Modeling & Analysis
# 405/10327

# Finding related functional neuroimaging volumes

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## Abstract

We describe an information retrieval system for finding related experiments in functional neuroimaging based on the activation volumes. Both sets of locations (e.g., local maxima) as well as summary images can be used.

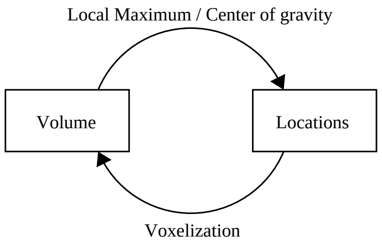
## Introduction

Identification of related research in functional neuroimaging can be done, e.g., by searching in bibliographic databases such as PubMed, browsing "table of contents" of scientific journals or searching BrainMap™ [5] with, e.g., behavioral or location criteria. Here we describe an image retrieval method based on activation information in 3D Talairach space. The information might either come in the form of a list of points representing activation hot spots or it might come as an activation volume, e.g., a volume of $t$-values from a statistical analysis of a functional neuroimaging data set. Our first goal is to establish a service comparable to "Related Articles" of PubMed.
Some image retrieval systems are based on text description of images, but others have combined it with extracted features from the image, e.g., color, texture, shape and keywords. We work entirely with the gray level of the image.
Earlier descriptions of our work are available in [6].

## Which space?

The distances between the volumes can be computed in several different spaces.

- *Voxel space* where the distance is aggregated from the distance between the two corresponding voxel values from the two volumes.
- *Projected space* where the distance is computed in a subspace, e.g., if number of volumes $N$ is smaller than the number of voxels $P$ then the volumes can be represented in a small $N$-dimensional space rather than the large $P$-dimensional space.
- In *location space* the distance between volumes is computed as the distance between the hot spots (e.g, local maxima) in the functional volume.




Translation from volume/voxel to location representation is usually done by thresholding the volume followed by identification of local maxima (or minima) above the threshold. An other method finds the center of gravities of the connected components in a thresholded volume. Translation from the (set of) locations to the volume/voxel representation is done by *voxelization*.

## Voxelization

For voxelization we convolve every location $\mathbf{x}$ with a Gaussian distribution with isotropic covariance, — a method associated with kernel density estimation also called Parzen window or Specht kernel estimation [7]. Each location (represented by a 3-dimensional vector $\mathbf{x}$) is convoluted with an isotropic 3-dimensional Gaussian probability density function (PDF) with a width of $\sigma^2$, presently fixed to $\sigma = 10$mm. The combined PDF is the sum of all the Gaussian PDFs.
There are several issues which should be addressed:

- Each volume may have one or several locations associated with it. We can choose to normalize with the number of locations (so the volumes become a probability volumes).
- A *magnitude* is often associated with the location. In BrainMap™ this can have different units, e.g., "percent change of rCBF" or "ml/100g/min".
- A *sign* is sometimes associated with the value of the location. This could indicated a deactivation or a reversed contrast in a $t$-test. Other method, e.g., an $F$-test, will not direct produce a sign.

For the present application we normalize with the number of locations, we ignore the magnitude and handle the sign simply by negating the Gaussian PDF for "negative" locations.

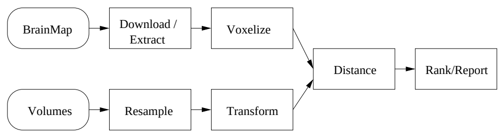
## Distance/similarity

We want to rank the volumes according how similar they are with each other. There are multiple ways in which the distance/similarity between the volumes can be measured, e.g.,

- If the volumes is are density volumes we can use information theoretic measures such as the Kullback-Leibler distance.
- By a correlation measure such as the inner product or the correlation coefficient [11].

## Data

As our primary data we will use the BrainMap™ database [5, http://ric.uthscsa.edu] which we download from the web. Bibliographic and location data is extracted and the location data are feed to the voxelization stage before computation of distances and ranking of related volume for each volume.




We supplements the location data from BrainMap™ with a few summary images from a functional neuroimaging study with cluster analysis [1]. The volumes are resampled and converted from MNI to the Talairach space [2].

## Example

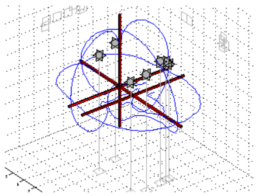
HTML web-pages with the resulting lists of related volumes are generated. The unrelated (or rather "antirelated") volumes are also reported. Also added are short bibliographic information, the list of locations and a Corner Cube visualization. An example from one of the 797 experiments presently used is shown below with an experiment from [3].

**Related volumes**

Jerne > Neuroinformatics > Related volumes > 100

(100) Shift R in R vis. field
*A PET study of visuospatial attention.*
Corbetta M, *Journal of Neuroscience* **13**(3):1202–1226, PMID: 8441008
[ BrainMap : paper 29 | exp 12 ]

| x | y | z |
|---|---|---|
| −25 | −52 | 38 |
| 27 | −52 | 43 |
| 23 | −52 | 47 |
| −23 | 6 | 45 |
| 14 | −55 | 51 |
| −8 | −59 | 45 |
| 7 | 16 | 45 |



Related volumes – correlated

(99) Shift L in R vis. field
*A PET study of visuospatial attention.*
Corbetta M, *Journal of Neuroscience* **13**(3):1202–1226, PMID: 8441008
[ BrainMap : paper 29 | exp 11 ]

(98) Shift R in L vis. field
*A PET study of visuospatial attention.*
Corbetta M, *Journal of Neuroscience* **13**(3):1202–1226, PMID: 8441008
[ BrainMap : paper 29 | exp 10 ]

(296) Saccades/anti–prostimulus
*Role of the human anterior cingulate cortex in the control of oculomotor, manual, and speech responses: a positron emission tomography study.*
Paus T, *Journal of Neurophysiology* **70**(2):453–469, PMID: 8410148
[ BrainMap : paper 108 | exp 10 ]

It shows two clusters of activations: one in the parietal lobe and an other in the frontal lobe. This pattern is repeated for the five most related experiments: Two others from the same study, two from [8] and one from [9].
The volume representation requires large amount of data. To reduce the amount of memory used a coarse sampling of 8mm is employed resulting in only 7752 voxels, the volumes × voxels matrix being $\mathbf{X}(797 \times 7752)$. With large data sets it might be an advantage to measure distance in the smaller location space rather than in the large voxel space.

## Other processing

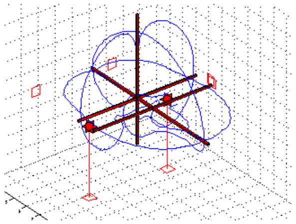
Once the data is in a common space other processing can be made: Indices based on image statistics can give a entry to or overview of the data. An example is the measure of the departure of a volume from the mean volume (across all volumes), — a novelty measure. The upper part of a list with ranked novelties for all volumes is shown below.

| Novelty | Entry |
|---|---|
| 1821310.156 | 265 *Cerebral Cortex* **5**:544–554, 1994 |
| 356553.719 | 469 |
| 226472.295 | 470 |
| 210379.745 | 681 , 1998 |
| 193692.603 | 19 *Science* **243**(4894 Pt 1):1071–1074, 1989, PMID: 2784226 |
| 171597.308 | 797 *Human Brain Mapping* **15**(3), 2002, PMID: 11835604 |
| 153851.347 | 555 *Proceedings of the National Academy of Sciences* **92**:5969–5972, 1995 |
| 152056.302 | 456 |
| 130419.741 | 279 *Unpublished*, 1995 |
| 129268.917 | 138 *Brain Topography* **5**(2):183–187, 1992, PMID: 1489648 |
| 117676.690 | 715 *Proceedings of the National Academy of Sciences* **93**(17):9212–9217, 1996, PMID: 8799180 |
| 115336.637 | 471 |
| 113322.474 | 717 *Proceedings of the National Academy of Sciences* **93**(17):9212–9217, 1996, PMID: 8799180 |

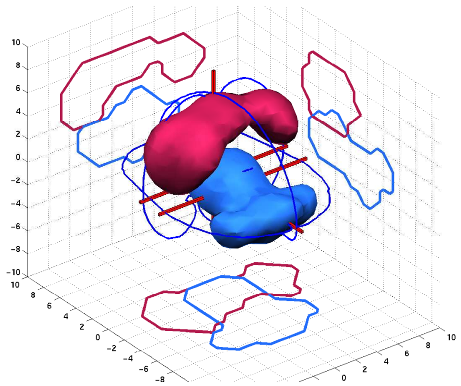
One of the top entries is [10] that associates the temporopolar cortex with anxiety. A later experiment found the signal could be extracranial [4].

(19) Induced anxiety
*Neuroanatomical correlates of anticipatory anxiety*
Reiman E M, *Science* **243**(4894 Pt 1):1071–1074, 1989, PMID: 2784226
[ BrainMap : paper 7 | exp 1 ]

| x | y | z |
|---|---|---|
| 47 | 15 | −26 |
| −43 | 17 | −24 |



An other method that can give an overview of the data is singular value decomposition. Isosurfaces in the 2nd eigenimage are shown below with thresholds at 5% and 95% of the number of voxels.



## Concluding remarks

- We have devised a method for finding related volumes in voxel and in "location" representation.
- We have applied it on data from primarily BrainMap™.
- A number of parameters can be optimized, e.g., kernel type, width estimation, handling of sign and magnitude information and distance measure.
- Some entries in the BrainMap™ database are meta-analyses and unpublished studies. These could be given small weight in the distance measure if they are not wanted.

## More information

- Some of the tools for this analysis is implemented in the *Brede* Matlab toolbox available at http://hendrix.imm.dtu.dk/software/brede/.
- The generated lists of related volumes are presently available from http://hendrix.imm.dtu.dk/services/jerne/.
- Lists of related volumes are also generated for the (anatomical) "volumes of interest" (see poster 490/10497).

## Acknowledgment

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## References

[1] Balslev D, et al. Cluster analysis of activity-time series in motor learning. *Human Brain Mapping*, 15:135–145, 2002.

[2] Brett M. The MNI brain and the Talairach atlas. http://www.mrc-cbu.cam.ac.uk/-Imaging/mnispace.html, 1999.

[3] Corbetta M, et al. A PET study of visuospatial attention. *The Journal of Neuroscience*, 13:1202–1226, 1993.

[4] Drevets WC, et al. PET images of blood flow changes during anxiety: Correction. *Science*, 256:1696, 1992.

[5] Fox PT and Lancaster JL. Neuroscience on the net. *Science*, 266:994–996, 1994.

[6] Nielsen FÅ. *Neuroinformatics in Functional Neuroimaging*. Ph.D. thesis, Informatics and Mathematical Modelling, Technical University of Denmark, Lyngby, Denmark, 2001.

[7] Nielsen FÅ and Hansen LK. Modeling of activation data in the BrainMap™ database: Detection of outliers. *Human Brain Mapping*, 15:146–156, 2002.

[8] Paus T, et al. Role of the human anterior cingulate cortex in the control of oculomotor, manual, and speech responses: a positron emission tomography study. *Journal of Neurophysiology*, 70:453–469, 1993.

[9] Petrides M, et al. Functional activation of the human frontal cortex during the performance of verbal working memory tasks. *Proc Natl Acad Sci USA*, 90:878–882, 1993.

[10] Reiman EM, et al. Neuroanatomical correlates of anticipatory anxiety. *Science*, 243:1071–1074, 1989.

[11] Van Horn JD, et al. The functional magnetic resonance imaging data center (fMRIDC): the challenges and rewards of large-scale databasing of neuroimaging studies. *Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences*, 356:1323 – 1339, 2001.