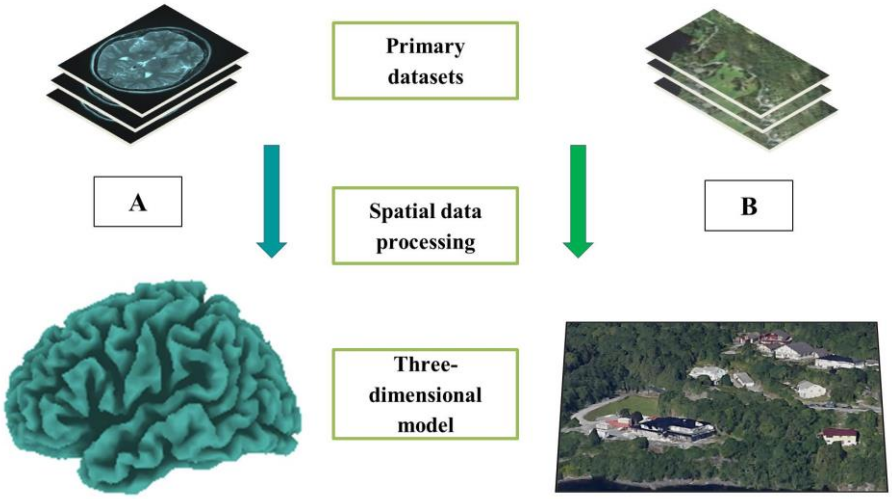

Figure 4. Spatial data processing: from sets of slides to the three-dimensional model in neuroimaging (A) and in satellite imagery (B) (map reproduced from https://www.google.com).

In practice, organization of layers in terms of separate functional areas is often provided, and is used in tasks of connectivity. For example, Robinson and Rolls reported the integration of layers in invariant visual object recognition (Robinson & Rolls, 2015).

3.2.2 Default mode network

The default mode network is a distinct brain feature that is activated when an individual engages in reflexion (Razi et al., 2015).

The concept of the default mode network was discussed by Simony et al. (Simony et al., 2016), in which the authors introduced the concept of inter-subject functional correlation, which isolates stimulus-dependent inter-region correlations between brains that are exposed to the same stimulus.

3.2.3 Multi-level structural and functional brain atlases

Multi-layer neuroimaging data obtained from various brain regions can be grouped within atlases. Multi-level atlases include numerous reports which combined into a single atlas.

One of the brain atlases is shown in Figure 5. This Brainnetome atlas (http://atlas.brainnetome.org/brainnetome.html) was generated in order to identify brain networks using multimodal neuroimaging techniques ranging from the highest-resolution scale (microtechniques, ultramicrotomy) to the most macroscopic scales (EEG, fMRI, and diffusion MRI), thereby allowing researchers to investigate the relationship between these scales (Fan et al., 2016).

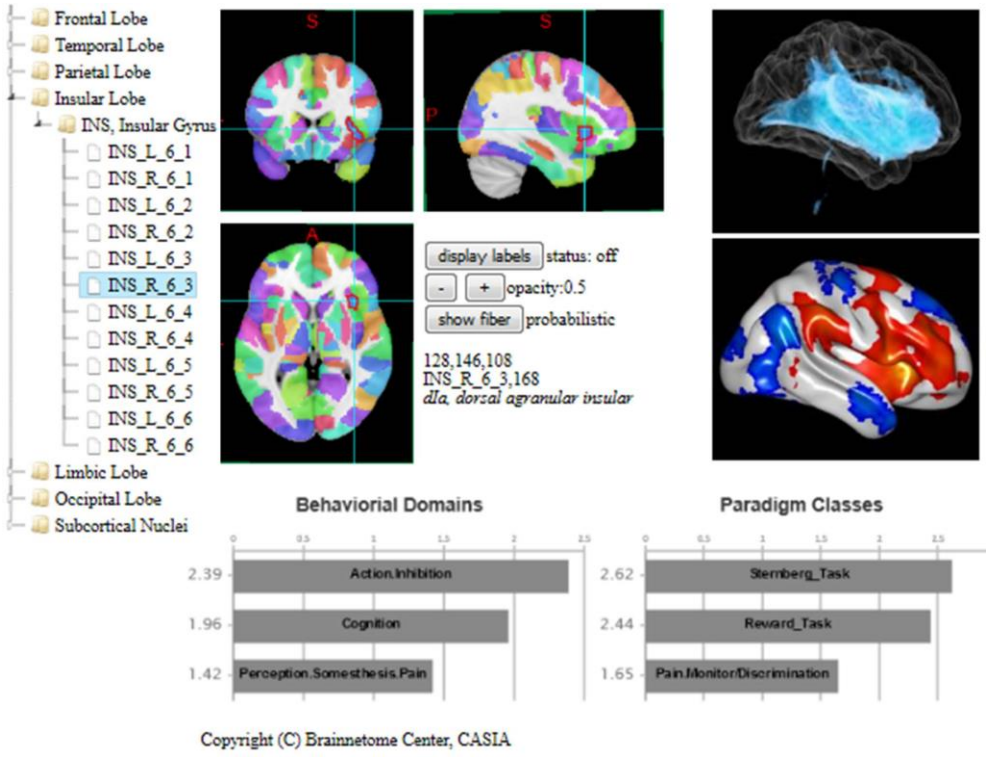

Figure 5. Brainnetome web-interface (reproduced from http://atlas.brainnetome.org/bnatlas.html).

Evans et al. summarized the brain atlases that are currently available (Evans et al., 2012). In review, they summarized the evolution of stereotaxic space, the creation of brain atlases, and future trends that can be expected in upcoming atlases.

3.3 Classification and parcellation of brain areas

Classifiers of brain areas are typically used for generating a brain atlas. For example, Glasser and colleagues delineated 180 areas in each hemisphere based on sharp changes in cortical architecture, function, connectivity, and/or topography (Glasser et al., 2016); in addition, they characterized 97 new areas by training a machine-learning classifier to recognize the multimodal "fingerprint" of each cortical area. The following criteria were used for parcellation: *I*) spatially overlapping gradient "ridges" between each pair of areas for at least

two independent areal feature maps; *II*) similar gradient ridges present in roughly corresponding locations in both hemispheres; *III*) gradients that are not correlated with artifacts; and *IV*) robust, statistically significant cross-border differences in the feature maps.

Although most structural brain atlases are delineated manually by region of interest, it is possible to automate these operations. For example, Wang et al. proposed a method for parcellating the brain into regions of interest based on connectivity by multi-class Hopfield network algorithm (Wang et al., 2016).

Data classifications generally apply "machine learning" methods, for example Support Vector Machines (SVMs) or Ensemble Tree Learning Techniques (Martinez-Murcia et al., 2016).

Mandelkow et al. compared several algorithms for classification, including Nearest Neighbor, Gaussian Naive Bayes, and Linear Discriminant Analysis; high accuracy in terms of discriminating fMRI response patterns is achieved using a large number of natural visual stimuli (Mandelkow et al., 2016).

3.4 Consolidation of temporal and spatial data in brain mapping

Modern studies performed comparative analyses between stationary data (MRI, fMRI) and dynamic data (EEG). To analyze EEG data all of the images are typically superimposed on an "average" brain, without taking into account topological features unique to individual brains. Such an approach often leads to systematic errors that can be eliminated with computational methods. Averaged static EEG maps can be overlaid on anatomical MRI-based maps.

Such a comparison between temporal and spatial data usually reveals that the computed EEG response is correlated with – but does not necessarily coincide with – active areas identified using fMRI. Recording fast EEG signals with high temporal resolution provides a higher level of detail than MRI and fMRI.

Therefore, combination of techniques can provide valuable information regarding the temporal structure and spatial distribution of the resting state networks under specific experimental and/or clinical conditions (Lehmann, 2010). For example, Yuan et al. reconstructed networks from high-resolution EEG data and performed spatial and temporal comparisons with fMRI data (Yuan et al., 2016).

There are two basic approaches to attenuate artifacts due to volume conduction: spatial filtering in combination with standard connectivity methods, or connectivity methods such as the weighted phase lag index that are blind to instantaneous connectivity that may reflect volume conduction artifacts (Cohen, 2014a).

Cohen reported that temporal fluctuations in oscillation peak frequency (also known as "frequency sliding") can be used for analyses at multiple scales within neuroscience (Cohen, 2014b).

Oscillation frequency appears to be a general principle that regulates brain function on multiple spatial and temporal scales, ranging from modulating spike timing in individual neurons to whole coordinating brain networks during cognition and the resting state.

Simultaneous multiscale study of brain activity signals leads to the detection of time lag (delay interval) between the signals (Figure 6).

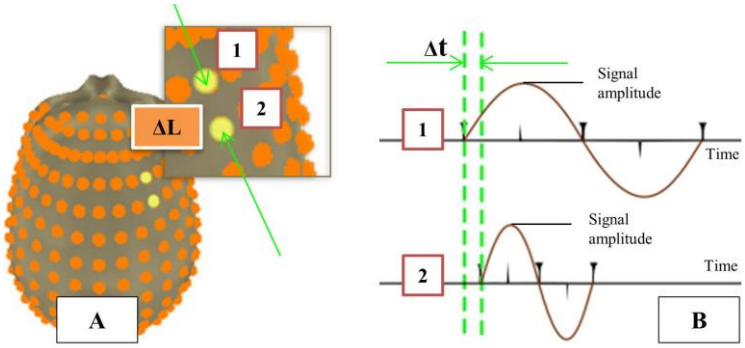

Figure 6. A. Distance between electrodes 1 and 2 (ΔL). B. Time lag between electrodes 1 and 2 (Δt).

3.5 Topography and connectivity in spatio-temporal processes

3.5.1 Effects of topography in the measurement of brain activity

Vertebrate brains generally contain two kinds of tissue: grey matter on the surface, which contains local networks of neurons that are wired by dendrites and mostly local axons, and white matter inside, which contains long-range axons that implement global communication (Wen & Chklovskii, 2005).

Shapes of brain curves, such as sulci, gyri and fissures, should be explored in 3D modelling, similar to how mountain topography is considered in 3D.

Subsurface connections improve level of communications, similar to tunnels in the hills (Figure 7 A).

Plane model of the brain shapes is shown in Figure 7B. Model of the interaction of neurons is shown in Figure 7C: convergence of curved surfaces could modify a possibility of connection.

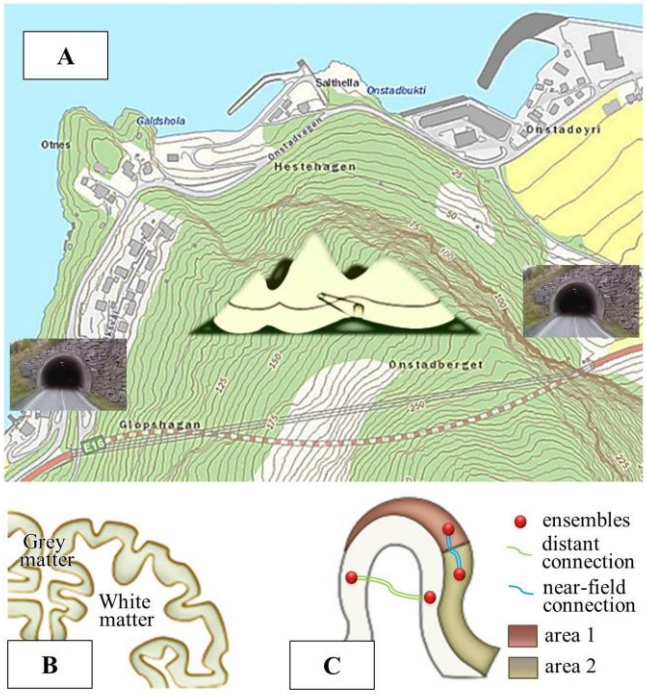

Figure 7. A. One-level objects tend to join together by topography (map to the underlying layer reproduced from https://www.visitnorway.com). B. Plane model of the brain shapes. C. Ensembles from different brain areas can support distant and near-field connections.

3.5.2 Sensor positions

To define the reference points are often used computational methods. For example, the software package LORETA (http://www.uzh.ch/keyinst/loreta) calculates the density distribution of sources using raw data in the form of electric potentials recorded at the scalp (event-related potentials, and cross-spectra EEG recordings).

The fact that the brain surface is curved has a significant strong impact on the overall measuring activity of ensembles of different segments. Figure 8 shows that measurements of activity are carried out with the scalp, and the electrodes are located distantly from the active sources.

Brain without electrodes and arrangement of the electrodes on the scalp in LORETA software are shown in Figure 8A, 8B, and arrangement of the electrodes relative to the slice is shown in Figure 8C.

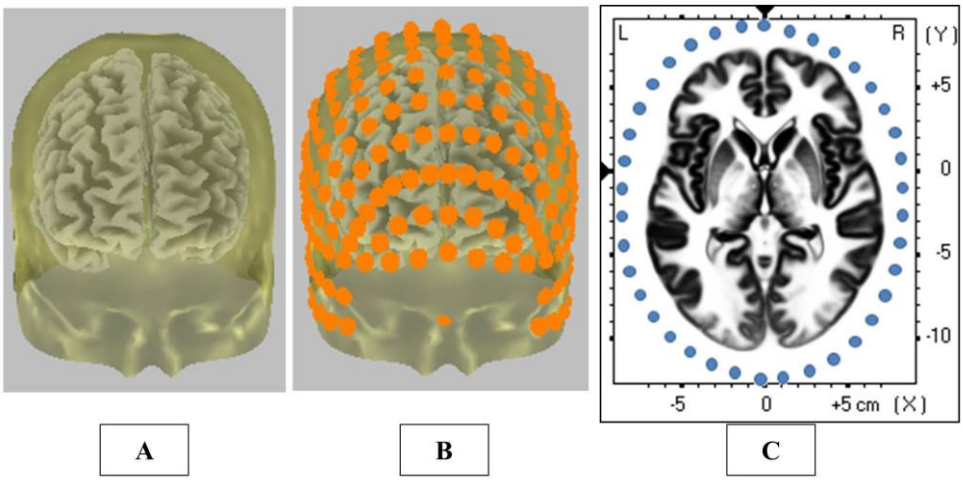

Figure 8. A. Brain without electrodes and B. Arrangement of the electrodes on the scalp in Loreta software. C. Arrangement of the electrodes relative to the slice.

To interpret brain activity various models are used, ranging from a representation of the brain as a sphere to the most accurate representation of the brain's topographic surface. Understanding the impact of neural topography on the resulting measure of brain activity is essential in analyzing interactions and connectivities between various areas of the brain (Thivierge & Marcus, 2007; Guntupalli et al., 2016).

3.5.3 Tractography

Fiber tract trajectories are coherently organized pathways of white matter in the brain. Tractography allows researchers to calculate contiguous fiber tract trajectories using discrete diffusion tensor MRI data (Basser et al., 2000) and to visualize the orientation and integrity of these pathways in the brain.

A map of structural connectivity can be generated as a combination of diffusion imaging and probabilistic tractography. A map of functional connectivity can be generated based on spatio-temporal correlations derived from resting-state fMRI data (Van Essen et al., 2014).

Maps of brain connectivity are being developed in order to reproduce the direction of anatomical and functional connectivity between distinct units, as well as 2D and 3D geomaps are constructed for visualizing the movements (Figure 9).

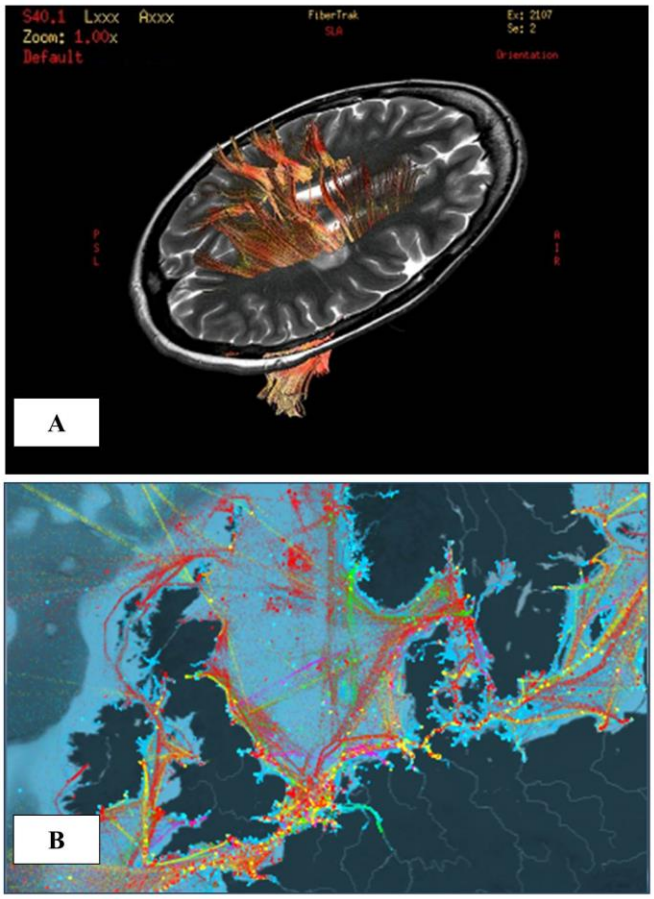

Figure 9. A.Brain fiber tract trajectories. B. Shipping Tracks (reproduced from https://www.shipmap.org).

4. SCALES AND REFERENCE POINTS IN BRAIN MAPPING

4.1 An analysis of spatially distributed brain activity

An analysis of spatially distributed brain activity should include the following considerations:

- The choice of coordinate systems for describing the observations;
- Multi-scale data properties;
- Individuality factors;
- The quality of the measurement techniques; and
- The specificity of the brain areas being analyzed.

The coordinate systems in brain activity measurements (EEG, MEG, etc.) are usually defined in terms of anatomical landmarks on the surface of the head; in contrast, the coordinate systems for neuroimaging (MRI, fMRI, CT) are usually defined in terms of slices inside the head.

The most commonly used coordinate systems are the Talairach Atlas (http://www.talairach.org) and the MNI (Montreal Neurological Institute) stereotaxic coordinates (for more details, see the Appendix).

MNI coordinates in Loreta software (http://www.uzh.ch/keyinst/loreta) shown at Figure 10, coordinate conversion MNI/ Talairach also is possible in this software.

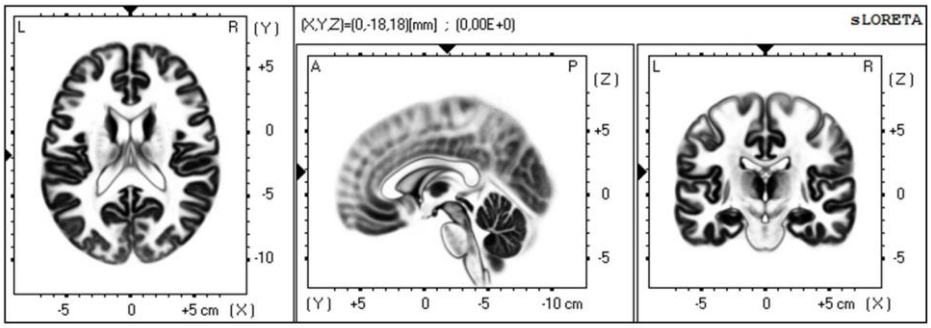

Figure 10. MNI coordinates in Loreta software.

Toro & Burnod introduced representations of the cortical anatomy with the intention of simplifying visualization of the principal sulci and other anatomical landmarks that serve as the axes of the geometric model (Toro & Burnod, 2003). Van Essen used a surface-based coordinate system to visualize the cerebral cortex (Van Essen et al., 1998).

A thorough overview of coordinate systems is available at FieldTrip (Oostenveld et al., 2011) (http://www.fieldtriptoolbox.org).

Coordinate grids for Allen Human Brain Atlas (http://www.brain-map.org) are shown in Figure 11.

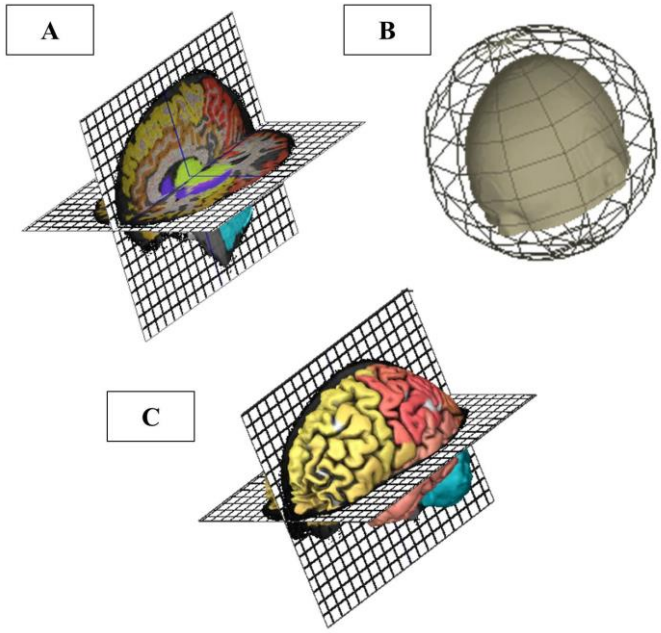

Figure 11. Coordinate grids for Allen Human Brain Atlas in Brain Explorer 2: A. Grids of sagittal and horizontal sections. B. Compass. C. 3D Atlas.

Multi-scale data properties lead to the necessity of generalization of the signals during transitions to wide scales. In addition, part of the observed signal is considered to be noise by the statistical analysis; typically, most of EEG signals can be filtered out as "random noise" and ignored in the subsequent analysis. The ratio of signal-to-noise is defined for each scale.

With respect to individuality factors, it is usually not possible to use a generalized brain map for all participants; a particular map must be compiled for each participant. However, with studies that do not require high precision (for example, to identify the onset of an epileptic seizure), a generalized brain atlas is generally acceptable. Individual brain structure can be considered invariant within a single set of measurements, and these data can be used as the basis for analyzing dynamic data.

In brain mapping, it is necessary to consider the features of the measurement, including the accuracy and relative location of the sensors. In addition, systematic errors may occur due to changes in physiological factors such as heart rate, blood oxygen saturation, and blood pressure (Ghosh Hajra et al., 2016).

Some brain areas can duplicate the cortex function. The majority of the human cerebellum maps to cerebral association networks in an orderly manner that includes a mirroring of the prominent cerebral asymmetries (Buckner, 2013).

With regard to all of the above-mentioned problems, GIS technologies may provide a suitable solution, including methods for working on various scales and with various reference points.

4.2 Scales

4.2.1 Sets of scales

The major sets of scales (and their dimensions) for brain mapping can be defined as follows: cells (10^{-6} m), ensembles (groups of cells; 10^{-4} m), and brain regions (10^{-2} m); the appropriate research methods should be used for each of these scales.

A complete multi-level map of an individual human brain – at the resolution required for mechanistic explanations – will need to represent the morphology, physiology, subcellular, and molecular architecture of neurons (and a similar number of non-neuronal cells) (Frackowiak & Markram, 2015).

4.2.2 Measurement accuracy and noise

The scale is determined primarily by the resolution of the measuring device. Thus, the spatial resolution of fMRI studies is defined by the ability of the equipment to distinguish between boundaries in the brain. Spatial resolution is measured by the size of the voxels, ranging from 4-5 mm to 1 mm (for example, in MRI). Scanning time increases directly with an increasing number of voxels and number of slices. One voxel typically includes approximately a few million neurons.

Marblestone et al. outlined the physical principles governing brain activity mapping using optical, electrical, magnetic resonance, and molecular modalities of neural recording (Marblestone et al., 2013). The authors noted that the recording of activity is limited by the low multiplexing capacity of electrodes and by their lack of intrinsic spatial resolution. In addition, optical methods are constrained by the scattering of visible light in brain tissue, and magnetic resonance is hindered by diffusion and relaxation time scales of protons.

When resolution is improved, noise typically increases. Moreover, noise can be noticed as a phenomenon, which is associated with different scales. Indeed, the choice of scale determines the filter settings to reduce noise. The ability to distinguish between noise and the true signal can affect the amount of data included in the final analysis. Consolidation data in multi-scale project allows researchers carefully to filter or to reduce the noise.

4.3 Reference points

4.3.1 Significance of reference points

In the brain, reference points are biologically significant points with coordinate description. Reference points are essential for integrating datasets obtained from different sources.

Individual anatomical and physiological reference points can be allocated based on the spatial and functional features of an individual brain and are based on characteristic surface features and/or measured activity. Lines of interest and areas of interest are identified using a similar approach.

Individual reference points can be mapped to an existing general brain atlas in order to specify functional locations or to update coordinates. Thus, points of interest, lines of interest, and regions of interest (often abbreviated POIs, LOIs, and ROIs, respectively) can serve as a basis for linking disparate data and for generalizing.

The various types of reference points are summarized in Table 2.

Table 2. Types of reference points

Type	Description
I. Internal reference points	
Anatomical points	Internal anatomical points (landmarks) are based on the structure of parts of the brain
Functional points	The points identified using blood oxygen level-dependent (BOLD) contrast imaging show changes in the brain's state
Dynamic points of brain activity	The "point of neuron activity" is a group of brain cells with stable, detectable activity
II. Sensor position	
Points of observation (can be used as the relative origin of coordinates)	Locations of the electrodes and sensors are taken into account when determining the relative coordinate system
Biomarkers	Biomarkers provide a selection of places of interest in the tissue microstructure
III. Brain cells for coordination and navigation	
Place cells, grid cells, head-direction cells, and boundary cells	Positioning systems in the brain

4.3.2 Anatomical and physiological landmarks

Landmarks are generally used to describe the shapes of brain structures and for parcellation. The shape of sulci is used to measure brain variability (Durrleman et al., 2007) and topological components of sulci are used as landmarks (Mangin et al., 2015). Functional reference points for brain activity are calculated using robust and similar values of measured parameters.

Zhang et al. formulated the detection of anatomical landmark and boundaries as a classification problem (Zhang et al., 2012) in which a shape repository/dictionary is constructed using manually delineated organ contours and/or surfaces.

Liu et al. presented algorithms to automatically detect and match landmark curves on cortical surfaces in order to obtain optimal parameters of brain conformation (Liu et al., 2006). The authors proposed an automated landmark curve-tracing method based on the principal directions established by the local Weingarten matrix.

Sergejeva et al. proposed a standardized set of anatomical landmarks for registering whole-brain imaging datasets obtained from mouse and rat brains, in particular for integrating experimental image data in the Waxholm Space atlas (Sergejeva et al., 2015).

New parcellation system for the orbitofrontal cortex using automated anatomical labeling was described by Rolls (Rolls et al., 2015).

4.3.3 Points of neuronal activity

To solve the dynamic problems associated with neural activity, it is essential to know the location of neurons or neuronal ensembles that are being measured. In many types of biological experiments, researchers simply operate with aggregate data, without providing any reference to coordinates.

An accurate method to overcome this issue is the registration of "points of neuron activity" by electrodes that are implanted in the brain. However, even with such registration, interference from neighboring units of activity can distort the detected signals, making it difficult to locate the precise source of the activity. EEG electrodes are spaced rather widely apart; the source of the signals recorded from neuronal ensembles can be determined only by computational methods (see section 3.5.2).

5. PATTERN RECOGNITION IN NEUROIMAGING

In this section we present the possibilities of GIS applications for the pattern recognition and comparative analysis of electronic medical records.

5.1 Primary data

Primary electronic medical records for analysis were obtained from the period 2012 through 2015. These data contain images obtained using various CT and MRI equipment.

View of primary images is shown in Figure 12.

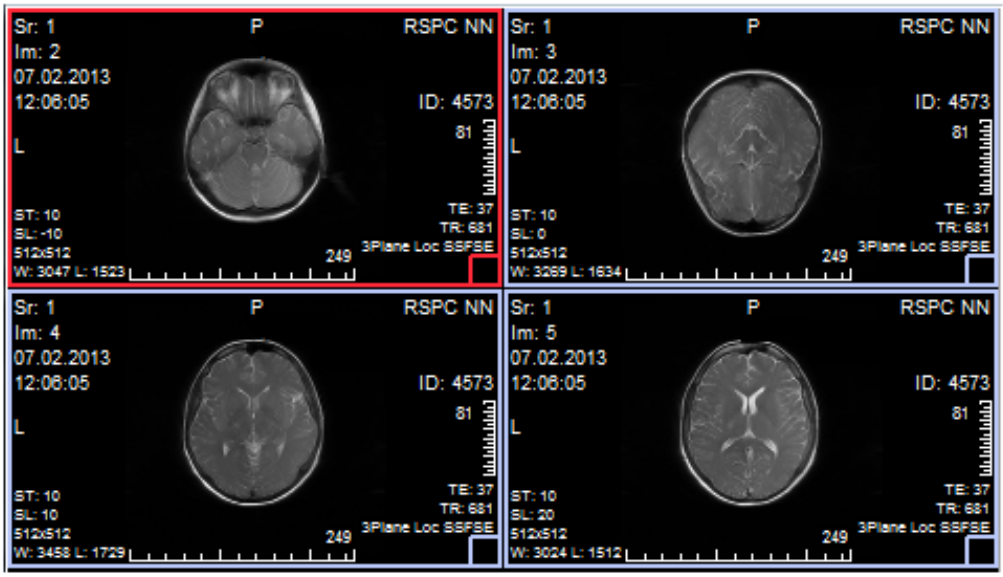

Figure 12. Primary neuroimaging dataset.

5.2 Methods

Control primary image series were grouped by date and type of observation in MicroDicom (http://www.microdicom.com).

The data were processed with open source software, including additional analysis modules. The GIS methods applied in the data analysis are shown in

Table **3**.

Table 3. Data processing methods

Methods	Description	Tools
Contouring	Contouring allows converting raster data to vector. Isoline calculation with a given tolerance is performed using Gdal_contour plugin.	**Gdal_contour** generates a vector contour file from the input raster http://www.gdal.org/gdal_contour.html.
Selection of reference points	Plugin allows extracting nodes from isolines and polygon layers and then outputting extracted nodes as reference points.	**Extract nodes** is a tool for nodes extraction: http://docs.qgis.org/2.6/en/docs/user_manual/processing_algs/qgis/vector_geometry_tools/extractnodes.html.
Georeferencing of image series	To georeference an image, one first needs: to establish reference points, input the known local coordinates of these points, choose the coordinate system and other projection parameters and then minimize residuals. Residuals are the difference between the actual coordinates of the reference points and the coordinates predicted by the spatial model (Figure 13).	**Georeferencer Plugin** is a tool for snapping rasters to single coordinate system with help of reference points: http://docs.qgis.org/2.0/en/docs/user_manual/plugins/plugins_georeferencer.html.
ROIs identification	Subsets of samples of the tumor area are selected as regions of interest (ROIs). Vector ROIs are the basis for next template creation and classification.	**Semi-Automatic Classification** (https://fromgistors.blogspot.com/p/semi-automatic-classification-plugin.html) is a plugin for the semi-automatic supervised classification of images (in the work modified version was used).
Data Classification and Template Creation	DTclassifier helps to allocate data on the image with the same characteristics. How it works: (1)Selecting training datasets, (2)Selecting data to classify, (3)Refining templates.	**DTclassifier** (http://nextgis.com/projects/dtclassifier) is a plugin that allows classification of data in QGIS. It uses a particular classification algorithm - “decision trees” (Murthy, 1998).
Multilayers Comparison	To compare parameter data from different layers the analytical tools of fTools Plugin are used. It provides a growing suite of spatial data management and analysis functions that are both fast and functional.	**fTools Plugin** for analysis functions: http://docs.qgis.org/2.8/en/docs/user_manual/plugins/plugins_ftools.html.

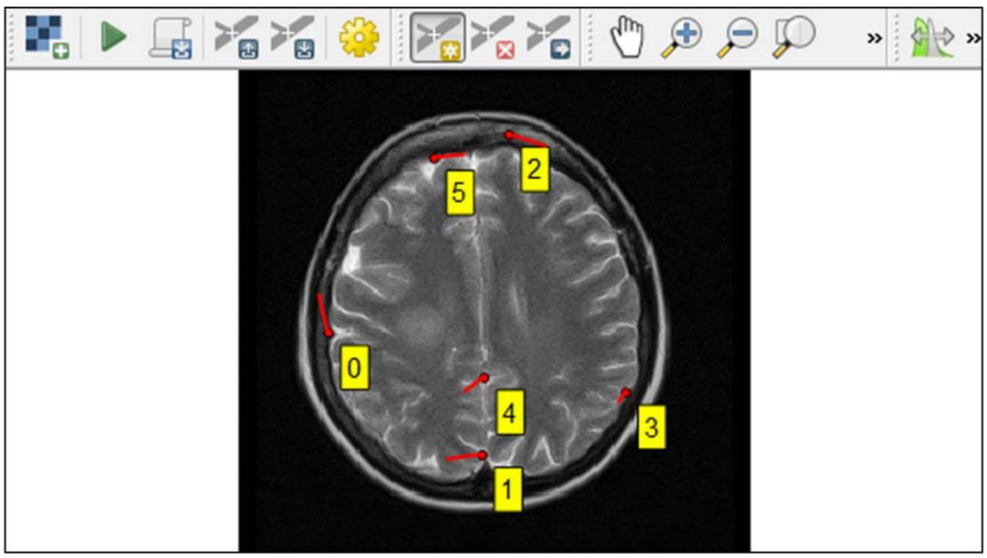

Figure 13. Georeferencer Plugin in QGIS.

5.3 Results

Example of selected ROIs (tumor areas) and comparison of tumor sizes at different times is shown in Figure 14.

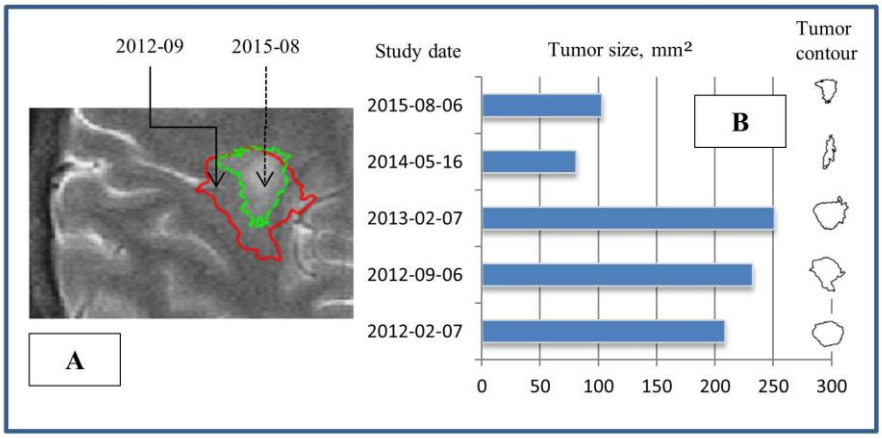

Figure 14. A. Example of selected ROIs (tumor areas). B. Comparison of tumor sizes at different times (tumor contours with maximum section square are shown in the right column).

6. PERCEPTION OF EXTERNAL ROUTES AND INTERNAL TRACTS

6.1 Perception of spatial information

Neuroscientists and geoscientists can actively interact in researching of the brain's perception of external space and the brain's orientation in space.

The study of the brain's perception of spatial information includes a wide range of tasks, including visual object recognition and locomotion.

Using high-resolution fMRI scanning, Peer et al. found that mental orientation in space and time produces a sequential posterior–anterior pattern of activity in each participant's brain (Peer et al., 2015).

Guntupalli et al. presented a linear model of shared representational spaces in the human cortex and models of cortical patterns of neural responses with individual-specific topographic basis functions (Guntupalli et al., 2016).

Neural responses in the visual cortex are governed by topographic mapping from retinal locations to cortical responses. At the voxel population level, early visual cortex activity enables the accurate decoding of stimuli locations (Roth, 2016).

6.2 Positioning systems in the brain

Grid-based methods are well-knowing in geoinformatics. 2D or 3D grid lines define the coordinate system and provide a unique reference to space features (Figure 15).

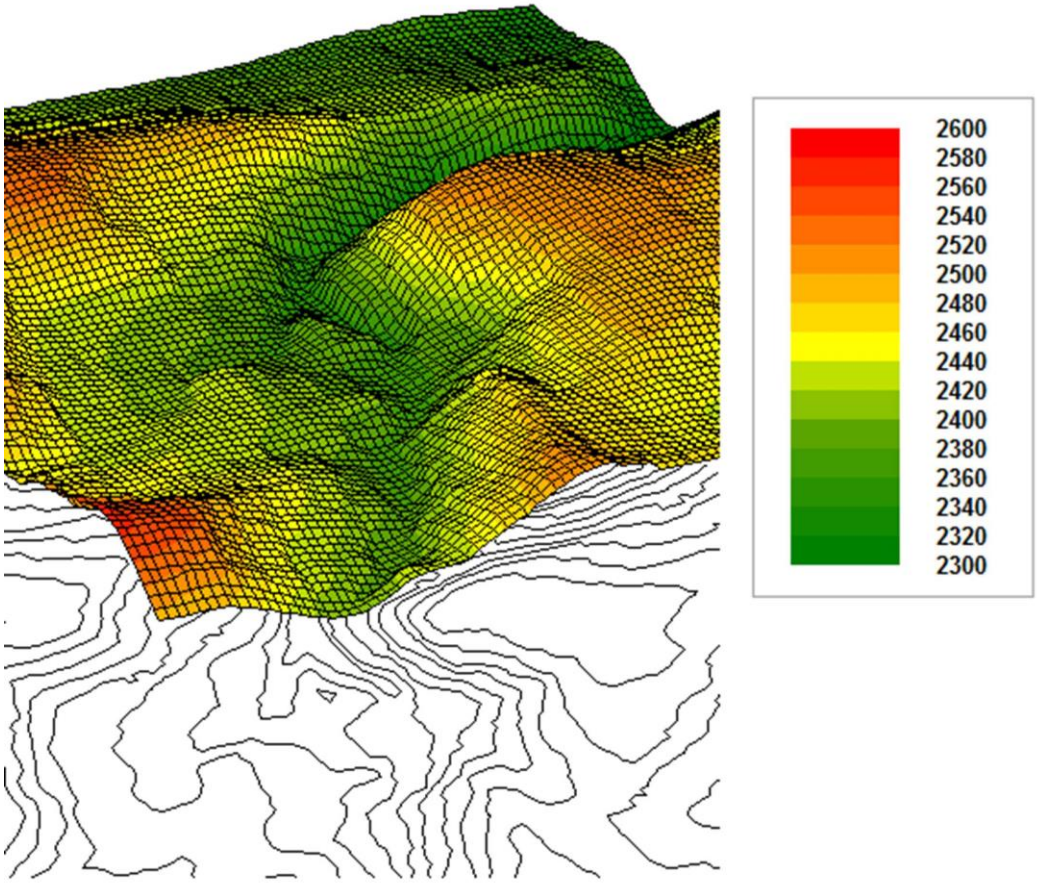

Figure 15. 3D grids and contour lines**.**

Grid reference tools are usually applied in a large number of GIS. These methods seem artificial and invented exclusively for calculations. But as shown in recent studies, the brain itself contains biological structures that are directly responsible for both navigation and recognition (Moser et al., 2014; Stemmler, et al., 2015).

The types of brain cells associated with navigation were summarized by Chersi and Burgess (Chersi & Burgess, 2015). In their review, the authors described the following four cell types: *I*) place cells, which typically fire in a restricted portion of the environment; *II*) directional grid cells or ‘‘conjunctive’’ cells, whose grid-like spatial firing is also modulated by head direction; *III*) head-direction cells, which typically fire in a narrow range of allocentric directions; and *IV*) boundary cells, which typically fire at a specific distance from an environmental boundary along a specific allocentric direction.

In 2014, the Nobel Prize in Physiology or Medicine was shared, with half of the prize awarded to John O’Keefe, and the other half awarded jointly to May-Britt Moser and Edvard Moser “for their discoveries of cells that constitute a positioning system in the brain” (http://www.nobelprize.org/nobel_prizes/medicine/laureates/2014).

O’Keefe concluded that the hippocampus generates numerous maps that are represented by the collective activity of place cells. Results obtained by May-Britt Moser and Edvard Moser confirmed that grid cells are activated in a unique spatial pattern, and collectively these cells constitute a coordinate system that allows for spatial navigation.

Border cells, grid cells, and head-direction cells form the elements of a metric representation of local space, and are likely used when an animal navigates through its environment (Moser & Moser, 2011). In the hippocampus, place cells are remapped when the environment changes (Miao et al., 2015; Colgin et al., 2008).

Unlike place cells, grid cells have several properties that facilitate navigation (Bush et al., 2015). Grid cells recorded at the same electrode location share several metric properties, including spacing, orientation, and field size (Hafting et al., 2005).

The grid cell network is intrinsically organized, with the grid cells clustered in separate, independent grid maps with distinct scales, orientations, and asymmetries (Moser, 2016).

Grid cells provide a metric of the neural representation of space, similar to the way in which head-direction cells provide a directional frame of reference. As a result, each environment is represented by a unique combination of active place cells and place fields (Buzsaki & Moser, 2013).

Model of grid- and place-cells' activity is shown in Figure 16.

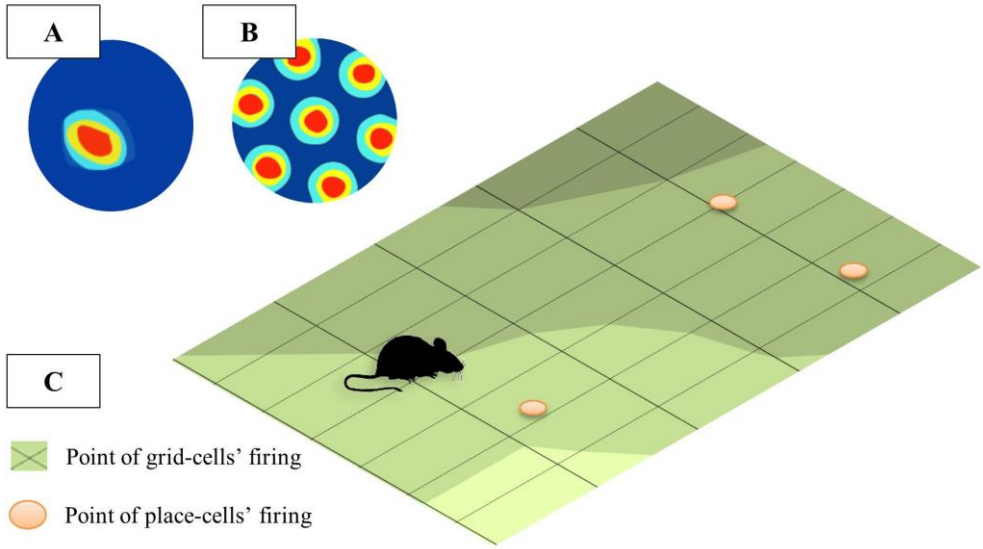

Figure 16. A. Model of place cell firing. B. Model of grid cell firing. C. Model of grid and place cells' activity.

The optimal configurations of spatial scales for grid cell firing in the context of noise and uncertainty were reported by Towse et al., who concluded that such configurations can be changed (Towse et al., 2014).

Oscillatory dynamics and place field maps reflect the processing of sequence and place memory (Cabral et al., 2014). Oscillatory dynamics of grid cells contribute to the processing of space-time, including the speed of movement. Theta-band oscillatory dynamics of grid cell were also described by Towse (Towse et al., 2014).

Optogenetics and pharmacogenetics techniques are used to study individual cells, including grid cells (Miao et al., 2015). Optogenetics uses light to alter neural processing at the level of single spikes and synaptic events, providing a widely adaptable tool for genetically targeted optical control of neural activity (Boyden et al., 2005). These technologies apply light to control biological processes within targeted cells *in vivo*, with high temporal precision, thereby allowing researchers to develop generalized strategies for targeting cells based on morphology and/or tissue topology (Gradinaru et al., 2010).

But results of Krupic et al. provide compelling evidence for the idea that environmental boundaries compete with the internal organization of the grid cell system to drive grid firing. Grid cell activity cannot provide a universal spatial metric in all environments (Krupic et al., 2015).

6.3 Reference points and interpolation in navigation tasks

Our brains are continuously engaged in the selection and construction of a route. Poucet et al.

focus on the information carried by grid cells, their relationship to place cells and the role of grid cells in navigation and also discussed a framework provided by landmark stimuli or by information about motion of animal (Poucet et al., 2013).

To create a generalized representation of space, one must create a cognitive map of the environment by integrating observations over extended periods of time and by inferring spatial structure from perceptions and the effects of his/her actions (Kuipers & Levitt, 1988). The Wayfinding Scale route strategy (Kremmyda et al., 2016) can be used in both spatial navigation and spatial anxiety.

To solve navigation tasks, reference points determine the behavioral strategy for the route, and the perceptions of "place" and "object" are interrelated in navigation. In other words, the parameters of "object" vary depending on the position, and the parameters of "place" vary depending on the objects included.

In 1970, Waldo Tobler introduced the first law of geography (Tobler, 1970), which states "everything is related to everything else, but near things are more related than distant things." This principle can serve as the basis for the spatial analysis of continuous data on the same scale.

Points with well-known attributes can serve as reference points in tasks that lack – or have excess – information. These points can also serve as a basis for creating a generalized coordinate system.

In geostatistical interpolation techniques (for example, kriging), well-known attributes of reference points can be transferred to nearby points.

Deterministic interpolation techniques create surfaces from measured points, (http://desktop.arcgis.com/en/arcmap/latest/extensions/geostatistical-analyst/deterministic-methods-for-spatial-interpolation.htm) based on either the extent of similarity (inverse distance weighted) or the degree of smoothing (radial basis functions).

The interpolation of data regarding the space between points with well-known attributes allows one to create new routes or modify existing routes.

7. CONCLUSIONS

As a result of analogous experiences in spatial data processing, researchers in the neuroscience and geoscience fields communicate in nearly the same language and use similar tools and techniques.

In this review, we summarized the areas of interest common to brain mapping and GIS mapping, including:

- Processing large numbers of images;
- Rapid conversion of coordinates in individual brains;
- Precise positioning of brain activity and neuroimaging data in the map of an individual brain;
- Optimization of classifiers using existing GIS classifiers;
- Modelling of dynamic brain maps and investigating brain connectivity; and
- Positioning and navigation tasks.

8. APPENDIX

8.1 Basic standards

Digital Imaging and Communications in Medicine (DICOM) is a standard for handling, storing, printing, and transmitting information in medical imaging. The DICOM Standard

now specified a network protocol utilizing TCP/IP, defined the operation of Service Classes beyond the simple transfer of data. DICOM was also structured as a multi-part document in order to facilitate extension of the standard. Additionally, DICOM defined Information Objects not only for images but also for patients, studies, reports, and other data grouping (http://dicom.nema.org).

The MNI Coordinate System originated at the Montreal Neurological Institute and Hospital and is used to normalize anatomical 3D datasets.

Talairach coordinates (http://www.talairach.org) is a 3D coordinate system of the human brain, which is used to map the location of brain structures independent from individual differences in the size and overall shape of the brain.

Bias between MNI and Talairach Coordinates is shown in (Lancaster et al., 2007).

A perennial source of confusion in brain mapping has been the small but significant differences between stereotaxic spaces owing to the different strategies for creating the template. The origin of the MNI152 templates is shifted approximately by + 3.5 mm in Z and + 2.0 mm in Y relative to Talairach space. Various methods have been proposed to minimize these differences (Evans et al., 2012).

During the measurements, the sensors occupy a certain position, which can be calculated, for example, in Subject Coordinate System (SCS / CTF) – (http://neuroimage.usc.edu/brainstorm/CoordinateSystems), where coordinates are specified relative to the calculated characteristic points of participants.

8.2 Data exchange standards

The brain is a complex organ consisting of various areas with specialized functions. The cartographic representation provides a conceptual framework for understanding the unique roles of cognitive systems in facilitating behavioral adaptability (Mattar et al., 2015).

Flexible standards regarding data exchange and data sharing are essential for creating robust and meaningful convergent neuroimaging data obtained from different sources. Integration projects such as BrainMap (Laird et al., 2011) have been developed in response to the needs of researchers in the fields of structural and functional neuroimaging.

Gorgolewski et al. attempted to organize and describe the output of neuroimaging experiments (Gorgolewski et al., 2016). Specifically, the authors used the XML-based Clinical Experiment Data Exchange (XCEDE) scheme to provide standards for describing neuroimaging data.

The same group published a practical guide for neuroimaging research (Gorgolewski & Poldrack, 2016). In this guide, the authors cover three major topics in open science (data, code, and publications), and they propose using the Brain Imaging Data Structure to organize data.

8.3 Brain mapping software

FSL (FMRIB Software Library) (http://fsl.fmrib.ox.ac.uk) is a comprehensive library of analysis tools for fMRI, MRI and DTI brain imaging data. It runs on Apple and PCs (both Linux, and Windows via a Virtual Machine), and is very easy to install. Most of the tools can be run both from the command line and as GUIs ("point-and-click" graphical user interfaces).

SPM (Statistical Parametric Mapping, http://www.fil.ion.ucl.ac.uk/spm) software package has been designed for the analysis of brain imaging data sequences. The sequences can be a series of images from different cohorts, or time-series from the same subject. The current release is designed for the analysis of fMRI, PET, SPECT, EEG and MEG.

Loreta (http://www.uzh.ch/keyinst/loreta) is a software for analysis of low resolution brain electromagnetic tomography.

Brain Explorer 2 (http://community.brain-map.org/display/BrainExplorer/Home) is a desktop software application for viewing brain anatomy and gene expression data in 3D.

NeuroVIISAS (neuro Visualization, Imagemapping, Information System for Analysis and Simulation) (http://139.30.176.116/neuroviisas.html) is an open framework for integrative data analysis, visualization and population simulations.

AAL (Automated anatomical labelling) (http://www.cyceron.fr/index.php/en/plateforme-en/freeware) is a software package dependent upon the Matlab and SPM programs, typically used in functional neuroimaging-based research.

NEST (The Neural Simulation Tool) (http://www.nest-simulator.org) is a simulator for spiking neural network models that focuses on the dynamics, size and structure of neural systems rather than on the exact morphology of individual neurons.

Brainstorm (http://neuroimage.usc.edu/brainstorm/Introduction) is a collaborative, open-source application dedicated to the analysis of brain recordings: MEG, EEG, fNIRS, ECoG, depth electrodes and animal electrophysiology.

BrainVISA (http://www.brainvisa.info) provides a complete, modular, infrastructure for neuroimaging software. It helps organizing heterogeneous software and data and provides a common general graphical interface for users.

FreeSurfer (http://surfer.nmr.mgh.harvard.edu) is an open source software suite for processing and analysing brain MRI images.

3D Slicer (https://www.slicer.org) is an open source software platform for medical image informatics, image processing, and three-dimensional visualization. Built over two decades through support from the National Institutes of Health and a worldwide developer community, Slicer brings free, powerful cross-platform processing tools to physicians, researchers, and the general public.

8.4 Brain Mapping organizations

The Organization for Human Brain Mapping (OHBM) (www.humanbrainmapping.org) is the primary international organization dedicated to using neuroimaging to discover the organization of the human brain.

The Human Brain Project (HBP) (www.humanbrainproject.eu) aims to collect, explain and simulate the functions of the human brain at different levels of hierarchical complexity. The HBP idea is to federate and integrate the data, thus making use of an abundance of biological information from the different levels of brain organization. Data mining will be used to extract sets of rules that constitute definitions of homogeneous groupings of patients or subjects (Frackowiak et al., 2016).

The goal of the Blue Brain Project (http://bluebrain.epfl.ch) is to build biologically detailed digital reconstructions and simulations of the rodent, and ultimately the human brain. The project's novel research strategy exploits interdependencies in the experimental data to obtain dense maps of the brain, without measuring every detail of its multiple levels of organization (molecules, cells, micro-circuits, brain regions, whole brain).

International Neuroinformatics Coordinating Facility (INCF) (https://www.incf.org) develops collaborative neuroinformatics infrastructure and promotes the sharing of data and computing resources to the international research community.

REFERENCES

Andriole, K.P., Wolfe, J.M., Khorasani, R., Treves, S.T., Getty, D.J., et al. 2011. Optimizing Analysis, Visualization, and Navigation of Large Image Data Sets: One 5000-Section CT Scan Can Ruin Your Whole Day. *Radiology*, 259 (2): 346–62.

Baillet, S., Mosher, J.C., and Leahy, R.M. 2001. Electromagnetic brain mapping. *IEEE Signal Processing Magazine*, 18 (6): 14–30.

Barbeito, A., Painho, M., Cabral, P., and O'neill, J. 2015. A topological multilayer model of the human body. *Geospatial Health*, 10 (2): 199–204.

Basser, P.J., Pajevic, S., Pierpaoli, C., Duda, J., and Aldroubi, A. 2000. In vivo fiber tractography using DT-MRI data. *Magnetic Resonance in Medicine*, 44 (4): 625–32.

Boyden, E.S., Zhang, F., Bamberg, E., Nagel, G., and Deisseroth, K. 2005. Millisecond-timescale, genetically targeted optical control of neural activity. *Nature Neuroscience*, 8 (9): 1263–68.

Buckner, R.L. 2013. The cerebellum and cognitive function: 25 years of insight from anatomy and neuroimaging. *Neuron*, 80 (3): 807–15.

Bush, D., Barry, C., Manson, D., and Burgess, N. 2015. Using Grid Cells for Navigation. *Neuron*, 87 (3): 507–20.

Buzsaki, G., and Moser, E.I. 2013. Memory, navigation and theta rhythm in the hippocampal-entorhinal system. *Nature Neuroscience*, 16 (2): 130–8.

Cabral, H.O., Vinck, M., Fouquet, C., Pennartz, C.M.A., Rondi-Reig, L., et al. 2014. Oscillatory dynamics and place field maps reflect hippocampal ensemble processing of sequence and place memory under NMDA receptor control. *Neuron*, 81 (2): 402–15.

Chersi, F., and Burgess, N. 2015. The Cognitive Architecture of Spatial Navigation: Hippocampal and Striatal Contributions. *Neuron*, 88 (1): 64–77.

Cohen, M.X. 2014a. Effects of time lag and frequency matching on phase-based connectivity. *Journal of Neuroscience Methods*, 250: 137–46.

Cohen, M.X. 2014b. Fluctuations in Oscillation Frequency Control Spike Timing. *Journal of Neuroscience*, 34 (27): 8988–98.

Colgin, L.L., Moser, E.I., and Moser, M.-B. 2008. Understanding memory through hippocampal remapping. *Trends in Neurosciences*, 31 (9): 469–77.

Durrleman, S., Pennec, X., et al. 2007. Measuring brain variability via sulcal lines registration: a diffeomorphic approach. *Medical Image Computing and Computer-Assisted Intervention*, 10 (Pt 1): 675-82.

Evans, A.C., Janke, A.L., Collins, D.L., and Baillet, S. 2012. Brain templates and atlases. *NeuroImage*, 62 (2): 911–22.

Fan, L., Li, H., Zhuo, J., Zhang, Y., Wang, J., et al. 2016. The Human Brainnetome Atlas: A New Brain Atlas Based on Connectional Architecture. *Cerebral Cortex*, 26 (8): 3508-26.

Frackowiak, R., Ailamaki, A., and Kherif, F. 2016. Federating and Integrating What We Know About the Brain at All Scales: Computer Science Meets the Clinical

Neurosciences. In *Micro-, Meso- and Macro-Dynamics of the Brain*, eds. Gyorgy Buzsaki and Yves Christen: 157–170. Cham: Springer International Publishing.

Frackowiak, R., and Markram, H. 2015. The future of human cerebral cartography: a novel approach. *Philosophical Transactions of the Royal Society B*, 370 (1668): 20140171.

Ghosh Hajra, S., Liu, C.C., Song, X., Fickling, S., Liu, L.E., et al. 2016. Developing Brain Vital Signs: Initial Framework for Monitoring Brain Function Changes Over Time. *Frontiers in Neuroscience*, 10: 211.

Glasser, M.F., Coalson, T.S., Robinson, E.C., Hacker, C.D., Harwell, J., et al. 2016. A multi-modal parcellation of human cerebral cortex. *Nature*, 536 (7615): 171-8.

Gorgolewski K.J., Auer T., Calhoun V.D., Craddock R.C., Das S., et al. 2016. The brain imaging data structure, a format for organizing and describing outputs of neuroimaging experiments. *Scientific Data*, 3: 1–9.

Gorgolewski, K.J., and Poldrack, R.A. 2016. A practical guide for improving transparency and reproducibility in neuroimaging, PLoS Biol., 14 (7): e1002506.

Gradinaru, V., Zhang, F., Ramakrishnan, C., Mattis, J., Prakash, R., et al. 2010. Molecular and Cellular Approaches for Diversifying and Extending Optogenetics. *Cell*, 141 (1): 154–65.

Guntupalli, J.S., Hanke, M., Halchenko, Y.O., Connolly, A.C., Ramadge, P.J., et al. 2016. A Model of Representational Spaces in Human Cortex. *Cerebral Cortex*, 26 (6): 2919-34.

Hafting, T., Fyhn, M., Molden, S., Moser, M.-B., and Moser, E.I. 2005. Microstructure of a spatial map in the entorhinal cortex. *Nature*, 436 (7052): 801–6.

Kremmyda, O., Hufner, K., Flanagin, V.L., Hamilton, D.A., Linn, J., et al. 2016. Beyond Dizziness: Virtual Navigation, Spatial Anxiety and Hippocampal Volume in Bilateral Vestibulopathy. *Frontiers in Human Neuroscience*, 10: 139.

Krupic, J., Bauza, M., Burton, S., Barry, C. and O'Keefe, J. 2015. Grid cell symmetry is shaped by environmental geometry. *Nature*, 518 (7538): 232–35.

Kuipers, B.J., and Levitt, T.S. 1988. Navigation and Mapping in Large Scale Space. *AI Magazine*, 9 (2): 25.

Laird, A.R., Eickhoff, S.B., Fox, P.M., Uecker, A.M., Ray, K.L., et al. 2011. The BrainMap strategy for standardization, sharing, and meta-analysis of neuroimaging data. *BMC Research Notes*, 4: 349.

Lancaster, J.L., Tordesillas-Gutierrez D., Martinez, M., Salinas, F., Evans, A., et al. 2007. Bias Between MNI and Talairach Coordinates analyzed using the ICBM-152 brain template. *Human Brain Mapping*, 28 (11): 1194–205.

Lehmann, D. 2010. Multimodal analysis of resting state cortical activity. *NeuroImage*, 52 (4): 1173–4.

Lui, L.M., Wang, Y., Chan, T.F., and Thompson, P.M. 2006. A landmark-based brain conformal parametrization with automatic landmark tracking technique. *Medical Image Computing and Computer-Assisted Intervention*, 9 (Pt 2): 308-15.

Mandelkow, H., de Zwart, J.A., and Duyn, J.H. 2016. Linear Discriminant Analysis Achieves High Classification Accuracy for the BOLD fMRI Response to Naturalistic Movie Stimuli. *Frontiers in Human Neuroscience*, 10: 128.

Mangin, J.F., Auzias, G., Coulon, O., Sun, Z.Y., Riviere, D., et al. 2015. Sulci as Landmarks. Brain Mapping: *An Encyclopedic Reference*, 2: 45–52.

Marblestone, A.H., Zamft, B.M., Maguire, Y.G., Shapiro, M.G., Cybulski, et al. 2013. Physical principles for scalable neural recording. *Frontiers in Computational Neuroscience*, 7: 137.

Martinez-Murcia, F., Gorriz, J., Ramirez, J., and Ortiz, A. 2016. A Spherical Brain Mapping of MR Images for the Detection of Alzheimer's Disease. *Current Alzheimer Research*, 13 (5): 575–88.

Mattar, M.G., Cole, M.W., Thompson-Schill, S.L., and Bassett, D.S. 2015. A Functional Cartography of Cognitive Systems. *PLoS Computational Biology*, 11 (12): e1004533.

Miao, C., Cao, Q., Ito, H.T., Yamahachi, H., Witter, M.P., Moser, M.-B., and Moser, E.I. 2015. Hippocampal Remapping after Partial Inactivation of the Medial Entorhinal Cortex. *Neuron*, 88 (3): 590–603.

Mikula, S., Trotts, I., Stone, J., and Jones, E.G. 2007. Internet-Enabled High-Resolution Brain Mapping and Virtual Microscopy. *NeuroImage*, 35 (1): 9-15.

Moser, E.I., Roudi, Y., Witter, M. P., Kentros, C., Bonhoeffer, T., and Moser, M.-B. 2014. Grid cells and cortical representation. *Nature Reviews Neuroscience*, 15 (7): 466–81.

Moser, M.-B, and Moser, E.I. 2011. Crystals of the brain. *EMBO Molecular Medicine*, 3 (2): 69–71.

Moser, M.-B. 2016. Brain Maps for Space. In *Seminal Contributions to Modelling and Simulation: 30 Years of the European Council of Modelling and Simulation*, eds. Khalid Al-Begain and Andrzej Bargiela: 7–9. Cham: Springer International Publishing.

Murthy, S.K. 1998. Automatic construction of decision trees from data: A multi-disciplinary survey. *Data Mining and Knowledge Discovery*, 2 (4), 345–89.

Oostenveld, R., Fries, P., Maris, E., and Schoffelen, J.M. 2011. FieldTrip: Open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. *Computational Intelligence and Neuroscience*, 2011: 156869.

Peer, M., Salomon, R., Goldberg, I., Blanke, O., and Arzy, S. 2015. Brain system for mental orientation in space, time, and person. *Proceedings of the National Academy of Sciences*, 112 (35): 11072–7.

Poucet, B., Sargolini, F., Song, E.Y., Hangya, B., Fox, S., et al. 2013. Independence of landmark and self-motion-guided navigation: a different role for grid cells. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 369 (1635): 20130370.

Razi, A., Kahan, J., Rees, G., and Friston, K.J. 2015. Construct validation of a DCM for resting state fMRI. *NeuroImage*, 106: 1–14.

Robinson, L., and Rolls, E.T. 2015. Invariant visual object recognition: biologically plausible approaches. *Biological Cybernetics*, 109 (4–5): 505–35.

Rolls, E.T., Joliot, M., and Tzourio-Mazoyer, N. 2015. Implementation of a new parcellation of the orbitofrontal cortex in the automated anatomical labeling atlas. *NeuroImage*, 122: 1-5.

Roth, Z.N. 2016. Functional MRI Representational Similarity Analysis Reveals a Dissociation between Discriminative and Relative Location Information in the Human Visual System. *Frontiers in Integrative Neuroscience*, 10: 16.

Sergejeva, M., Papp, E.A., Bakker, R., Gaudnek, M.A., Okamura-Oho, Y., et al. 2015. Anatomical landmarks for registration of experimental image data to volumetric rodent brain atlasing templates. *Journal of Neuroscience Methods*, 240: 161-9

Simony, E., Honey, C.J., Chen, J., Lositsky, O., Yeshurun, Y., et al. 2016. Dynamical reconfiguration of the default mode network during narrative comprehension. *Nature Communications*, 7: 12141

Stemmler, M., Mathis, A., and Herz, A. 2015. Connecting Multiple Spatial Scales to Decode the Population Activity of Grid Cells. *Science Advances*, 1 (11): e1500816.

Thivierge, J.P., and Marcus, G.F. 2007. The topographic brain: from neural connectivity to cognition. *Trends in Neurosciences*, 30 (6): 251–9.

Tobler, A.W.R. 1970. A Computer Movie Simulating Urban Growth in the Detroit Region. *Science*, 46 (2): 234–40.

Toro, R., and Burnod, Y. 2003. Geometric atlas: Modeling the cortex as an organized surface. *NeuroImage*, 20 (3): 1468–84.

Towse, B.W., Barry, C., Bush, D., and Burgess, N. 2014. Optimal configurations of spatial scale for grid cell firing under noise and uncertainty. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, 369 (1635): 20130290.

Van Essen, D.C., Drury, H., Joshi, S., and Miller, M.I. 1998. Functional and structural mapping of human cerebral cortex: solutions are in the surfaces. *Proceedings of the National Academy of Sciences of the United States of America*, 95 (3): 788–95.

Van Essen, D.C., Jbabdi, S., Sotiropoulos, S.N., Chen, C., Dikranian, K., et al. 2014. Mapping Connections in Humans and Non-Human Primates: Aspirations and Challenges for Diffusion Imaging. In *Diffusion MRI (Second Edition)*, eds. Heidi Johansen-Berg and Timothy E.J. Behrens. 337–358. Academic Press: San Diego.

Wang, Q., Chen, R., JaJa, J., Jin, Y., Hong, L.E., et al. 2016. Connectivity-Based Brain Parcellation: A Connectivity-Based Atlas for Schizophrenia Research. *Neuroinformatics*, 14 (1): 83–97.

Wen, Q., and Chklovskii, D.B. 2005. Segregation of the brain into gray and white matter: a design minimizing conduction delays. *PLoS Computational Biology*, 1 (7): e78.

Yuan, H., Ding, L., Zhu, M., Zotev, V., Phillips, R., et al. 2016. Reconstructing Large-Scale Brain Resting-State Networks from High-Resolution EEG: Spatial and Temporal Comparisons with fMRI. *Brain Connectivity*, 6 (2): 122–35.

Zhang, S., Zhan, Y., and Metaxas, D.N. 2012. Deformable segmentation via sparse representation and dictionary learning. *Medical Image Analysis*, 16 (7): 1385–96.