Meta-analysis and information retrieval in functional neuroimaging

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ABSTRACT

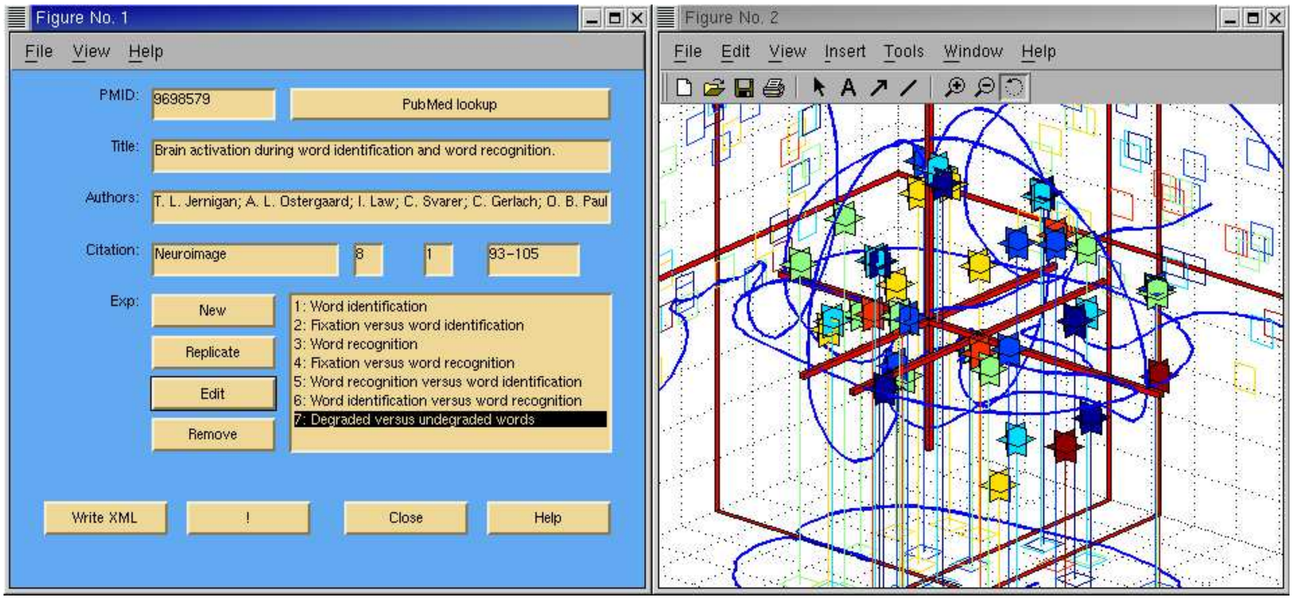
Functional neuroimaging databases containing stereotaxic coordinates allow for automated meta-analyses and image-based information retrieval. Based on data from BrainMap and our own small "Brede" database we describe systems that produce probabilistic anatomical atlases, find "related volumes" and discover novelty and global patterns using voxelization with adaptive kernel density estimation and by applying ordinary unsupervized techniques such as singular value decomposition, independent component analysis and K-means clustering.

OUTLINE

- The data: "Brede" and BrainMap databases.
- Modeling "locations".
- Conditional probability densities
  - Anatomical atlas.
  - Novelty detection: Conditional outlier detection.
  - Functional volumes modeling.
- Finding related volumes/experiments
  - Novelty of an experiment.
  - Singular value decomposition (SVD).
  - Independent component analysis (ICA).
  - Left/right asymmetry.

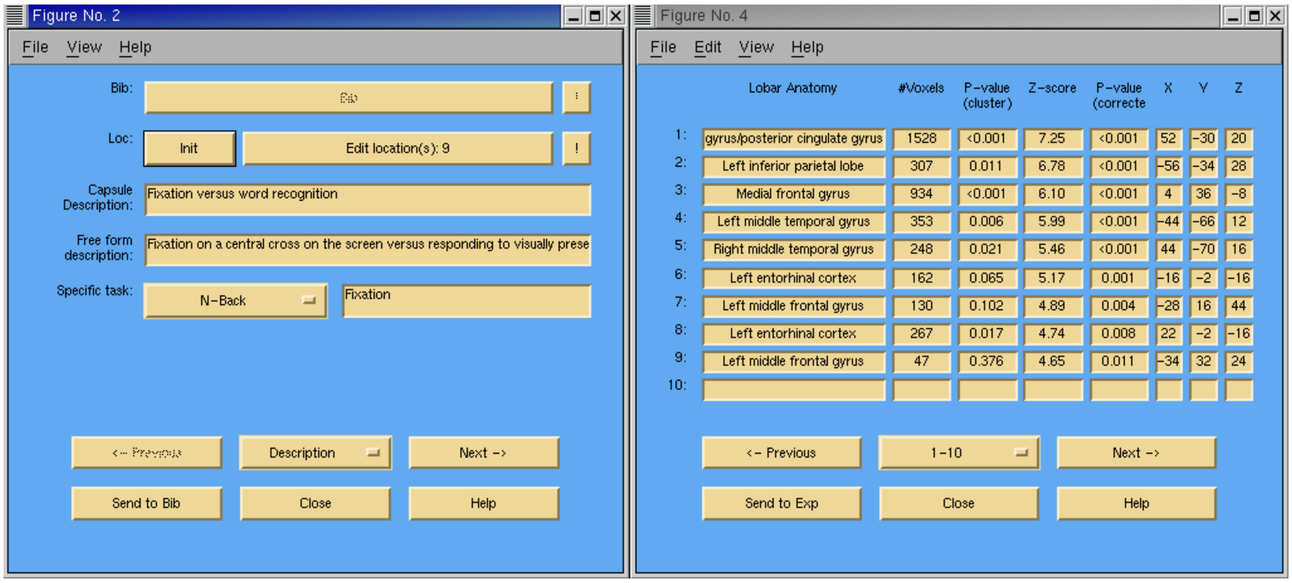
- "Modeling of activation data in the BrainMap database: Detection of outliers". HBM 15(3):146–156, 2002 March.
- "Finding related functional neuroimaging volumes". Submitted to *Artificial Intelligence in Medicine*, 2002 September.

NEUROIMAGING DATABASES



- Functional neuroimaging databases
  - Raw data-based: fMRIDC, Neurogenerator.
  - Stereotactic coordinate-based: BrainMap, BrainMap DBJ, Brede.
  - Related: PubMed, CocoMac, . . .
- Example: “Brede”
  - Main component: Stereotactic coordinates.
  - Bibliographic information taken from PubMed,
  - Linked to other databases: PubMed, fMRIDC.
  - “Poor man’s XML” (pXML)

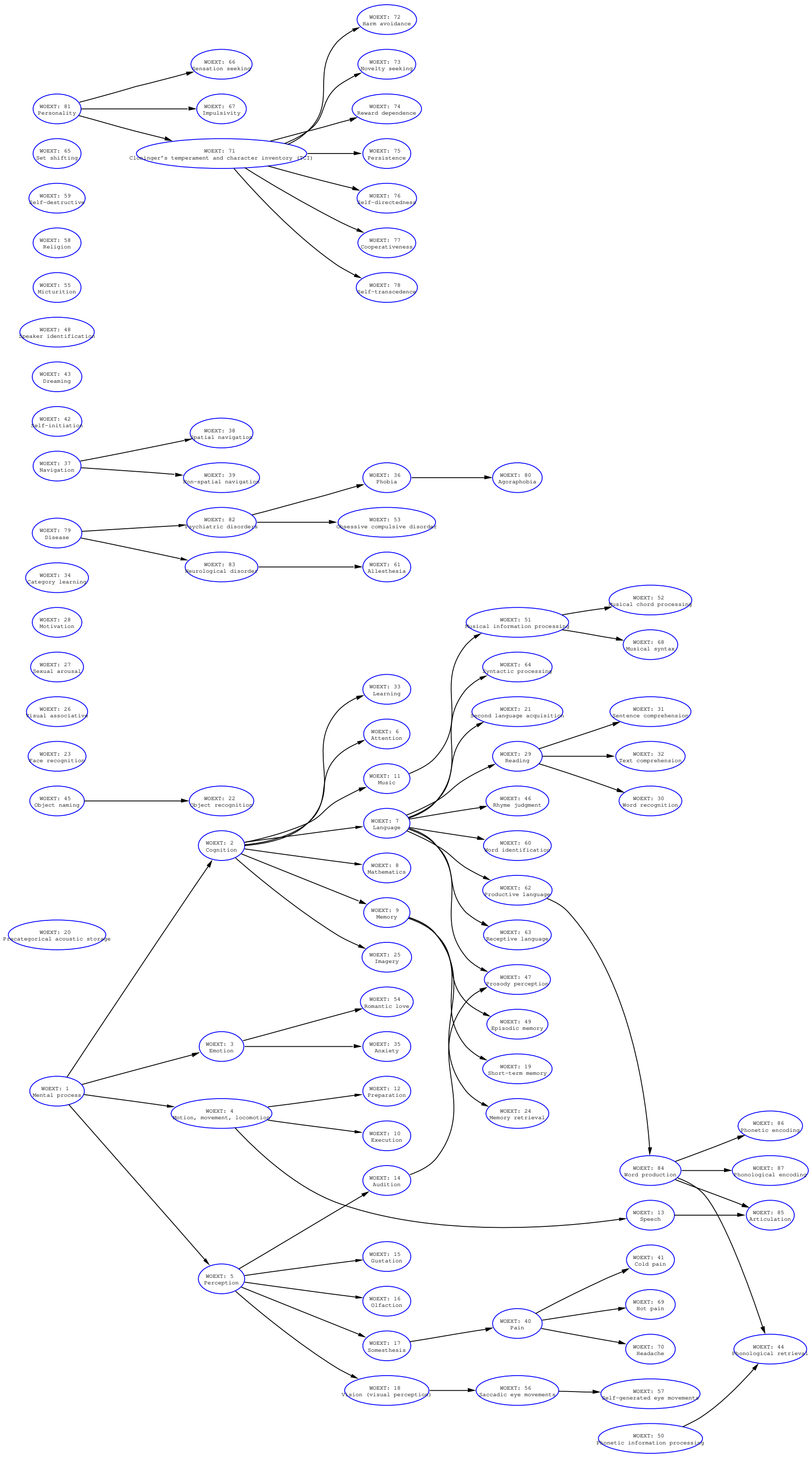
BREDE DATABASE



- Brede data model heavily inspired by BrainMap database (Fox and Lancaster, 1994): Paper (bibliographic information), experiment (summary image, paradigm, stimulus/response), location (stereotactic coordinates).
- Data entry with a Matlab program for the information in "experiments" and "locations".
- Supplement to BrainMap:

	BrainMap	Brede
Papers	225	40
Experiments	771	134
Locations	7683	882
Year	1985–1998	1997–2003

"EXTERNAL" INFLUENCE COMPONENTS



“EXTERNAL” COMPONENTS CLOSE UP

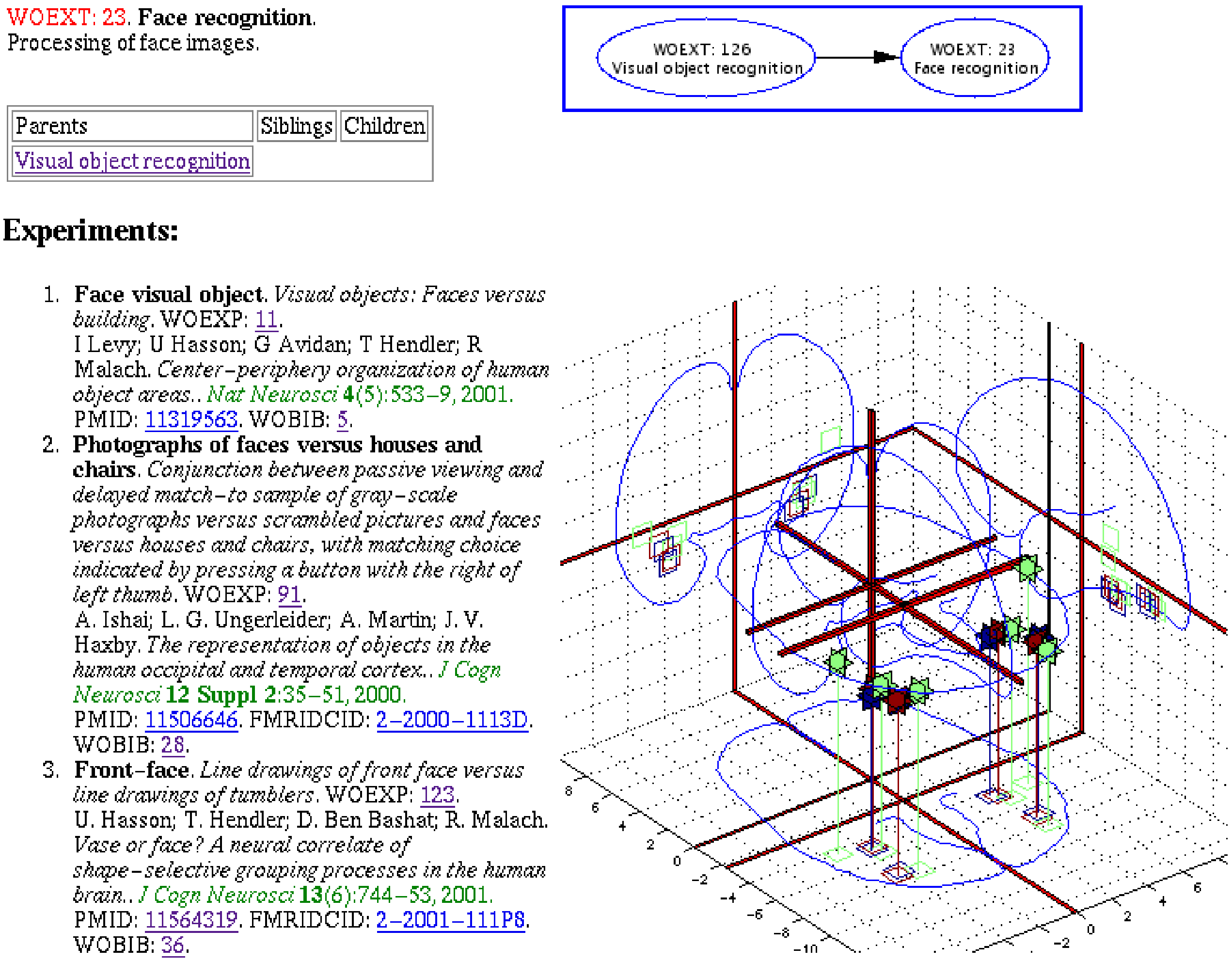


Figure 1: “Face recognition” external influence component.

- “External” influence components (e.g., cognitive components) organized in a directed acyclic graph with links to MeSH descriptor data.
- Corner Cube visualization (Rehm et al., 1998).
- Clickable graphs generated with *dot* (Koutsofios and North, 1996).

MODELING LOCATIONS AND VOLUMES

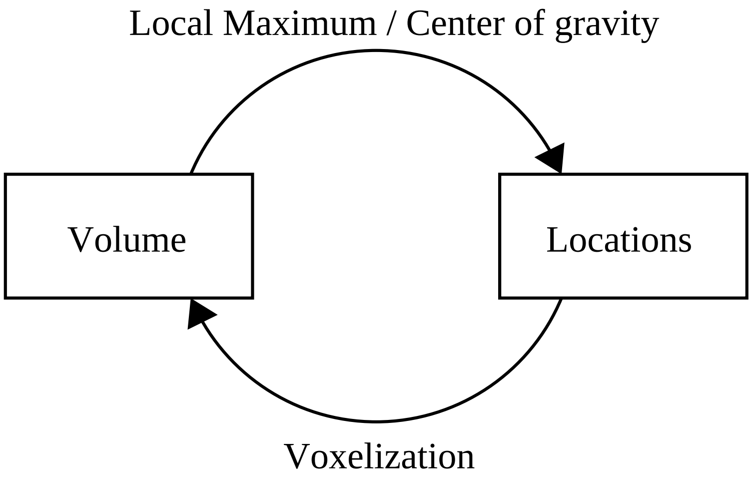


Figure 2: "Voxelization": From peak/local maxima or center of gravity to volume.

- From locations to volume: "Voxelization".
- Regard the "locations" as being generated from a distribution $p(\mathbf{x})$, where $\mathbf{x}$ is in 3D Talairach space.
- Kernel methods (N kernels centered on each object: $\boldsymbol{\mu}_n$) with homogeneous Gaussian kernel in 3D Talairach space $\mathbf{x}$

$$\hat{p}(\mathbf{x}) = \frac{1}{N} \sum_{n}^{N} (2\pi\sigma^2)^{-3/2} \exp\left(-\frac{1}{2\sigma^2}(\mathbf{x} - \boldsymbol{\mu}_n)^2\right) \quad (1)$$

  σ^2 fixed or optimized with leave-one-out cross-validation.
- Condition on, e.g., anatomical label, behavioral domain c: $p(\mathbf{x}|c)$

ANATOMICAL ATLASES

(precuneus) precuneus

Asymmetry: −0.09005 (left: −1, right: +1)

SPM ANALYZE volume (MNI, symmetric,
Sigma=4.44769mm, 79 x 95 x 68, 2.0mm x 2.0mm x 2.0mm)
– precuneus–mni–sym.hdr (1 Kb)
– precuneus–mni–sym.img (2042 Kb)

VRML2 file (250 Kb)

Talairach			BrainMap		
x	y	z	Paper	Exp	Loc
−2	−60	24	27	2	8
−2	−60	20	27	2	9
14	−46	36	29	5	4
12	−55	45	29	5	5
8	−57	36	29	10	4
7	−71	36	29	10	5
18	−57	53	29	11	5
12	−42	45	29	11	6
−18	−48	47	29	11	7
8	−59	51	29	11	8
...	...	...	...	...	...

82 coordinates (total)

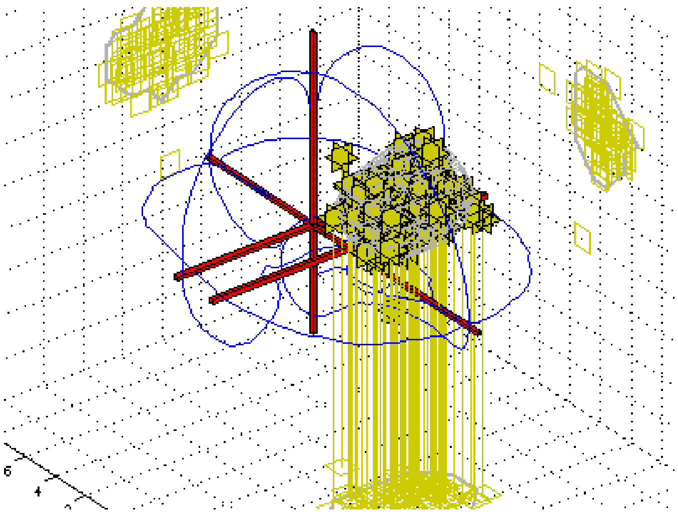


Figure 3: "Precuneus" web-page with data from BrainMap from a part of the 3935 labeled locations.

- Conditioning on anatomical label $p(\mathbf{x}|c = \text{precuneus})$.
- Extract word and subphrases from the "Lobar anatomy" field in BrainMap, e.g., "Occipital gyrus" → "occipital gyrus", "occipital" "gyrus".
- Web-page for each label with Corner Cube visualization and probabilistic ANALYZE volumes in MNI-space.
- Collaborative atlas.
- Dependent on use and common activation.

THE WORD "LOBE"

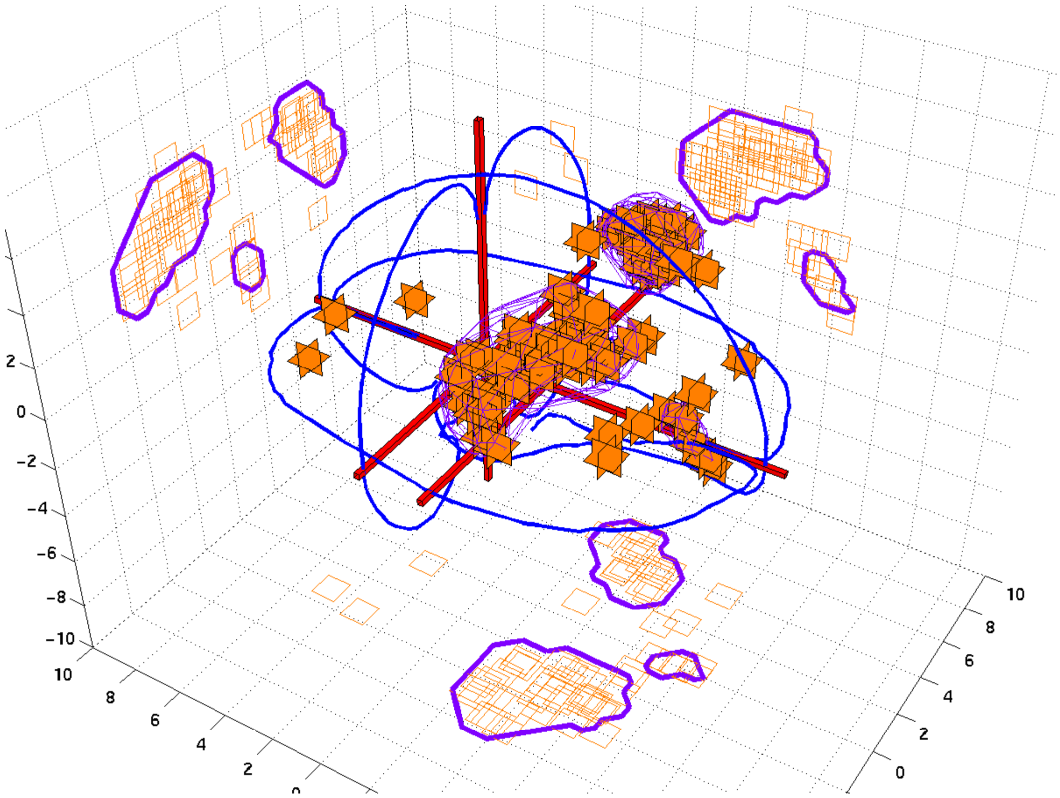


Figure 4: Probability density estimation of "lobe". The blue/magenta wire-frame model is the second stage probability density estimate at a $P_{\mathrm{HPD}} = 0.5$ threshold, and the orange glyphs are the "lobe" BrainMap locations.

Count	Lobar Anatomy
60	inferior parietal lobe
10	superior parietal lobe
6	midline occipital lobe
2	limbic lobe
1	subgyral frontal lobe
1	paracentral parietal lobe
1	medial occipital gyrus/temporal lobe
1	medial frontal lobe

- "Lobe" location is focused in specific areas.

NOVELTY DETECTION

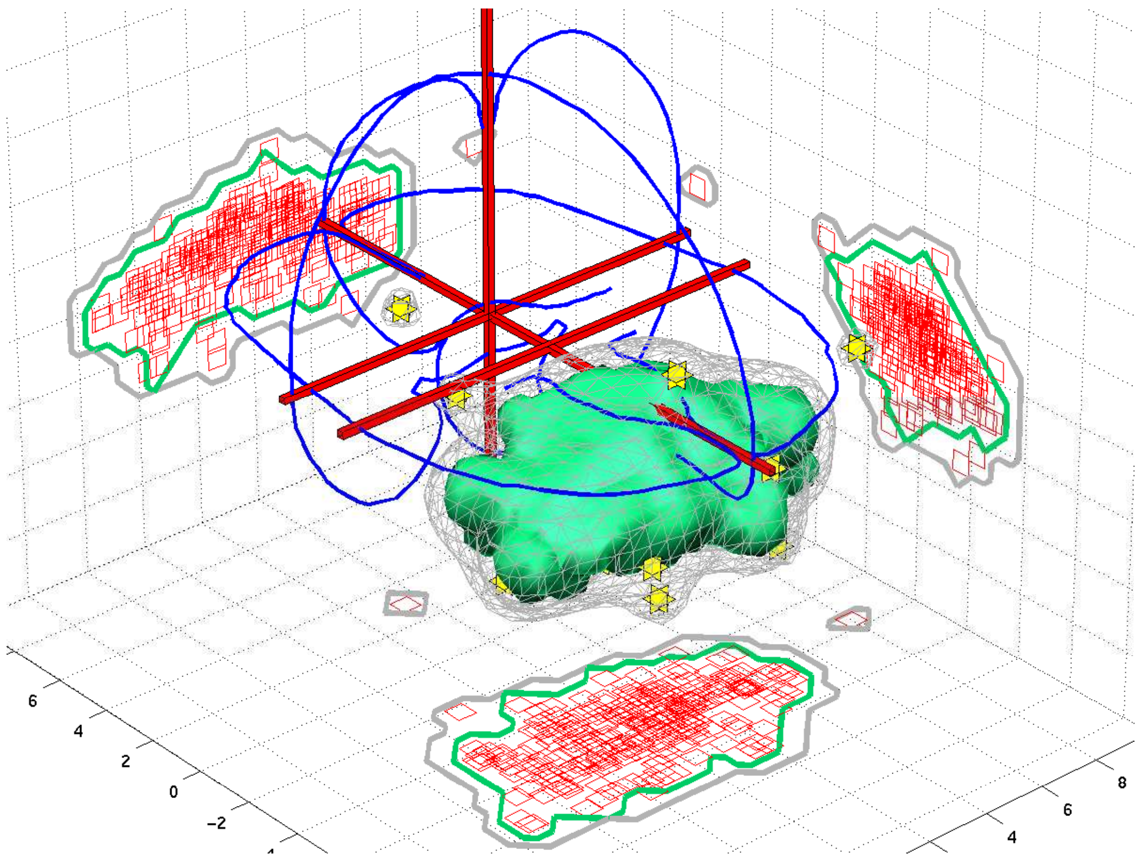


Figure 5: Densities from cerebellum locations. Yellow glyphs are the original BrainMap locations. Grey wireframe: Isosurface in the first level probability density estimate. Green surface: Isosurface in the second level.

- Novelty detection: Discover unsual entries.
- Condition on anatomical label: $p(\mathbf{x}|c = \text{cerebellum})$.
- Evaluate each location with respect to its probability densities: its "novelty".
- Robust estimate of $p(\mathbf{x})$ by excluding the 5% most extreme locations in a two-stage scheme.
- Rank all locations with respect to novelty.

"MANUAL" INVESTIGATION OF OUTLIERS

No.	BrainMap	x	y	z	BrainMap label	Comment	Reference
1	267, 2, 1	−5	7	540	SMA	Millimeter and centimeter for z-coordinate confused during BrainMap entry	(Buckner et al., 1996, table 4, entry 1)
2	29, 10, 8	48	−23	−51	Lateral superior parietal	Resolved: Transcription mistake.	(Corbetta et al., 1993, table 5)
3	141, 1, 10	35	150	28	Dorsolateral prefrontal	Millimeter and centimeter for y-coordinate confused during BrainMap entry	(Kosslyn et al., 1994, table 2, entry 10)
4	249, 1, 59	−31.8	48.1	2.2	Subgyral frontal lobe	Correct	S. K. Brannan, 1997, Unpublished
5	280, 1, 9	24	−70	−24	Dorsal parietal cortex	Is labeled "Right cerebellum" in the article	(Schlösser et al., 1998, table 1, entry 9)
6	4, 2, 7	−6	42	−8	Cerebellum — superior anterior	Not possible to find the foci in the article.	(Petersen et al., 1988)
7	280, 1, 7	38	24	−8	Dorsolateral parietal	Is labeled "Right orbitofrontal cortex" in the article	(Schlösser et al., 1998, table 1, entry 7)
8	249,1,29	−2	26	16	Limbic Lobe	Correct	S. K. Brannan, 1997, Unpublished
9	277, 3, 3	−50	−42	−14	Inferior frontal gyrus, posterior	Is labeled "inferior temporal gyrus posterior (area 37)" in the article	(Owen et al., 1996, table 2, entry 3)
10	115, 2, 5	−38	54	0	Middle temporal gyrus	Not resolved.	(Shaywitz et al., 1995, page 155)
11	19,2,17	24	−47	38	Frontal	Not resolved	(Pardo et al., 1991, Table 1a, entry 17)
12	47,4,1	−36	32	28	Medial frontal lobe	Correct	(George et al., 1994)
13	65, 2, 23	57	26	45	Anterior cingulate	Millimeter and centimeter for x-coordinate confused during BrainMap entry.	(O'Sullivan et al., 1994, table 4, entry 10)
14	52, 1, 2	36	−46	36	Inferior frontal gyrus	Probably misunderstanding of the text during entry. The foci is around supramarginal gyrus and the denoted "BA40".	(Becker et al., 1994, page 287)
15	61, 1, 12	−24	42	4	Temporal/insular	Resolved: Transcription mistake.	(Tulving et al., 1994, table 1)

Table 1: BrainMap outliers. The entries are ordered according to novelty. The second column indicates the paper, experiment and location identifier of the BrainMap database. The third to fifth column are x, y and z with the "reported" coordinates from BrainMap (not the corrected "Talairach 1988" coordinates).

“FUNCTIONAL VOLUMES MODELING”

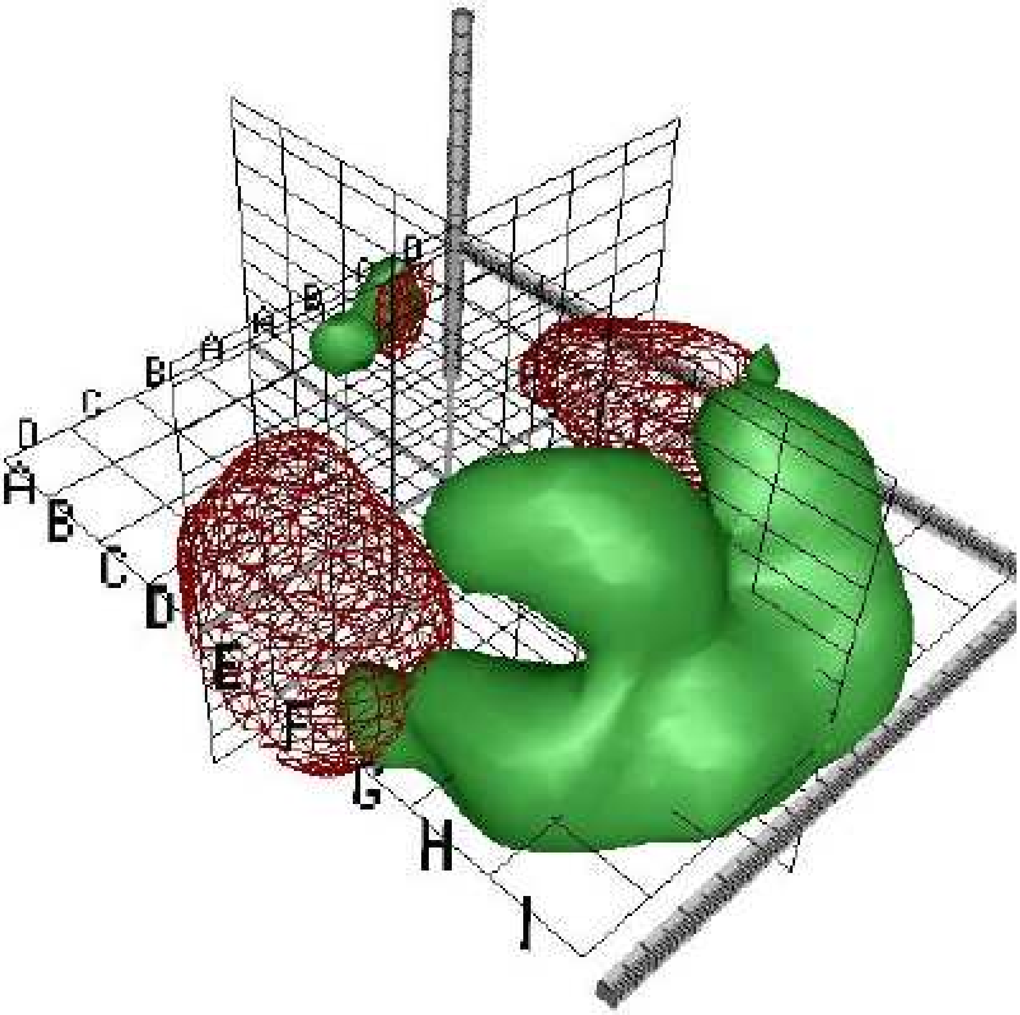
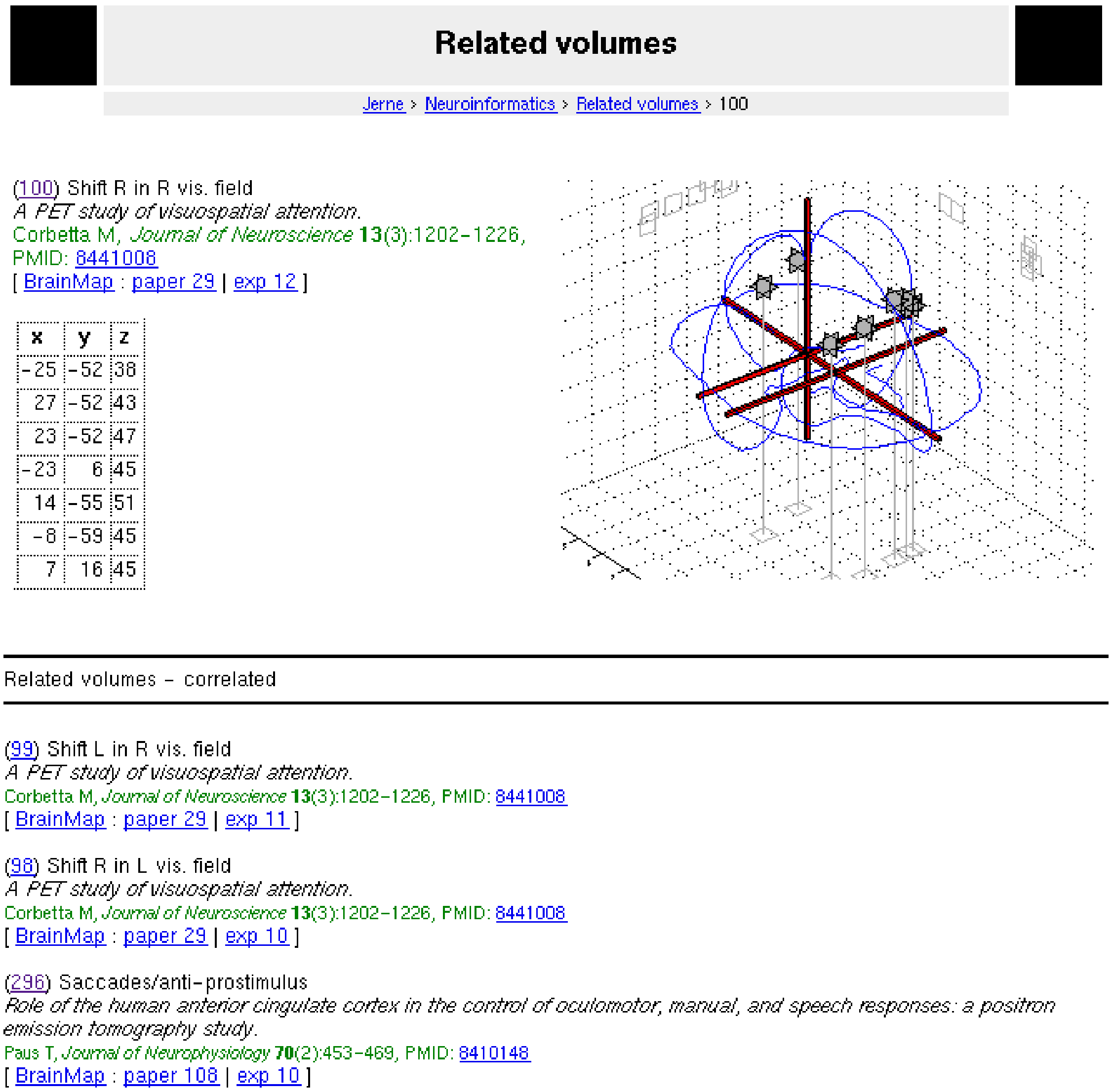


Figure 6: Densities from “Vision” and “Audition” behavioral paradigm, e.g., $p(\mathbf{x}|\mathrm{behavior} = \text{"vision"})$. VRML97 screenshot. Data from BrainMap

- Condition on “behavior”: “Functional volumes modeling” (Fox et al., 1997).
- Kernel density modeling on locations for single word reading (Turkeltaub et al., 2002).

FINDING RELATED VOLUMES



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]

Figure 7: Result page with automatically generated corner cube visualization (Corbetta et al., 1993). Two cluster of activations. Data from BrainMap.

- Each experiment a volume: $p(\mathbf{x}|\text{experiment} = 100)$ sampled on a fixed 8mm grid.
- Location data can be compared to volume data.
- Sorted list of similar volumes.

IMAGE-BASED INDICES: NOVELTY

Novelty	Entry
14278.361	265 Allison T, McCarthy G,Nobre A,Puce A,Belger A. *Human extrastriate visual cortex and the perception of faces, words, numbers, and colors* . *Cerebral Cortex* **5**:544–554, 1994.
2795.242	469 McGinnis S, –. *ROI Template II*.
1775.454	470 McGinnis S, –. *ROI Template II*.
1649.295	681 McGinnis S, –. *Anxiety Metanalysis.* , 1998.
1518.474	19 Reiman E M, Fusselman M J,Fox P T,Raichle M E. *Neuroanatomical correlates of anticipatory anxiety*. *Science* **243**(4894 Pt 1):1071–1074, 1989. PMID: 2784226.
1345.256	797 Daniela Balslev; Finn Årup Nielsen; Sally A. Frutiger; John J. Sidtis; Torben B. Christiansen; Claus Svarer; Stephen C. Strother; David A. Rottenberg; Lars K. Hansen; Olaf B. Paulson; I. Law. *Cluster analysis of activity–time series in motor learning*. *Human Brain Mapping* **15**(3), 2002. PMID: 11835604.
1206.135	555 Kawashima R, O'Sullivan B T,Roland P E. *Positron–emission tomography studies of cross–modality inhibition in selective attentional tasks: closing the "mind's eye"*. *Proceedings of the National Academy of Sciences* **92**:5969–5972, 1995.
1192.062	456 McGinnis S, –. *ROI template I*.
1022.440	279 Davis W, –. *Testing*. *Unpublished*, 1995.

Figure 8: The top of the novelty list.

- Novelty for an experiment, here: The normalized inner product with the mean volume, i.e., related to the angle between volume and mean volume.
- Unconditional novelty: Should not be as sensitive as a conditional novelty.
- Highest scoring:
  - (Allison et al., 1994): Only EEG study in the database, only x and y coordinates are given.
  - (Reiman et al., 1989): Perhaps a muscle "activation". Correction: (Drevets et al., 1992).
  - (Balslev et al., 2002): Perhaps a motion artifact.

IMAGE-BASED INDICES: SVD

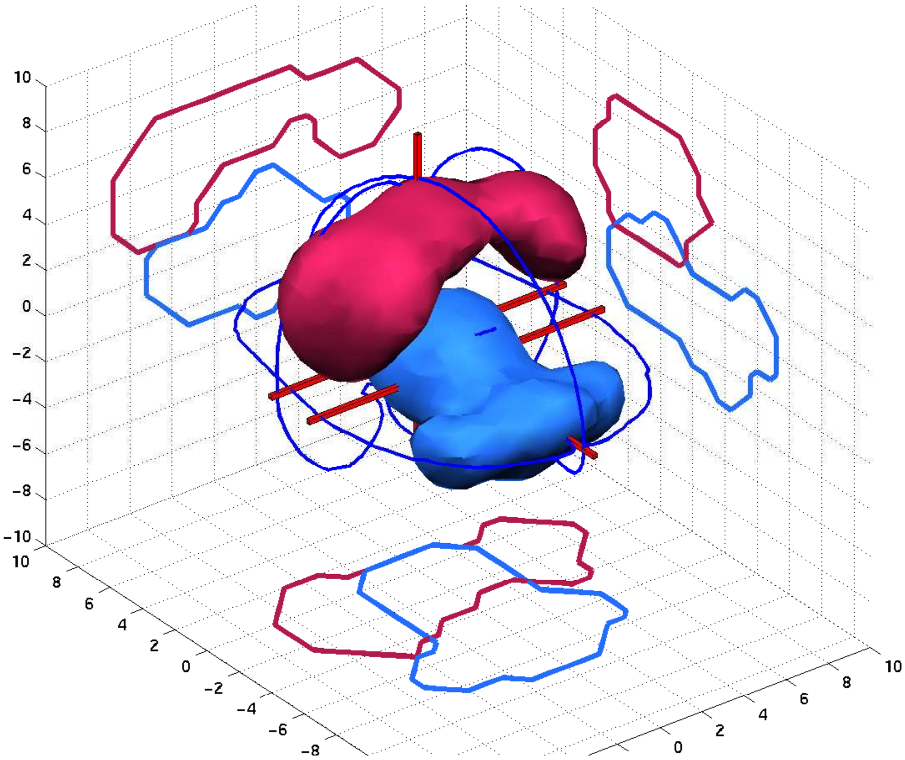


Figure 9: Both ends of the second eigenimage $\mathbf{v}_2$ from an analysis of data from BrainMap.

- Singular value decomposition of the (experiment $\times$ voxel) data matrix: $\mathbf{ULV}^\mathsf{T} = \mathrm{svd}(\mathbf{X})$. Columns of $\mathbf{V}$ is called eigenimages.
- Second eigenimage: One end interpreted as sensorimotor("upper extremity movements", "thumb-finger opposition"), other end as visual ("Watch virtual reality right hand grasping objects").
- Higher components have increasing spatial frequency.

IMAGE-BASED INDICES: ICA

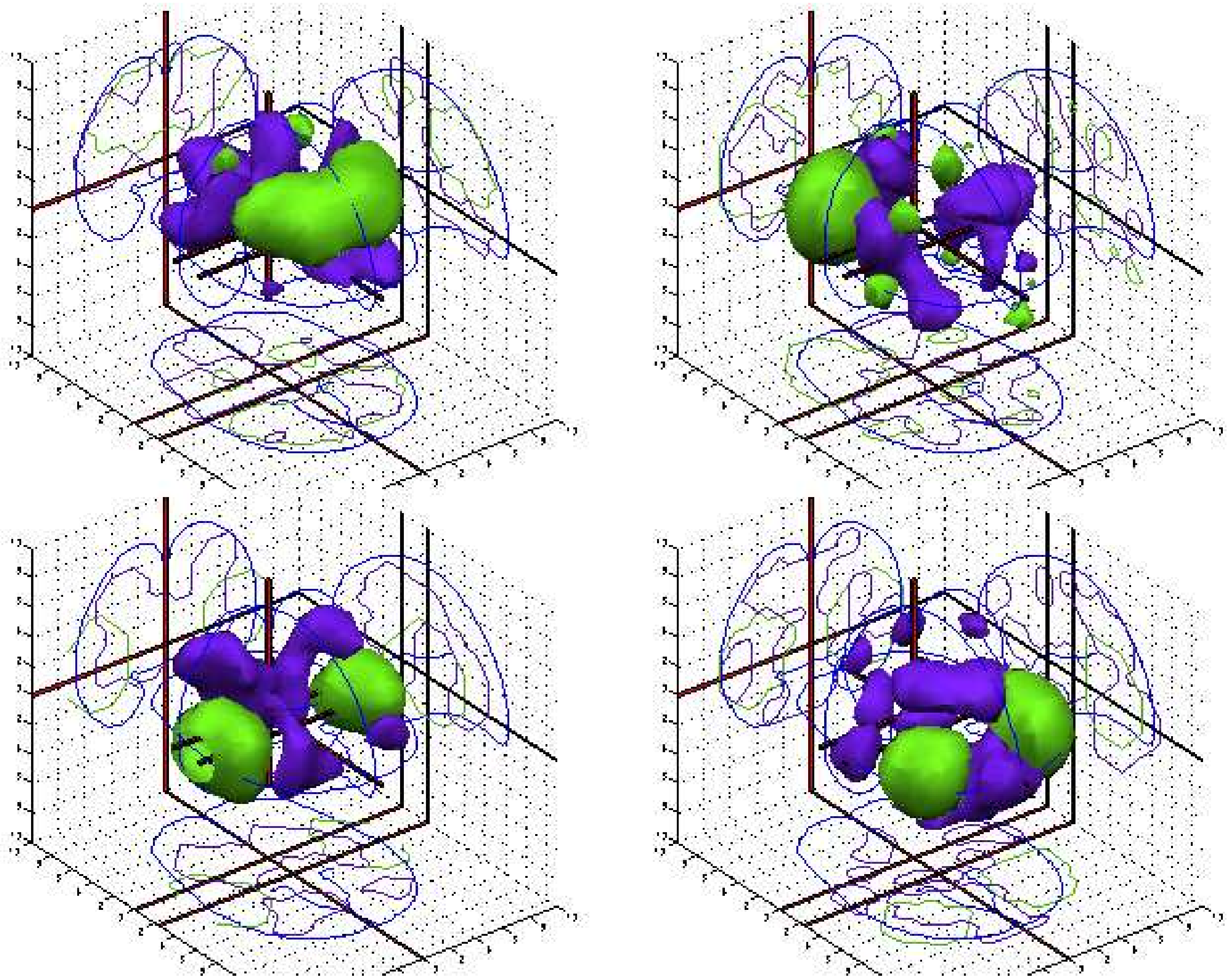


Figure 10: Both ends of the third to sixth source images $\mathrm{s}_3, \ldots, \mathrm{s}_6$. Data from Brede.

- Independent component analysis of the $\mathbf{X}(\text{experiment} \times \text{voxel})$ data matrix: $\mathbf{AS} = \text{ica}(\mathbf{X})$. $\mathbf{A}$ is the mixing matrix, $\mathbf{S}$ the sources.
- ICA components: hand movement, visuospatial, words/verbs, audition, visual motion.

IMAGE-BASED INDICES: ASYMMETRY

Rank	Probability	Total	Left	Right	Anatomical label
1	0.00171	13	1	12	anterior cerebellum
2	0.00183	44	12	32	vermis
3	0.00195	9	0	9	calcarine sulcus
4	0.00591	20	4	16	calcarine
5	0.00693	38	11	27	cerebellar vermis
6	0.00781	7	0	7	right
7	0.01983	290	127	163	cerebellum
8	0.03125	5	0	5	homologue
9	0.03125	5	0	5	temporal occipital
10	0.03125	5	0	5	broca homologue
11	0.03125	5	0	5	cerebrum
12	0.05923	15	4	11	colliculus

Table 2: Right dominant brain asymmetry.

- "Experiment" left/right asymmetry: Count the number of locations in the left side X

$$P_{\mathrm{Bin}} = \sum_{0}^{X} \begin{pmatrix} N \\ X \end{pmatrix} 0.5^N. \tag{2}$$

  Normalize the value to $[-1; +1]$ range

$$a = 1 - 2P_{\mathrm{Bin}}. \tag{3}$$

- For anatomical labels the measure will be biased due to correlated entries: an author within a paper tend to use the same labeling scheme.
- Left dominate (-1): 'motor', 'area', 'cortex', . . . , 'broca s area'.
- Right dominate (+1): 'anterior cerebellum',

CONCLUSION

- Modeling 3D Talairach coordinates with kernel density estimators.
- Visualization with Corner Cube Environments.
- Novelty detection, finding related experiments, functional volumes modeling.
- Brede neuroinformatics toolbox: Primarily written in Matlab. Includes the Brede database in XML. http://hendrix.imm.dtu.dk/software/brede/.
- Results available on the Internet from hendrix.imm.dtu.dk more specifically http://hendrix.imm.dtu.dk/services/jerne/.
- Publications available from homepage http://www.imm.dtu.dk/~fn/.

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