Virtual brain mapping: Meta-analysis and visualization in functional neuroimaging

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ABSTRACT

Results from functional neuroimaging such as positron emission tomography and functional magnetic resonance are often reported as sets of 3-dimensional coordinates in Talairach stereotactic space. By utilizing data collected in the BrainMap database and from our own small XML database we can automatically model and visualize several studies at once. We model a set of 3-dimensional coordinates by a voxelization step where flexible probability density models such as kernel density estimators produce a voxel-volume representation of a study, allowing us to represent all coordinate data in one single data matrix.

By conditioning on elements in the databases other than the coordinate data, e.g., anatomical labels associated with many coordinates we can make conditional novelty detection identifying outliers in the database that might be errorneous entries or seldom occuring patterns. In the BrainMap database we found errors, e.g., stemming from confusion of centimeters and millimeters during entering and errors in the original article. Conditional probability density modeling also enables generation of probabilistic atlases and automatic probabilistic anatomical labeling of new coordinates. By conditioning on the behavioral domains associated with each study, e.g, the words ‘word’ and ’visual’, we can make virtual brain activations.

Voxelization also permits us to find related volumes, where query volumes are matched with database items and the most related volumes are found and returned in sorted lists. Image-based indices can be created by singular value decomposition and by matching individual volumes against eigenimages.

Individual experiments, sets of experiments as well as results from meta-analyses can be rendered as glyphs, cut-planes or isosurfaces in 3-dimensional Corner Cube Environments or exported as VRML97 and made available on the Internet, see http://hendrix.imm.dtu.dk.

OUTLINE

- Functional neuroimaging
- The BrainMap database
- Modeling “locations”
- Novelty detection
- Functional volumes modeling
- Finding related volumes
  - Novelty
  - SVD
  - Asymmetry
- Database in XML.
- Information visualization

FUNCTIONAL NEUROIMAGING

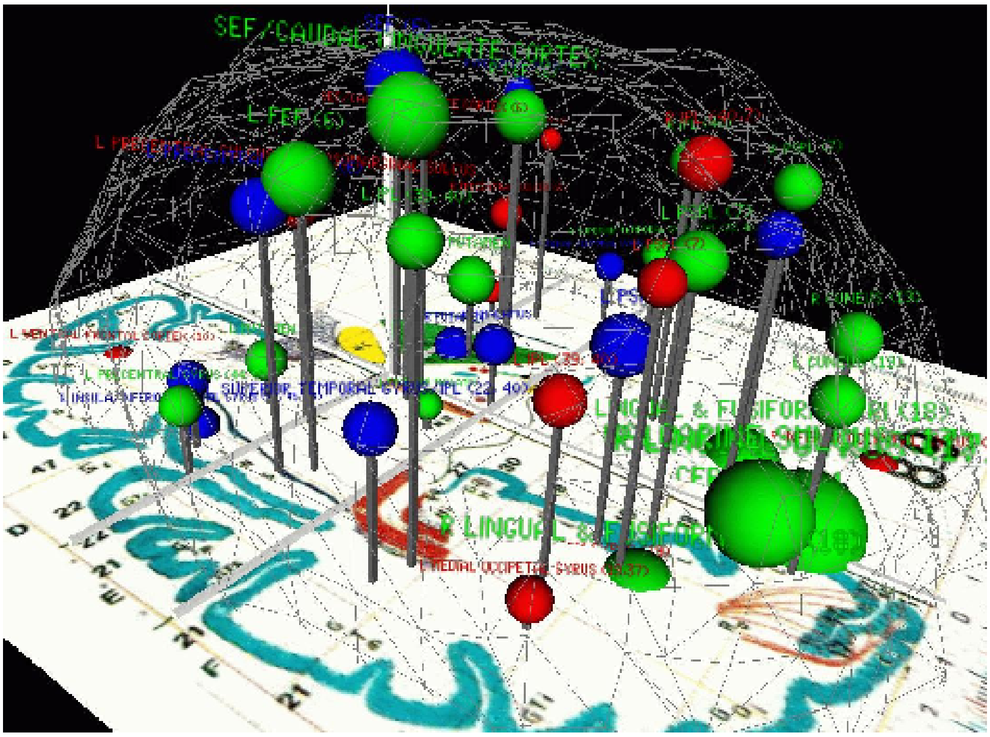
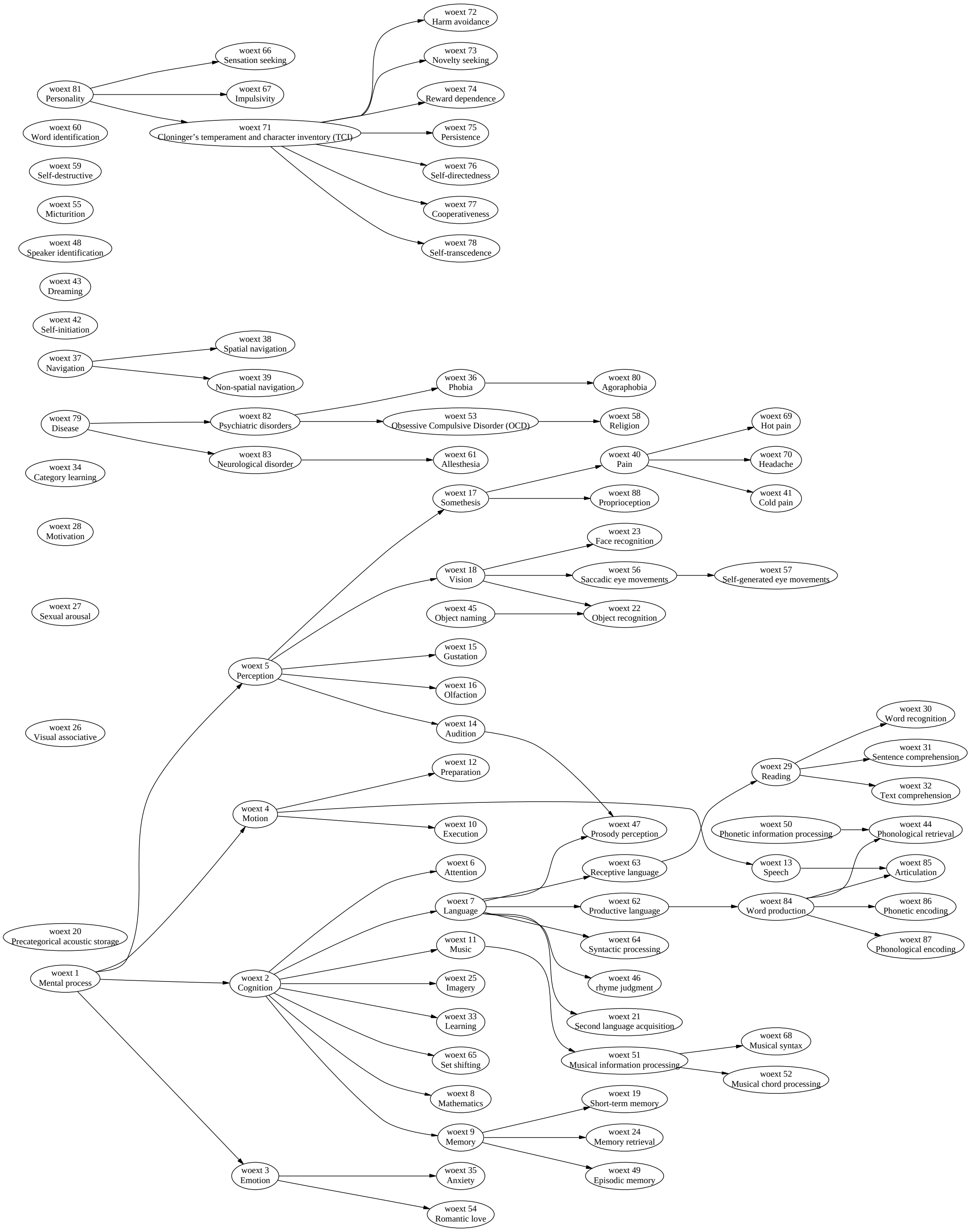


Figure 1: Locations from (Law, 1996): Saccadic eye movements.

- Functional neuroimaging, brain mapping: Finding cognitive components, e.g., “willed action”.
- 3 different data types + behavior
  - “Paper”: Bibliographic information, PubMed.
  - “Experiment” (contrast/summary image): Description of paradigm (stimulus/response/ instructions), scanner, volume or locations.
  - “Location”: 3D stereotactic coordinates (point) in Talairach space, anatomical/functional/ Brodmann labels, magnitude.

COGNITIVE COMPONENTS



THE BRAINMAP DATABASE

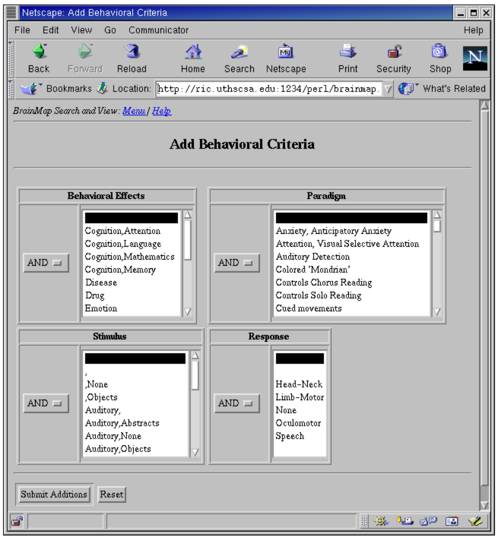


Figure 2: Behavioral criteria query web-page.

- *BrainMap* database: *Research Imaging Center*, San Antonio, Texas, http://ric.uthscsa.edu. (Fox and Lancaster, 1994)
- Consists of: Entry + Database + Search and View.
  - “BrainMap Entry”. Limited distribution.
  - Database. Oracle SQL Relational database.
  - “BrainMap Search & View”. Version with visualization for SUN computer. Internet version.
- Paper (225), Experiment (771), Location (7683, 3935 with anatomical and Brodmann labels).
- Superseded with the BrainMap DBJ http://www.brainmapdbj.org/.

LOCATIONS AND VOLUMES

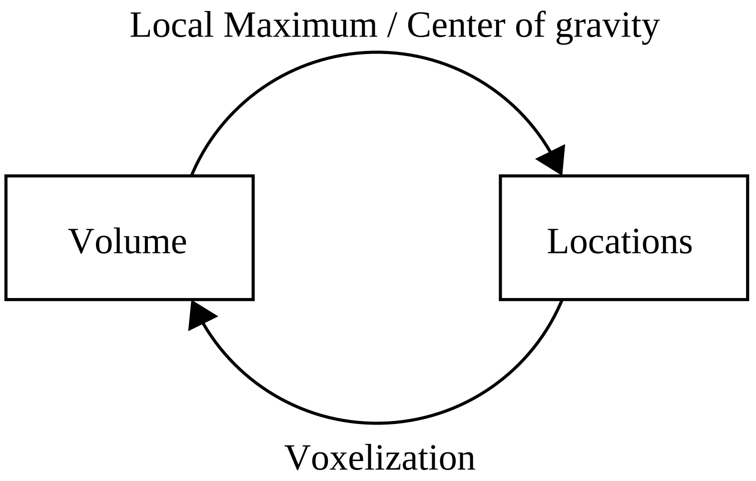


Figure 3: Voxelization.

- From volume to points:
  - Peak/local maxima
  - Center of gravity/mass.
- From points to volume: “Voxelization”
  - Regard the “locations” as being generated from a distribution $p(\mathbf{x})$, where $\mathbf{x}$ is in 3D Talairach space.
  - Models:
    - Simple parametric distribution. Problem with complex distributions, e.g., bimodal.
    - Mixture models. How many components. What width and shape.
    - Kernel method. What width and shape.

MODELING “LOCATIONS”

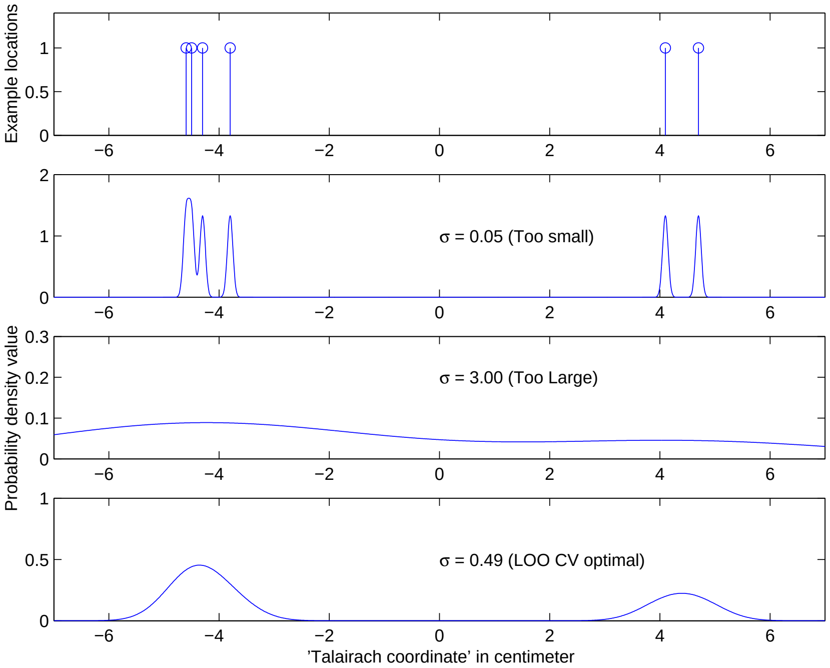


Figure 4: Example of probability density modeling

- Finite Gaussian mixture modeled with K determined by AIC and the covariance and center determined on different parts of the data set (Hansen et al., 2000b).
- “Kernel methods” (kernels centered on each object: $K = N$) with homogeneous Gaussian kernel

$$\hat{p}(\mathbf{x}) = N^{-1} \sum_{n}^{N} \tilde{p}_n(\mathbf{x}) \tag{1}$$

$$\tilde{p}_n(\mathbf{x}) = (2\pi\sigma^2)^{-3/2} \exp\left(-\frac{1}{2\sigma^2} (\mathbf{x} - \boldsymbol{\mu}_n)^2 \right) \tag{2}$$

MODELING OF ANATOMICAL LABELS AND 3D TALAIRACH LABELS

- Modeling the relation between *3D Talairach Coordinates* (three dimensional continuous value) and *anatomical labels* ("lobar anatomy" text field BrainMap field).
- Novelty detection: Discover unusual entries.

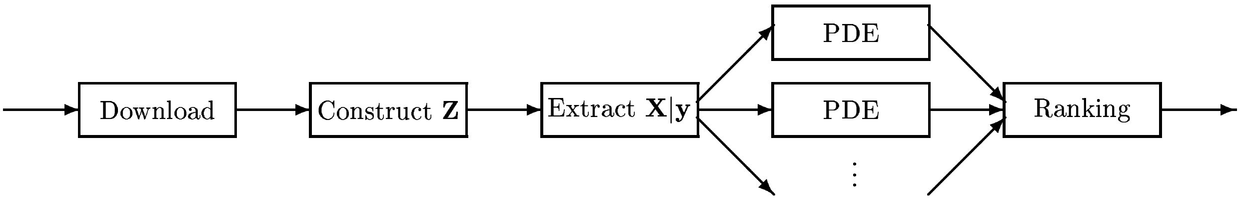
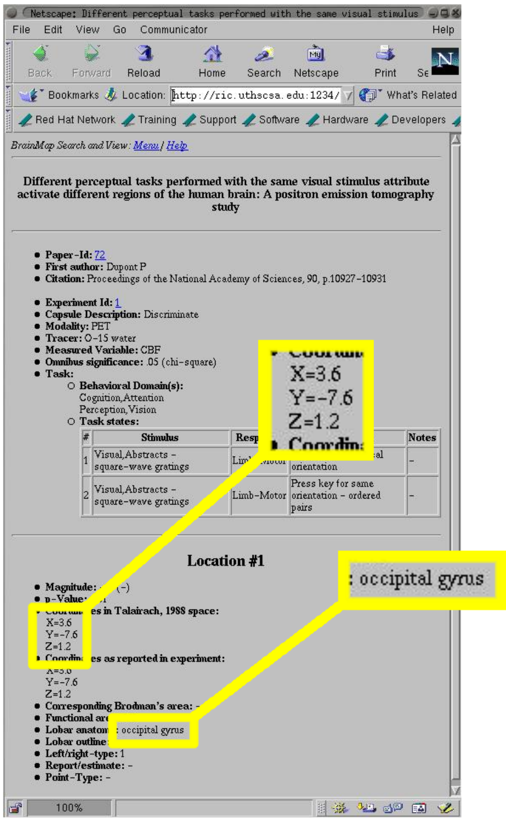


Figure 5: Processing scheme for finding outliers in BrainMap

- Download BrainMap web-page with a Perl/Matlab script.
- Construct a matrix $\mathbf{Z}(N \times P) = [\mathbf{X}, \mathbf{Y}]$ that contains N rows corresponding to $N = 3935$ locations.
- Extract submatrix $\mathbf{X}$ that contains Talairach coordinate for a given phrase.
- Construct probability density estimates (PDE) for each submatrix.
- Rank locations according to their density values.

EXTRACTING LOCATION DATA



BrainMap Search and View: *Menu* / *Help*

Different perceptual tasks performed with the same visual stimulus attribute activate different regions of the human brain: A positron emission tomography study

- **Paper-Id:** 72
- **First author:** Dupont P
- **Citation:** Proceedings of the National Academy of Sciences, 90, p.10927-10931

- **Experiment Id:** 1
- **Capsule Description:** Discriminate
- **Modality:** PET
- **Tracer:** O-15 water
- **Measured Variable:** CBF
- **Omnibus significance:** .05 (chi-square)
- **Task:**
  - **Behavioral Domain(s):** Cognition,Attention Perception,Vision
  - **Task states:**

#	Stimulus	Resp		Notes
1	Visual,Abstracts - square-wave gratings	Lim	al orientation	-
2	Visual,Abstracts - square-wave gratings	Limb-Motor	Press key for same orientation - ordered pairs	-

Location #1

- **Magnitude:** (-)
- **p-Value:**
- es in Talairach, 1988 space: X=3.6 Y=-7.6 Z=1.2
- es as reported in experiment: Y=-7.6 Z=1.2
- **Corresponding Brodman's area:** -
- **Functional are**
- **Lobar anatom** : occipital gyrus
- **Lobar outline**
- **Left/right-type:** 1
- **Report/estimate:** -
- **Point-Type:** -

Figure 6: Extraction of data from a "location".

- Extraction of Talairach coordinate. Example (3.6, -7.6, 1.2).
- Extraction of each word and phrase from the field "Lobar anatomy".
- Example "lateral superior parietal" → {"lateral", "superior", "parietal", "lateral superior", "superior parietal", "lateral superior parietal"}.
- Multiple data generated for one location.

MODELING OF ANATOMICAL LABELS AND 3D TALAIRACH LABELS

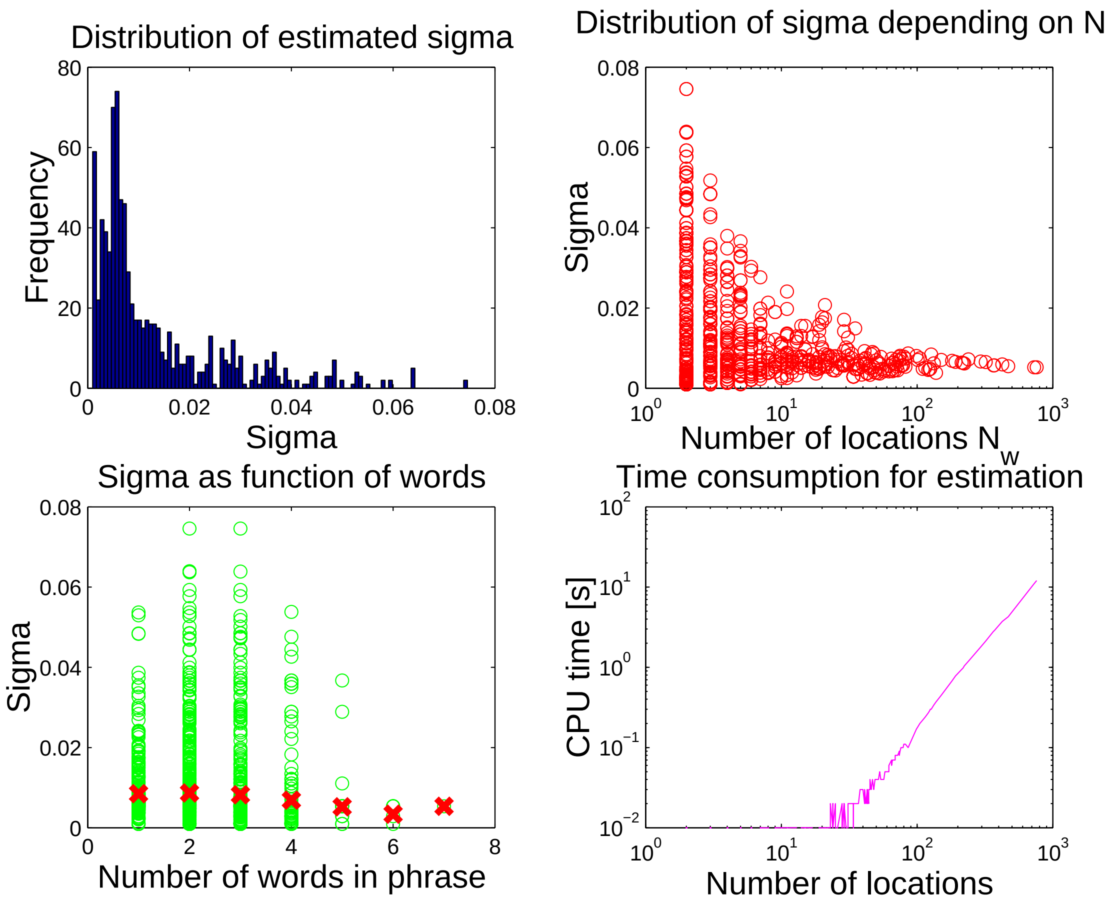


Figure 7: Sigma: width of kernel

- Conditional probability: $p(\mathbf{x}|c)$, where c is a word/phrase.
- Optimize kernel width σ with leave-one-out cross-validation.
- Robust estimate of $p(\mathbf{x})$ by excluding the 5% most extreme locations (as determined by their density value) in a two-stage scheme.

PDFS FOR LOCATION LABELS

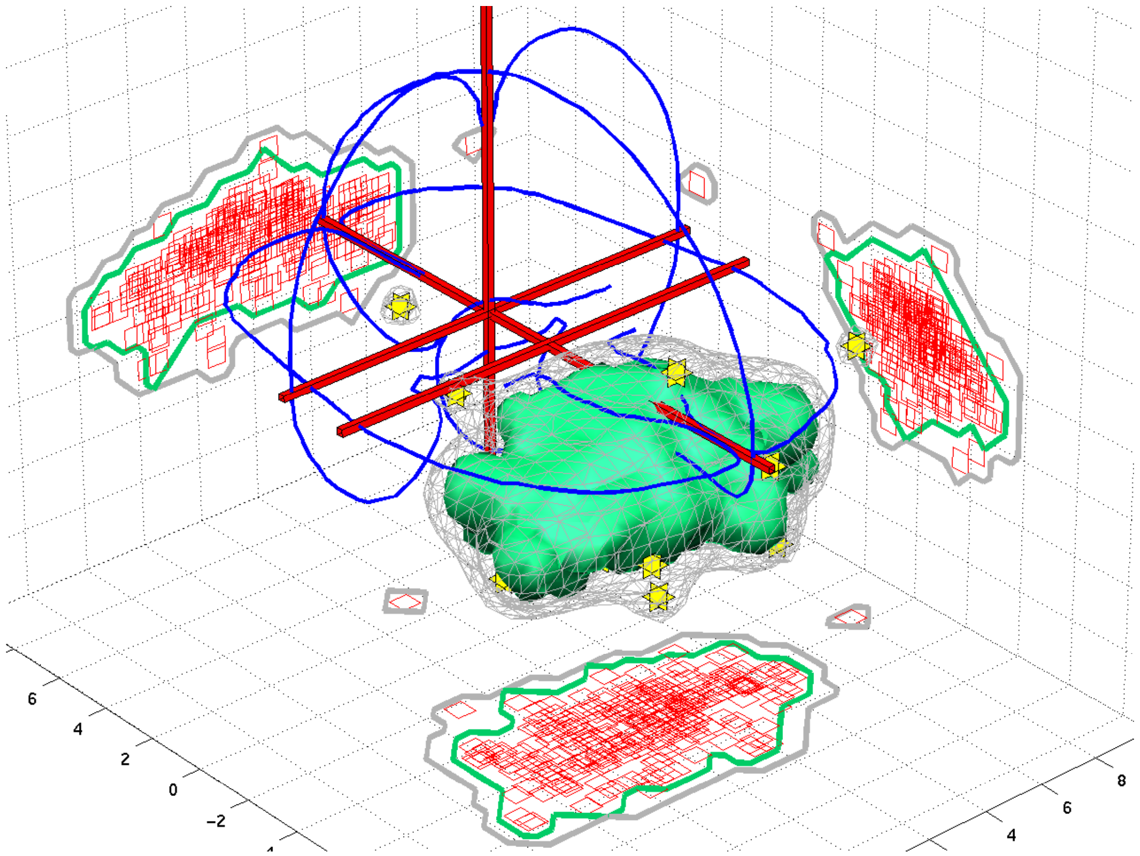
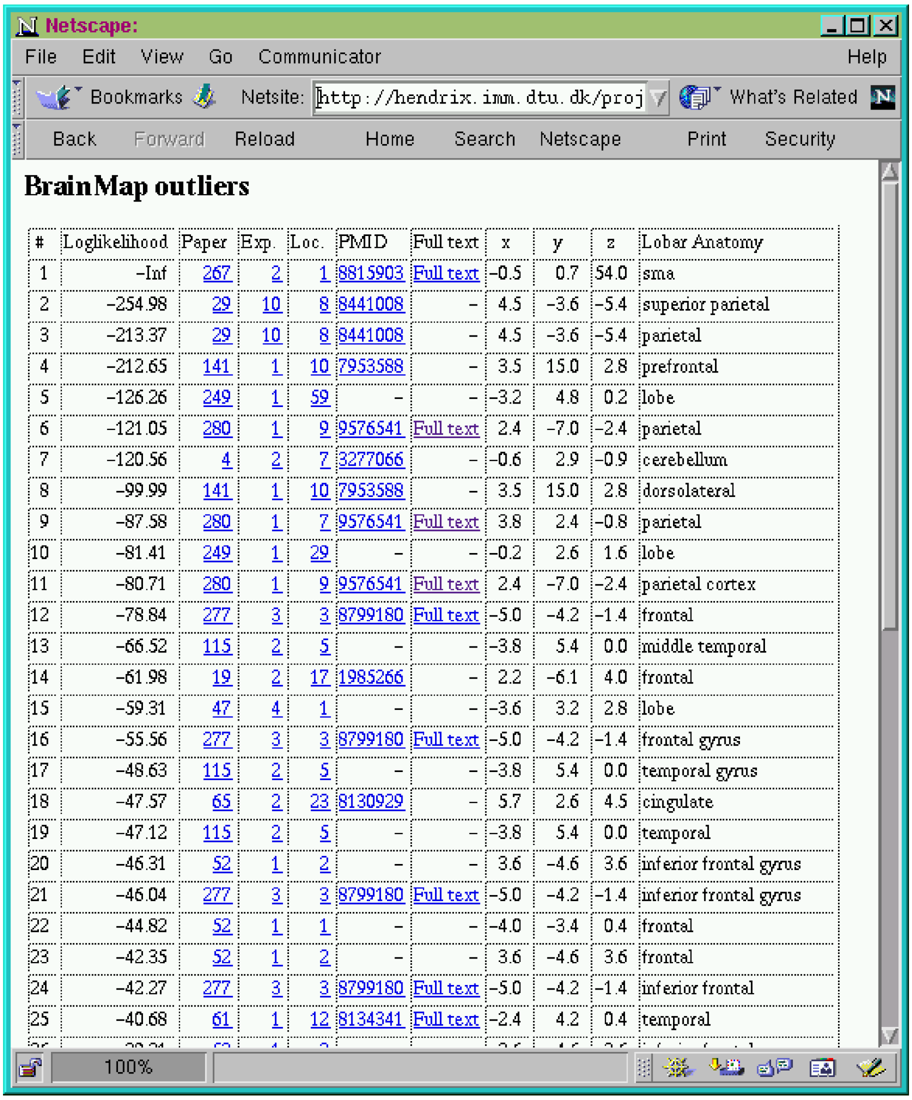


Figure 8: Densities from cerebellum locations. Yellow “points” are the BrainMap locations.

- Condition on anatomical label: $p(\mathbf{x}|c = \text{cerebellum})$.
- Corner Cube Enviroment (Rehm et al., 1997).
- Yellow glyphs: Original BrainMap locations.
- Grey wireframe: Isosurface in the first level probability density estimate.
- Green surface: Isosurface in the second level.

RANKING OF OUTLIERS



BrainMap outliers

#	Loglikelihood	Paper	Exp.	Loc.	PMID	Full text	x	y	z	Lobar Anatomy
1	-Inf	267	2	1	8815903	Full text	-0.5	0.7	54.0	sma
2	-254.98	29	10	8	8441008	-	4.5	-3.6	-5.4	superior parietal
3	-213.37	29	10	8	8441008	-	4.5	-3.6	-5.4	parietal
4	-212.65	141	1	10	7953588	-	3.5	15.0	2.8	prefrontal
5	-126.26	249	1	59	-	-	-3.2	4.8	0.2	lobe
6	-121.05	280	1	9	9576541	Full text	2.4	-7.0	-2.4	parietal
7	-120.56	4	2	7	3277066	-	-0.6	2.9	-0.9	cerebellum
8	-99.99	141	1	10	7953588	-	3.5	15.0	2.8	dorsolateral
9	-87.58	280	1	7	9576541	Full text	3.8	2.4	-0.8	parietal
10	-81.41	249	1	29	-	-	-0.2	2.6	1.6	lobe
11	-80.71	280	1	9	9576541	Full text	2.4	-7.0	-2.4	parietal cortex
12	-78.84	277	3	3	8799180	Full text	-5.0	-4.2	-1.4	frontal
13	-66.52	115	2	5	-	-	-3.8	5.4	0.0	middle temporal
14	-61.98	19	2	17	1985266	-	2.2	-6.1	4.0	frontal
15	-59.31	47	4	1	-	-	-3.6	3.2	2.8	lobe
16	-55.56	277	3	3	8799180	Full text	-5.0	-4.2	-1.4	frontal gyrus
17	-48.63	115	2	5	-	-	-3.8	5.4	0.0	temporal gyrus
18	-47.57	65	2	23	8130929	-	5.7	2.6	4.5	cingulate
19	-47.12	115	2	5	-	-	-3.8	5.4	0.0	temporal
20	-46.31	52	1	2	-	-	3.6	-4.6	3.6	inferior frontal gyrus
21	-46.04	277	3	3	8799180	Full text	-5.0	-4.2	-1.4	inferior frontal gyrus
22	-44.82	52	1	1	-	-	-4.0	-3.4	0.4	frontal
23	-42.35	52	1	2	-	-	3.6	-4.6	3.6	frontal
24	-42.27	277	3	3	8799180	Full text	-5.0	-4.2	-1.4	inferior frontal
25	-40.68	61	1	12	8134341	Full text	-2.4	4.2	0.4	temporal

Figure 9: Densities from cerebellum locations.

- Automatic generated list.
- Entries sorted according to novelty.
- 2nd and 3rd entry: More information in a phrase than in a word.

“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).

THE WORD "LOBE"

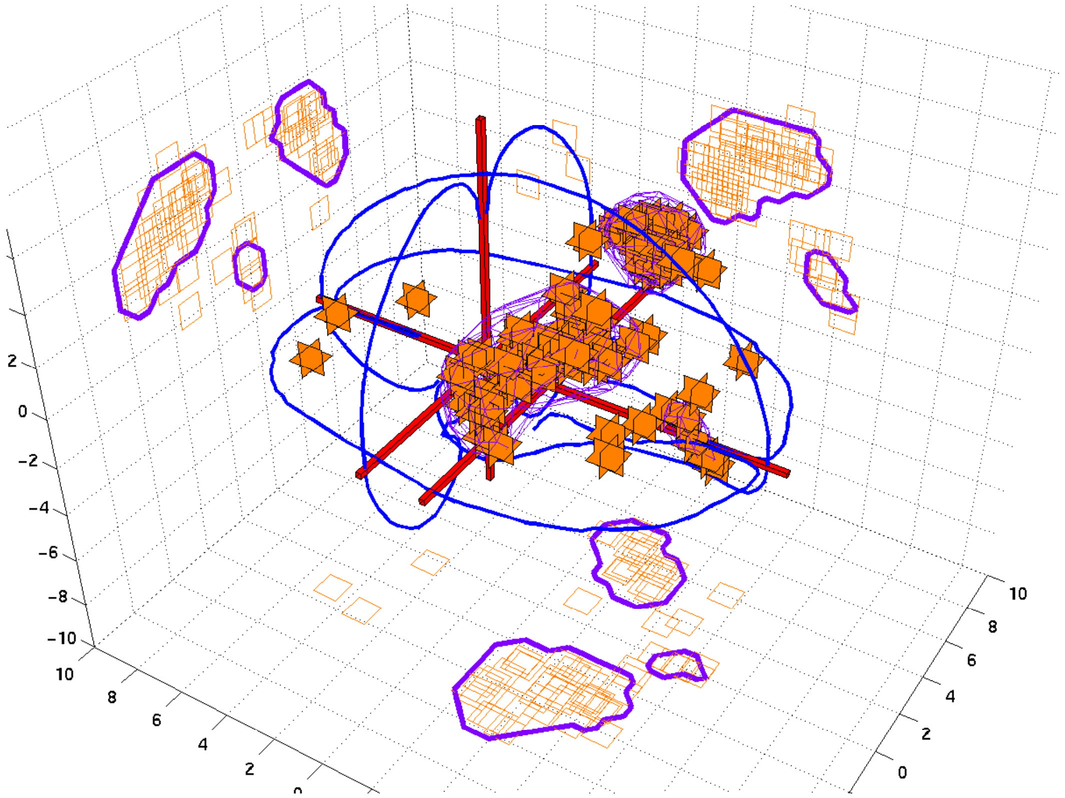


Figure 10: Probability density estimation of "lobe". The blue/magenta wire-frame model is the second stage probability density estimate at a $P_{\text{HPD}} = 0.5$ threshold, and the orange glyphs are the "lobe" BrainMap locations.

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.

OTHER BRAIN ATLASES

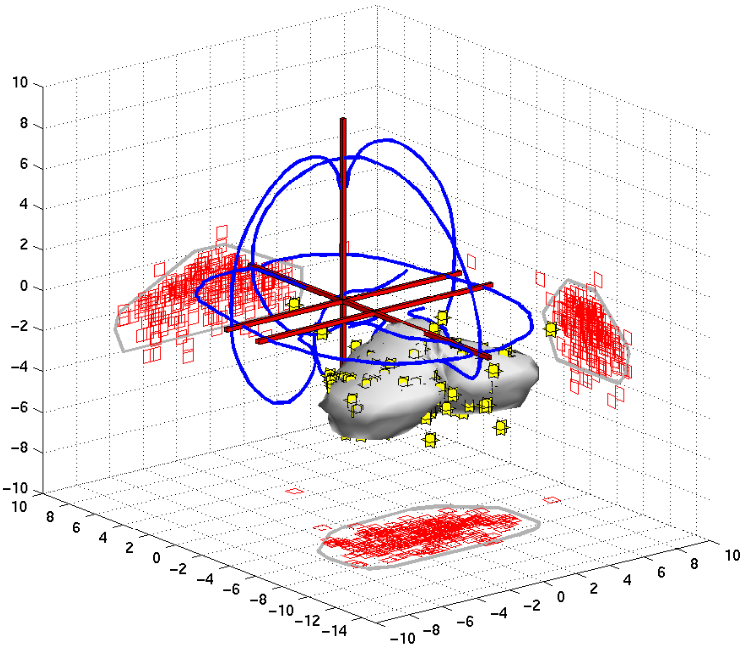


Figure 11: Talairach cerebellum.

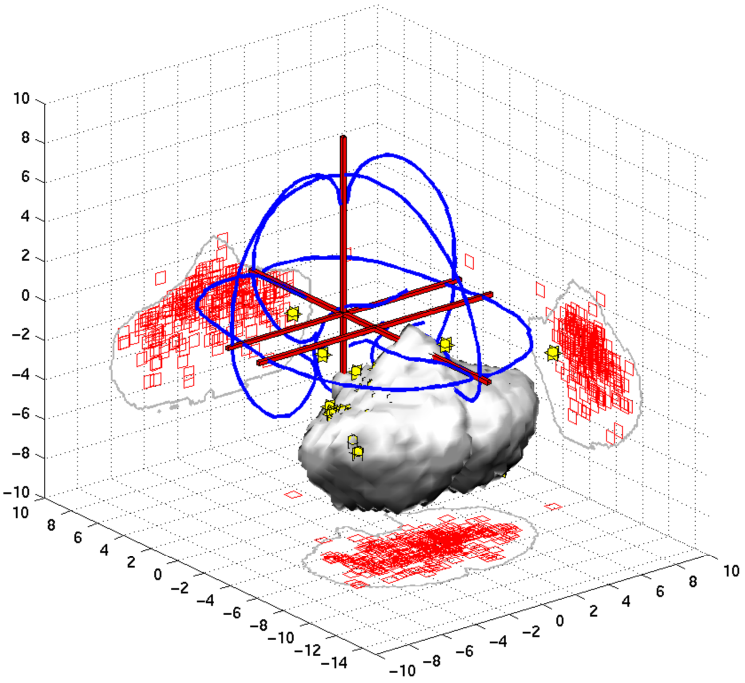
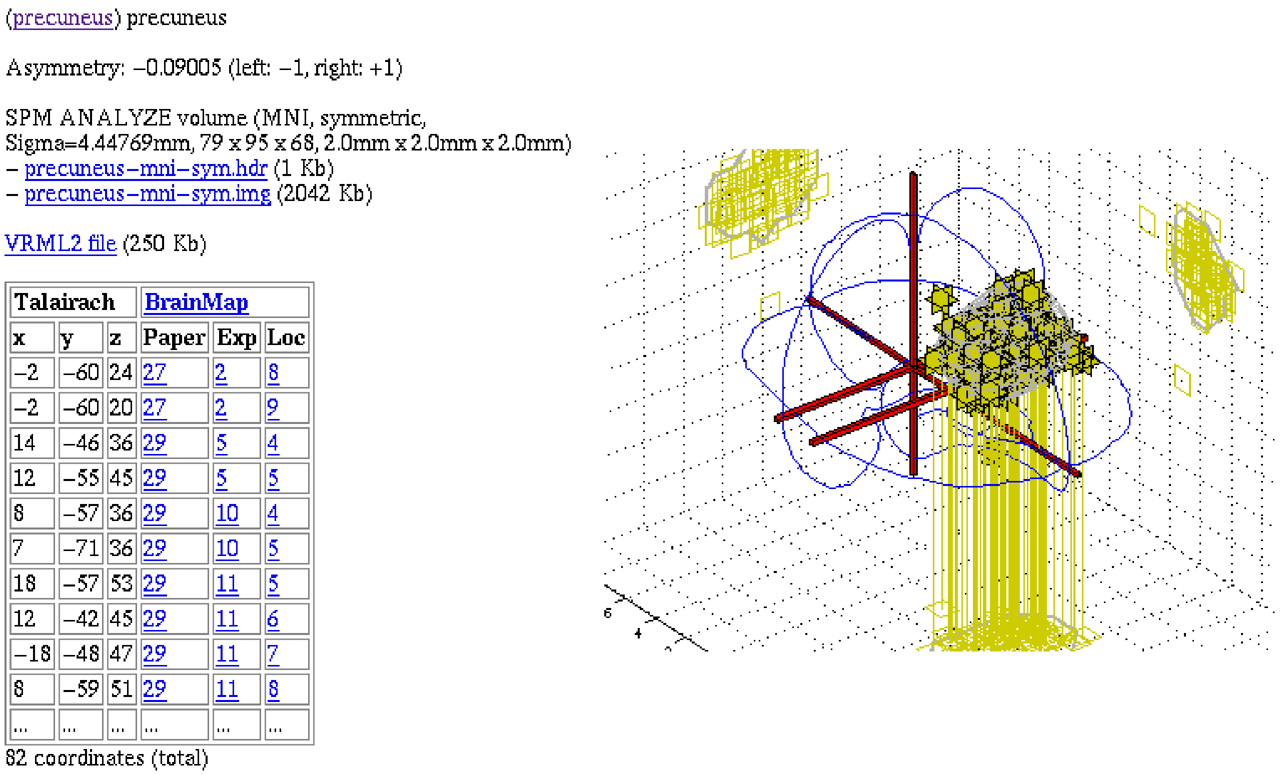


Figure 12: MNI cerebellum.

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)

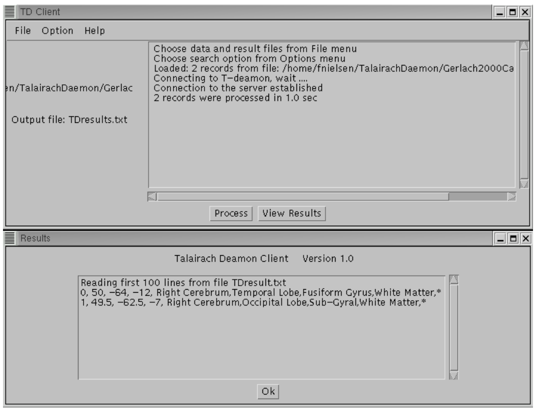
Talairach			BrainMap		
x	y	z	Paper	Exp	Loc
−2	−60	24	27	2	8
−2	−60	20	27	2	9
14	−46	36	29	5	4
12	−55	45	29	5	5
8	−57	36	29	10	4
7	−71	36	29	10	5
18	−57	53	29	11	5
12	−42	45	29	11	6
−18	−48	47	29	11	7
8	−59	51	29	11	8
...	...	...	...	...	...

82 coordinates (total)

Figure 13: “Posterior cingulate” web-page.

- Collaborative efforts sometimes better than individual experts
  - In modeling of fMRI with “consensus models” (Hansen et al., 2000a) where the average model perform better the individual models.
  - Information (artificial) markets (Pennock et al., 2001a; Pennock et al., 2001b) where Internet games (Foresight Exchange, HSX) make good predictors.

AUTOMATIC LABELING. PRIOR WORK



```
en/TalairachDaemon/Gerlac

Output file: TDresults.txt
```

```
Choose data and result files from File menu
Choose search option from Options menu
Loaded: 2 records from file: /home/fnielsen/TalairachDaemon/Gerlach2000Ca
Connecting to T-deamon, wait ....
Connection to the server established
2 records were processed in 1.0 sec
```

```
Talairach Deamon Client    Version 1.0
```

```
Reading first 100 lines from file TDresult.txt
0, 50, −64, −12, Right Cerebrum,Temporal Lobe,Fusiform Gyrus,White Matter,*
1, 49.5, −62.5, −7, Right Cerebrum,Occipital Lobe,Sub−Gyral,White Matter,*
```

Figure 14: Screenshot from the Talairach Daemon.

- Talairach coordinate → Neuroanatomical label.
- Digital brain atlas based:
  - Talairach Daemon based on Talairach and MNI atlas (Lancaster et al., 2000b; Lancaster et al., 1997). Java-based Internet service and stand-alone Java program (Lancaster et al., 2000a).
  - ANIMAL (Collins et al., 1995).
  - CIeMed (Nowinski et al., 1995) based on Talairach and Schaltenbrand (Schaltenbrand and Wahren, 1977). CD-ROM (Nowinski et al., 1997).
  - Harvard brain atlas (Kikinis et al., 1996) co-registered with MNI (Klein and Hirsch, 2001).

AUTOMATIC LABELING

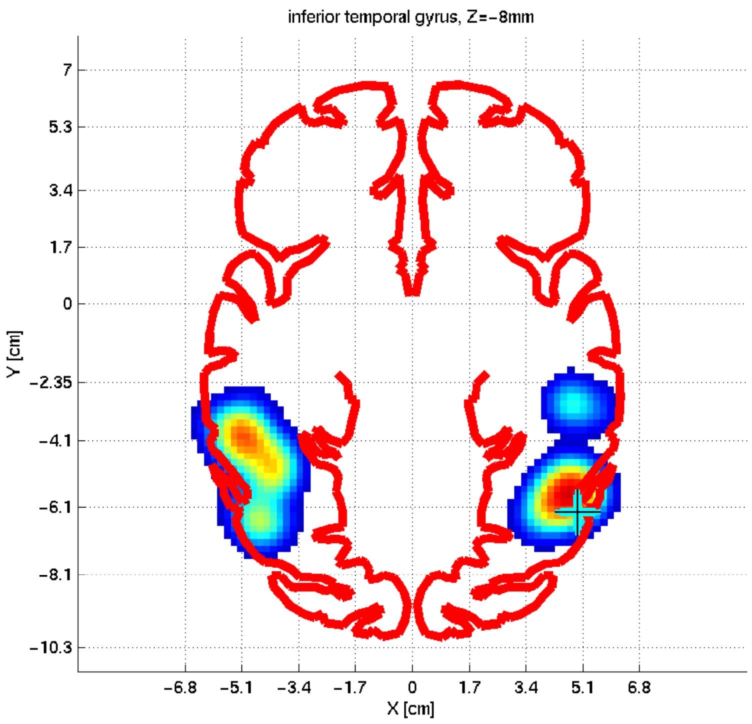


Figure 15: Probability density of "Inferior temporal gyrus".

- Automatic labeling through labeling in the literature via BrainMap.
- Generate densities for each of anatomical label. Here fixed width kernel density modeling and coarse sampling: 8mm.
- Sort on densities.
- Or generate distribution: $P(\mathbf{x}) = \sum_{p(\mathbf{x}')>p(\mathbf{x})} p(\mathbf{x}')$ and sort that.

AUTOMATIC LABELING: EXAMPLE

Labeler	Label
Christian Gerlach	R. Inferior temporal gyrus
TD (50, -64, -12)	Right Cerebrum,Temporal Lobe,Fusiform Gyrus,White Matter,*
TD (49.5, -62.5, -7)	Right Cerebrum,Occipital Lobe,Sub-Gyral,White Matter,*
TD (50, -64, -12)	Temporal_Lobe 100.00
TD (49.5, -62.5, -7)	Occipital_Lobe 7.70,Temporal_Lobe 62.35

Table 2: An example location: Talairach Daemon labeling. (Gerlach et al., 2000, table 1, entry 1): "R. Inferior temporal gyrus", (50, -64, -12), BA37. Brett's nonlinear transformation: MNI → (Brett) → Talairach: (49.5 -62.5 -7).

Density	P-value	#	Lobar anatomy
12472.34	0.9347557264	5	occipito
10143.67	0.9329029335	37	inferior temporal gyrus
15590.43	0.9264361436	4	occipito temporal
2528.44	0.9163056567	367	inferior
3917.70	0.9075731229	48	ventral
9671.07	0.9026819368	66	inferior temporal
15375.41	0.8024087613	7	ventral surface
15375.41	0.8024087613	7	surface
1200.74	0.7883446267	762	gyrus
9475.11	0.7713286841	22	inferior occipital
3607.68	0.8635240291	48	ventral
16900.23	0.8544980115	3	inferior temporal gyrus posterior
2091.93	0.8438028002	367	inferior
20796.17	0.8273447873	5	inferior lateral
8450.12	0.8225637414	6	temporal gyrus posterior
1862.94	0.8083775236	99	lateral
7395.51	0.7818767138	37	inferior temporal gyrus
6982.64	0.7533701307	66	inferior temporal
8632.66	0.7106316973	22	inferior occipital
7242.96	0.6965897412	7	gyrus posterior

Table 3: An example location: Labeled through BrainMap. With Brett's transformation above the line. # is the number of locations defining the volume.

“FUNCTIONAL VOLUMES MODELING”

- Condition on “behavior”.
- “Functional volumes modeling” (Fox et al., 1997; Fox et al., 1999; Fox et al., 2001). Single Gaussian on location for mouth area.
- Kernel density modeling on locations for single word reading (Turkeltaub et al., 2002; Turkeltaub et al., 2001).
- Discrimination between to sets of locations: Hotelling’s T^2 statistics (Christoff and Grabrieli, 2000, page 176), Multidimensional Kolmogorov-Smirnov (Duncan and Owen, 2000).
- Language studies with Brodmann areas (Indefrey and Levelt, 2000; Indefrey, 2001).
- Voxel-based method (Herskovits et al., 1999; Herskovits, 2000).
- Problem:
  - Behavior annotation is on the level of the experiment
  - Abstract and other bibliographic information are on a yet higher level.

DENSITIES FOR "BEHAVIOR"

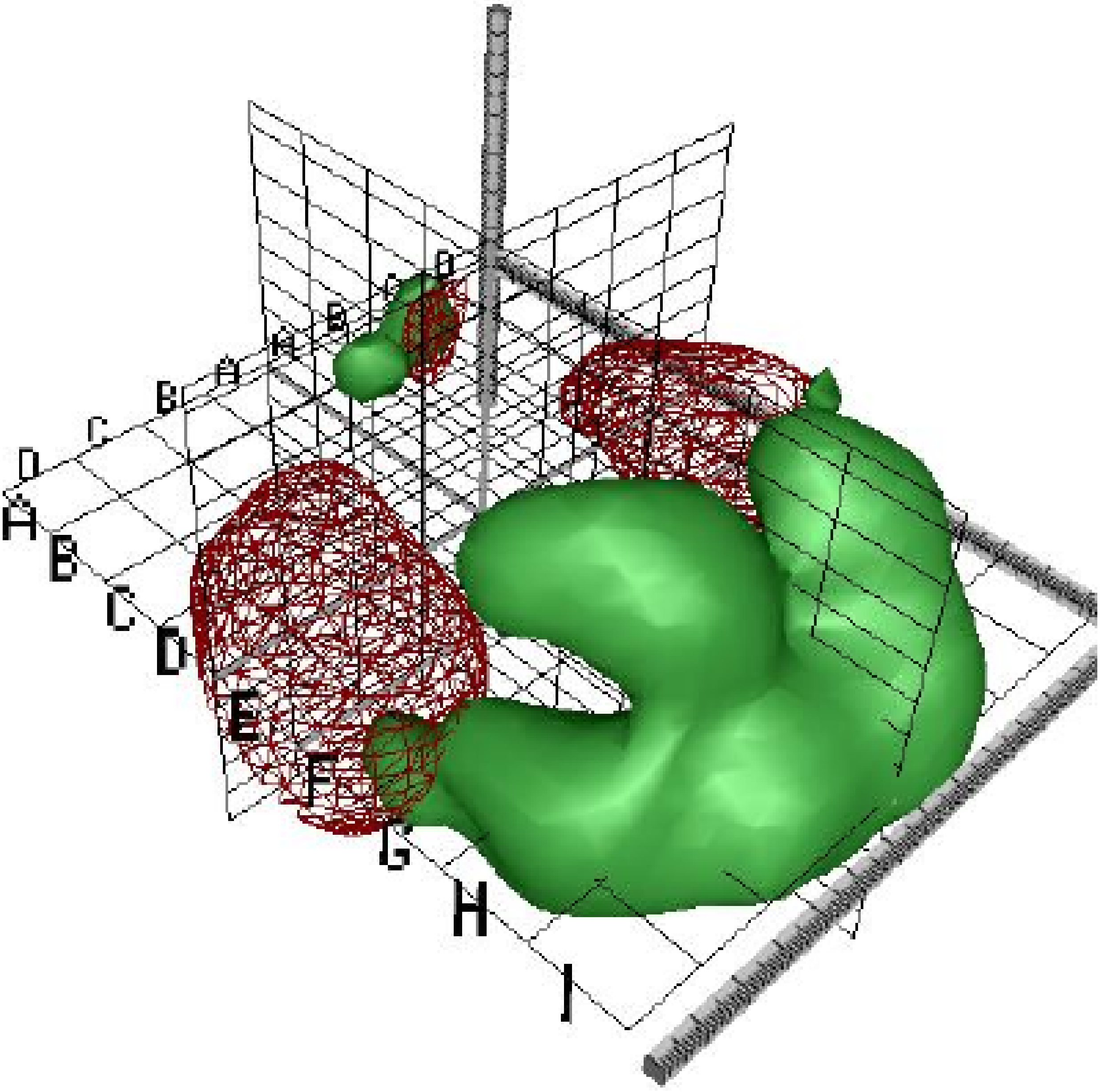


Figure 16: Densities from "Vision" and "Audition" behavioral paradigm, e.g., $p(\mathbf{x}|\text{behavior} = \text{"vision"})$. VRML97 screenshot.

DENSITIES FOR “BEHAVIOR”

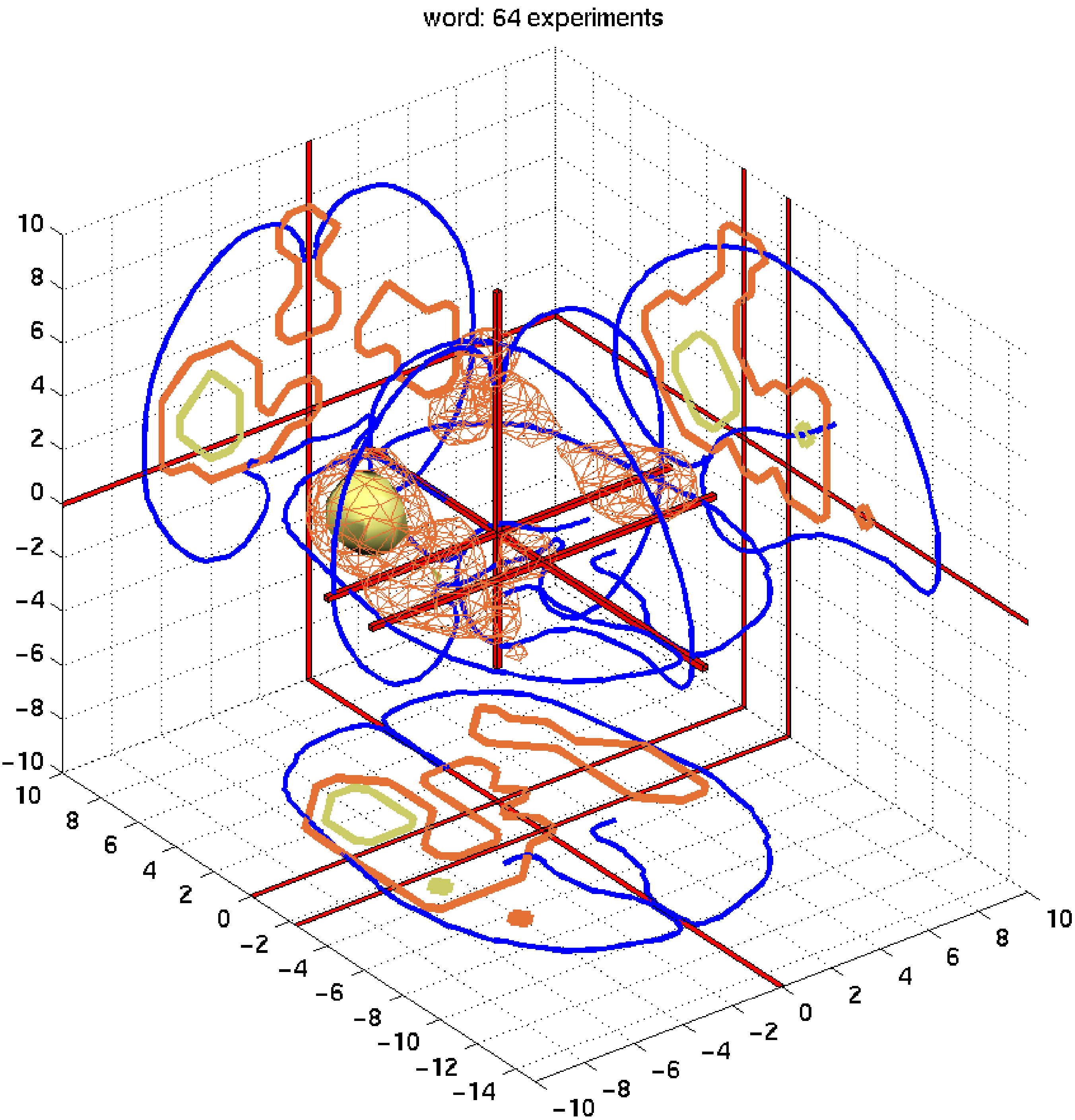


Figure 17: Densities from the word “word”.

IMAGE RETRIEVAL

- “Find related experiments”.
- Image based retrieval systems typically extract features, such as texture and color and/or surrounding text (Rui et al., 1999; Djeraba and Bouet, 1997).
- QBIC, commercial system by IBM (Flickner et al., 1995), example at http://www.hermitagemuseum.org.
- Web-based image retrieval systems
  - AltaVista, text-based search
  - WebSEEk (Smith and Chang, 1996a; Smith and Chang, 1996b)
- Medical image retrieval
  - CT-scans, query image with “stroke” or “acute blood” (Liu and Dellaert, 1998a; Liu and Dellaert, 1998b)
  - Other (Ford et al., 2001; Comaniciu et al., 1998)

FINDING RELATED VOLUMES

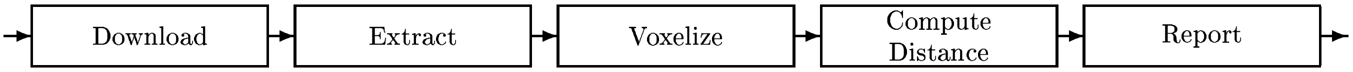


Figure 18: A processing scheme for finding related BrainMap experiments based on volume comparisons.

- Finding related functional neuroimaging volumes (Nielsen and Hansen, 2002; Nielsen, 2001).
- Data
  - Point data as “Experiments” from BrainMap with sets of locations.
  - Volumes, small set from a cluster analysis in PET (Balslev et al., 2002).
- Point data voxelized with Gaussian kernel on a coarse grid (8mm).
- Compute distances between volumes as the normalized inner product.
- Generation of static web-pages with sorted list of similar volumes and with links to BrainMap and Pubmed.
- For efficiency: Compute the distance in a subspace, or between the points.

EXAMPLE

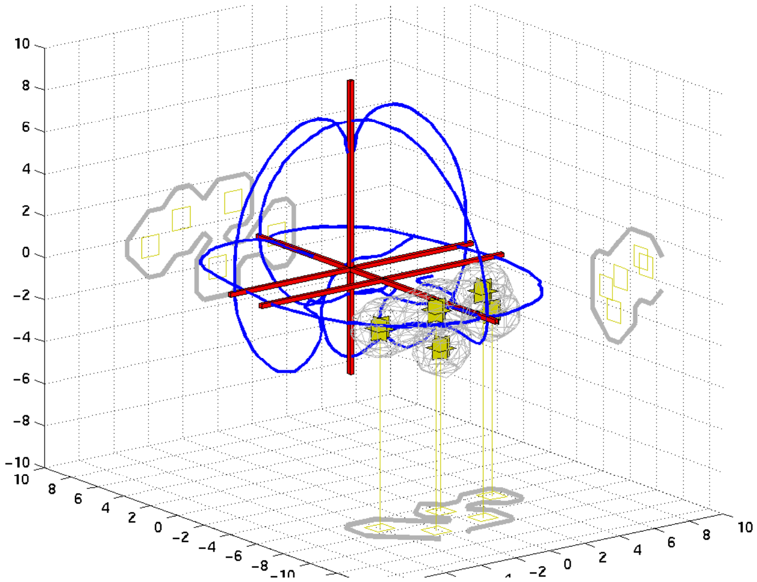


Figure 19: Query volume formed from (Sergent et al., 1992) — a letter and object (visual) processing paper with the 5 original points and an isosurface in the volume.

(3) Positron emission tomography study of letter and object processing: Empirical findings and methodological considerations
Sergent J, *Cerebral Cortex* **2**:68−80

Related volumes

(168) Neural correlates of category−specific knowledge
Martin A, *Nature* **379**:649−652

- (168*8) [BrainMap : paper | exp]

(114) Neuroanatomical analysis of functional brain images: validation with retinotopic mapping
Grabowski T J, *Human Brain Mapping* **2**:134−148

- (114*2) [BrainMap : paper | exp]

(189) Topographical representations of mental images in primary visual cortex
Kosslyn S M, *Nature* **378**:496−498

- (189*2) [BrainMap : paper | exp]

(12) Retinotopic organization of human visual cortex mapped with positron−emission tomography
Fox P T, *The Journal of Neuroscience* **7**:913−922

- (12*1) [BrainMap : paper | exp]

(12) Retinotopic organization of human visual cortex mapped with positron−emission tomography
Fox P T, *The Journal of Neuroscience* **7**:913−922

- (12*2) [BrainMap : paper | exp]

(3) Positron emission tomography study of letter and object processing: Empirical findings and methodological considerations
Sergent J, *Cerebral Cortex* **2**:68−80

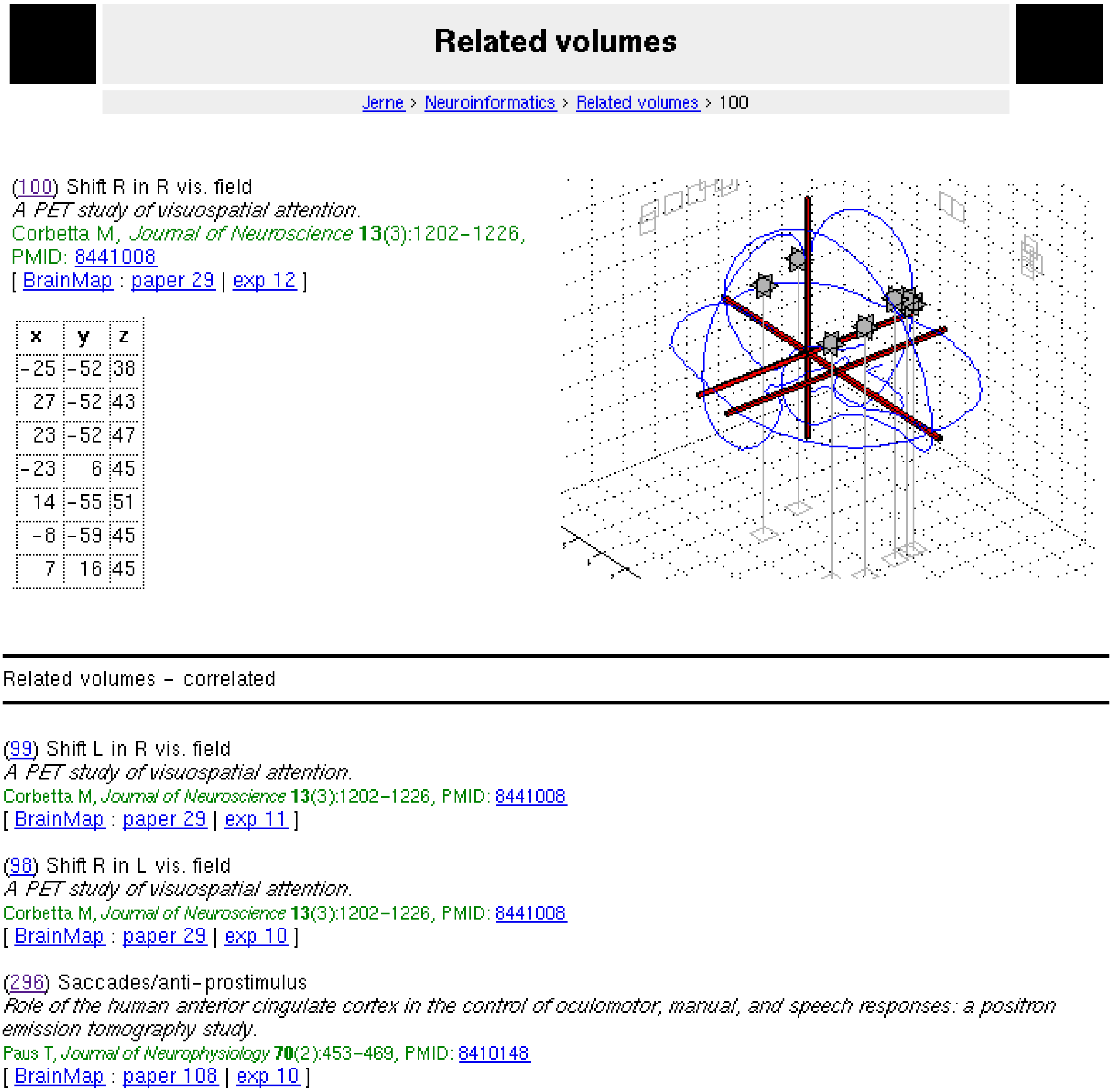
- (3*2) [BrainMap : paper | exp]

(36) Area V5 of the human brain: Evidence from a combined study using positron emission tomography and magnetic resonance imaging
Watson J D G, *Cerebral Cortex* **3**:79−94

- (36*1) [BrainMap : paper | exp]

Figure 20: Result list: All vision experiments.

EXAMPLE



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

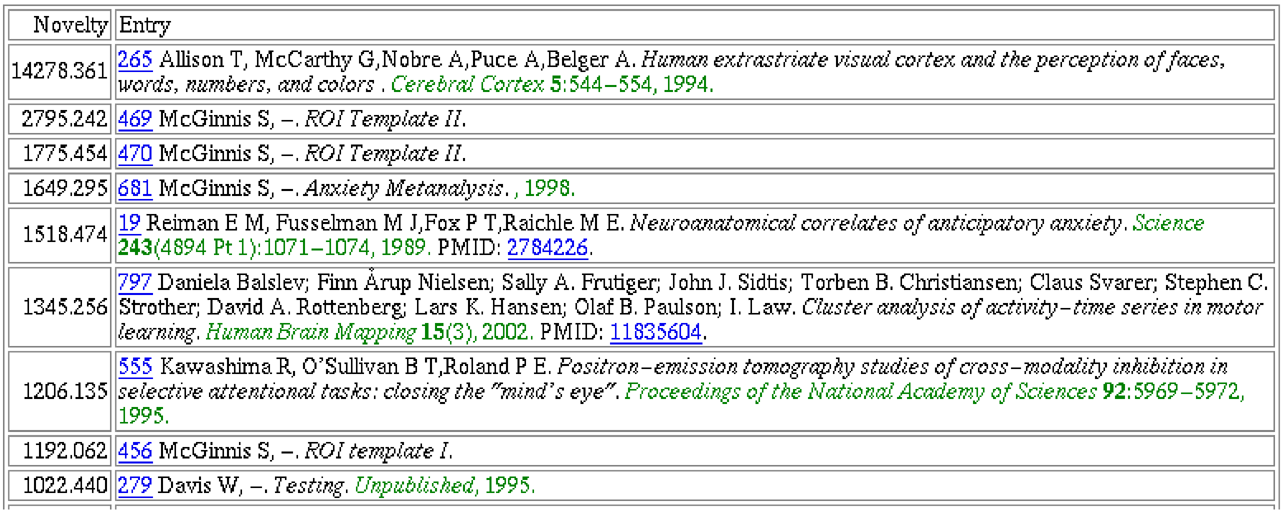
(99) Shift L in R vis. field
A PET study of visuospatial attention.
Corbetta M, *Journal of Neuroscience* **13**(3):1202-1226, PMID: 8441008
[BrainMap : paper 29 | exp 11]

(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 21: Result page with automatically generated corner cube visualization (Corbetta et al., 1993). Two cluster of activations.

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 22: 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

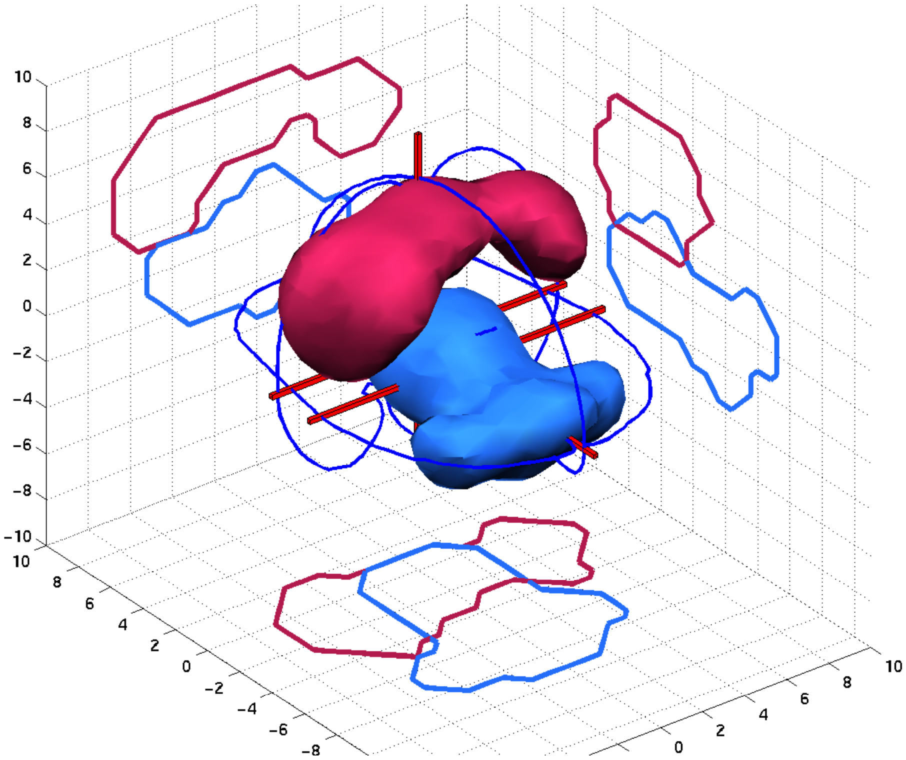


Figure 23: Both ends of the second eigenimage $\mathbf{v}_2$.

- Singular value decomposition of the (experiment × voxel) data matrix: $\mathbf{U}\mathbf{L}\mathbf{V}^{\mathsf{T}} = \mathrm{svd}(\mathbf{X})$. 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. Orthogonality problem. ICA?

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 4: Right dominant brain asymmetry.

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

$$P_{\text{Bin}} = \sum_{0}^{X} \binom{N}{X} 0.5^N \tag{3}$$

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

$$a = 1 - 2P_{\text{Bin}} \tag{4}$$

- 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’

A DATABASE IN XML

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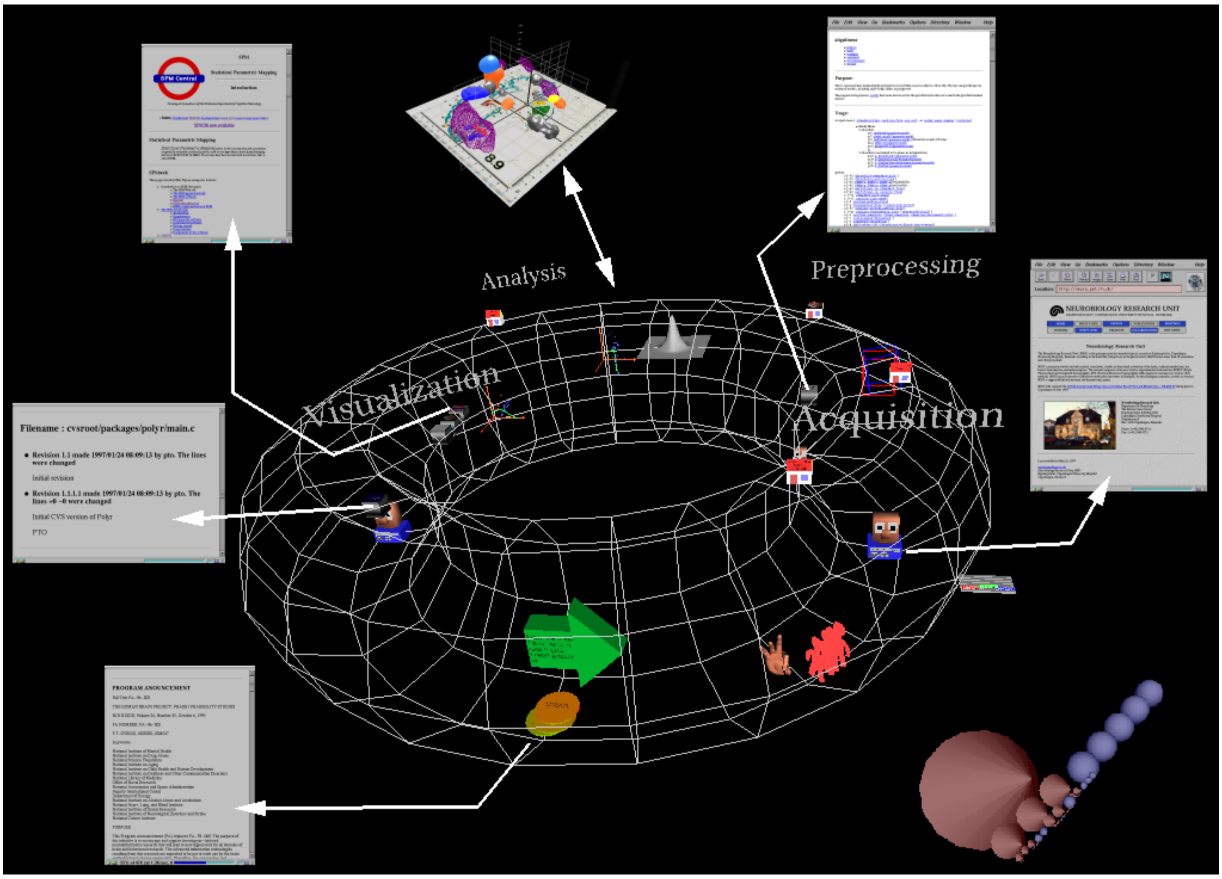
...
<title>Functional localization of pain perception in the human brain studied by PET.</title>
<ui>97235324</ui>
<volume>8</volume>
<year>1997</year>
<Exp>
  <type>exp</type>
  <capsuleDescription>Painful stimulation of the left hand</capsuleDescription>
  <freeFormDescription>Painful stimulation of the left hand by laser</freeFormDescription>
  <specificTask>Painful stimulation</specificTask>
  <numberOfSubjects>6</numberOfSubjects>
  <labOfExperiment>Kyoto University - Kyoto, Japan</labOfExperiment>
  <modality>PET</modality>
  <measuredVariable>CBF</measuredVariable>
  <tracer>O-15 Water</tracer>
...
```

- "Poor man's XML" (pXML): no attributes, no empty tags, only letters allowed in element tag names, two types (either simple text field or structure). A subset of XML as *Minimal XML* (Park, 2000) and *Canonical XML* (Boyer, 2001).
- Relatively easy to read with a recursive extended regular expression: 3–9 lines of Perl. Validation with definition DTD.
- Easy to distribute database
- Extensible definitions

```
<author>Van Essen, D. J.</author>
<Author>
  <surname>Van Essen</surname>
  <firstname>David</firstname>
  <initials>DJ</initials>
</Author>
```

- Matlab program to type in the information.

INFORMATION VISUALIZATION



Filename : cvsroot/packages/polyr/main.c

- Revision 1.1 made 1997/01/24 08:09:13 by pto. The lines were changed

  Initial revision

- Revision 1.1.1.1 made 1997/01/24 08:09:13 by pto. The lines +0 -0 were changed

  Initial CVS version of Polyr

  PTO

Figure 24: Information visualization as a process: Initial hypothesis, scanning, analysis and lastly interpretation, which links to the initial hypothesis.

- Information visualization example (Nielsen and Hansen, 1997): Visualize every kind of data that is generated in a neuroimaging study — supplement to textual information.
- Second item in Jakob Nielsen's: Top Ten Mistakes in Web Design": "Gratuitous Use of Bleeding-Edge Technology" (Nielsen, 1996)!?

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 a small XML database of results from functional neuroimaging.
- Results available on the Internet from hendrix.imm.dtu.dk more specifically hendrix.imm.dtu.dk/services/jerne/.

References

Allison, T., McCarthy, G., Nobre, A., Puce, A., and Belger, A. (1994). Human extrastriate visual cortex and the perception of faces, words, numbers, and colors. *Cerebral Cortex*, 4(5):544–554. PMID: 7833655.

Balslev, D., Nielsen, F. Å., Frutiger, S. A., Sidtis, J. J., Christiansen, T. B., Svarer, C., Strother, S. C., Rottenberg, D. A., Hansen, L. K., Paulson, O. B., and Law, I. (2002). Cluster analysis of activity-time series in motor learning. *Human Brain Mapping*, 15(3):135–145. http://www3.interscience.wiley.com/cgi-bin/abstract/89011762/. ISSN 1097-0193, [defkat.dk — bibliotek.dk].

Becker, J. T., Mintun, M. A., Diehl, D. J., Dobkin, J., Martidis, A., Madoff, D. C., and Dekosky, S. T. (1994). Functional neuroanatomy of verbal free recall: A replication study. *Human Brain Mapping*, 1(4):284–292.

Boyer, J. (2001). Canonical XML. W3C Recommendation Version 1.0, W3C.

Buckner, R. L., Raichle, M. E., Miezin, F. M., and Petersen, S. E. (1996). Functional anatomic studies of memory retrieval for auditory words and visual pictures. *The Journal of Neuroscience*, 16(19):6219–6235.

Christoff, K. and Grabrieli, J. D. E. (2000). The frontopolar cortex and human cognition: Evidence for a rostrocaudal hierarchical organization within the human prefrontal cortex. *Psychobiology*, 28(2):168–186. http://www-psych.stanford.edu:80/~kalina/papers/psbi2000.pdf. ISSN 0889-6313, [defkat.dk — bibliotek.dk].

Collins, D. L., Holmes, C. J., Peters, T. M., and Evans, A. C. (1995). Automatic 3-D model-based neuroanatomical segmentation. *Human Brain Mapping*, 3(3):190–208.

Comaniciu, D., Meer, P., Foran, D., and Medl, A. (1998). Bimodal system for interactive indexing and retrieval of pathology images. In *Proceedings of the 4th IEEE Workshop on Applications of Computer Vision (WACV'98), Princeton, NJ*, pages 76–81. ResearchIndex: http://citeseer.nj.nec.com/comaniciu98bimodal.html.

Corbetta, M., Miezin, F. M., Shulman, G. L., and Petersen, S. E. (1993). A PET study of visuospatial attention. *The Journal of Neuroscience*, 13(3):1202–1226. PMID: 8441008. ISSN 0270-6474, [defkat.dk — bibliotek.dk].

Djeraba, C. and Bouet, M. (1997). Digital information retrieval. In Golshani, F. and Makki, K., editors, *Sixth International Conference on Information and Knowledge Management*, pages 185–200. ACM, ACM Press.

Drevets, W. C., Videen, T. O., MacLeod, A. K., Haller, J. W., and Raichle, M. E. (1992). PET images of blood flow changes during anxiety: Correction. *Science*, 256(5064):1696. PMID: 1609283. A previous functional neuroimaging study found correlation between anxiety and the temporopolar region. This study finds that it is more likely muscle signal from teeth-clenching.

Duncan, J. and Owen, A. M. (2000). Common regions of the human frontal lobe recruited by diverse cognitive demands. *Trends in Neurosciences*, 23(10):475–483. http://www.sciencedirect.com/science/article/B6T0V-417MKDS-F/1/48e8aad434785265d476e00c6d76ecbf. ISSN 0378-5912, [defkat.dk — bibliotek.dk].

Flickner, M., Sawhney, H., Niblack, W., Ashley, J., Huang, Q., Dom, B., Gorkani, M., Hafner, J., Lee, D., Petkovic, D., Steele, D., and Yanker, P. (1995). Query by image and video content: The qbic system. *IEEE Computer*, 28(9):23–32. http://www.computer.org/computer/co1995/r9023abs.htm.

Ford, J., Makedon, F., Megalooikonomou, V., Shen, L., Steinberg, T., and Saykin, A. J. (2001). Spatial comparison of fMRI activation maps for data mining. *NeuroImage*, 13(6):S1302. http://www.apnet.com/www/journal/hbm2001/11743.html.

Fox, P. T., Huang, A., Parsons, L. M., Xiong, J.-H., Zamarippa, F., Rainey, L., and Lancaster, J. L. (2001). Location-probability profiles for the mouth region of human primary motor-sensory cortex: Model validation. *NeuroImage*, 13(1):196–209. PMID: 11133322. ISSN 1053-8119, [defkat.dk — bibliotek.dk].

Fox, P. T., Huang, A. Y., Parsons, L. M., Xiong, J.-H., Rainey, L., and Lancaster, J. L. (1999). Functional volumes modeling: Scaling for group size in averaged images. *Human Brain Mapping*, 8(2–3):143–150. PMID: 10524606. Special Issue: Proceedings of the BrainMap '98 Workshop.

Fox, P. T. and Lancaster, J. L. (1994). Neuroscience on the net. *Science*, 266(5187):994–996. PMID: 7973682.

Fox, P. T., Lancaster, J. L., Parsons, L. M., Xiong, J.-H., and Zamarripa, F. (1997). Functional volumes modeling: Theory and preliminary assessment. *Human Brain Mapping*, 5(4):306–311. http://www3.interscience.wiley.com/cgi-bin/abstract/56435/START.

George, M. S., Ketter, T. A., Parekh, B. A., Gill, D. S., Huggins, T., Marangell, L., Pazaglia, P. J., and Post, R. (1994). Spatial ability in affective illness: differences in regional brain activation during a spatial matching task ($H_2^{15}O$ PET). *Neuropsychiatry, Neuropsychology, and Behavioral Neurology*, 7(3):143–153.

Gerlach, C., Law, I., Gade, A., and Paulson, O. B. (2000). Categorization and category effects in normal object recognition. a PET study. *Neuropsychologia*, 38(13):1693–1703. PMID: 11099727. ISSN 0028-3932, [defkat.dk — bibliotek.dk].

Hansen, L. K., Nielsen, F. Å., Strother, S. C., and Lange, N. (2000a). Consensus inference in neuroimaging. *NeuroImage*, 13(6):1212–1218. PMID: 11352627. http://www.idealibrary.com/links/citation/1053-8119/13/1212.

Hansen, L. K., Sigurðsson, S., Kolenda, T., Nielsen, F. Å., Kjems, U., and Larsen, J. (2000b). Modeling text with generalizable Gaussian mixtures. In *Proceedings of ICASSP'2000*. Turkey. http://eivind.imm.dtu.dk/publications/1999/hansen.icassp2000.ps.gz. ResearchIndex: http://citeseer.nj.nec.com/hansen99modeling.html.

Herskovits, E. H. (2000). An architecture for a brain-image database. *Methods of Information in Medicine*, 39(4–5):291–297. PMID: 11191696. Description of the BRAID object-relational brain image database and related analysis methods (contingency tables, logistic regression) with examplification on two data sets.

Herskovits, E. H., Megalooikonomou, V., Davatzikos, C., Chen, A., Bryan, R. N., and Gerring, J. P. (1999). Is the spatial distribution of brain lesions associated with closed-head injury predictive of subsequent development of attention-deficit/hyperactivity disorder? analysis with brain-image database. *Radiology*, 213(2):389–394. PMID: 10551217. http://ditzel.rad.jhu.edu/papers/radiology1999.ps. ResearchIndex: http://citeseer.nj.nec.com/319461.html.

Indefrey, P. (2001). A meta-analysis of PET and fMRI experiments on syntactic parsing. *NeuroImage*, 13(6):S545. http://www.apnet.com/www/journal/hbm2001/10136.html.

Indefrey, P. and Levelt, W. J. M. (2000). The neural correlates of language production. In Gazzaniga, M. S., editor, *The New Cognitive Neurosciences*, chapter 59, pages 845–865. MIT Press, Cambridge, MA, 2nd edition.

Kikinis, R., Shenton, M. E., Iosifescu, D. V., McCarley, R. W., Saiviroonporn, P., Hokama, H. H., Robatino, A., Metcalf, D., Wible, C. G., Portas, C. M., Donnino, R. M., and Jolesz, F. A. (1996). A digital brain atlas for surgical planning, model-driven segmentation, and teaching. *IEEE Transactions on Visualization and Computer Graphics*, 2(3):232–241. http://www.spl.harvard.edu:8000/pages/papers/atlas/text.html.

Klein, A. and Hirsch, J. (2001). Automatic labeling of brain anatomy and FMRI brain activity. *NeuroImage*, 13(6, part 2):S174. http://www.academicpress.com/www/journal/hbm2001/10850.html.

Kosslyn, S. M., Alpert, N. M., Thompson, W. L., Chabris, C. F., Rauch, S. L., and Anderson, A. K. (1994). Identifying objects seen from different viewpoints, a PET investigation. *Brain*, 117:1055–1071.

Lancaster, J. L., Kochunov, P., Nickerson, D., and Fox, P. T. (2000a). Stand-alone java-base version of the Talairach Daemon database system. volume 11, page S923. Academic Press. . ISSN 1053-8119, [defkat.dk — bibliotek.dk].

Lancaster, J. L., Rainey, L. H., Summerlin, J. L., Freitas, C. S., Fox, P. T., Evans, A. C., Toga, A. W., and Mazziotta, J. C. (1997). Automated labeling of the human brain: A preliminary report on the development and evaluation of a forward-transform method. *Human Brain Mapping*, 5(4):238–242. ttp://www3.interscience.wiley.com/cgi-bin/abstract/56443/START. ISSN 1065-9471, [defkat.dk — bibliotek.dk]. Description of the Talairach Daemon for neuroanatomical labeling from Talairach coordinates.

Lancaster, J. L., Woldorff, M. G., Liotti, M., Freitas, C. S., Rainey, L., Kochunov, P. V., Nickerson, D., Mikiten, S. A., and Fox, P. T. (2000b). Automated Talairach atlas labels for functional brain mapping. *Human Brain Mapping*, 10(3):120–131. PMID: 10912591. Describes the Talairach Daemon and validation of the scheme through BrainMap labels, expert annotations and an activation study.

Law, I. (1996). *Saccadic Eye Movements, A Functional Brain Mapping Approach*. PhD thesis, Department of Neurology, Rigshospitalet, The University of Copenhagen, Copenhagen, Denmark. http://nru.dk/cgi-bin/extract?lawi1997c.

Liu, Y. and Dellaert, F. (1998a). A classification based similarity metric for 3d image retrieval. In *IEEE Conference on Computer Vision and Pattern Recognition (CVPR'98), Santa Babara, CA*, pages 800–805. http://www.cs.cmu.edu/afs/cs.cmu.edu/project/nist/ftp/cvpr98.ps.Z.

Liu, Y. and Dellaert, F. (1998b). Classification-driven medical image retrieval. In *DAPAR Image Understanding Workshop, IUW'98*. http://www.cs.cmu.edu/afs/cs.cmu.edu/project/nist/ftp/iuw.ps.Z.

Nielsen, F. Å. (2001). *Neuroinformatics in Functional Neuroimaging*. PhD thesis, Informatics and Mathematical Modelling, Technical University of Denmark, Lyngby, Denmark.

Nielsen, F. Å. and Hansen, L. K. (1997). Interactive information visualization in neuroimaging. In Ebert, D. S. and Nicholas, C. K., editors, *Workshop on New Paradigms in Information Visualization and Manipulation*, New York, New York. The Association of Computing Machinery, ACM Press. http://hendrix.imm.dtu.dk/staff/fnielsen/ps/Nielsen1997Interactive.ps.gz. ISBN 1581130511, [defkat.dk — bibliotek.dk — amazon.com — bn.com — isbn.nu].

Nielsen, F. Å. and Hansen, L. K. (2002). Finding related functional neuroimaging volumes. *NeuroImage*, 16(2). http://www.imm.dtu.dk/~fn/ps/Nielsen2002Finding_abstract.ps.gz. Presented at the 8th International Conference on Functional Mapping of the Human Brain, June 2–6, 2002, Sendai, Japan. Available on CD-Rom.

Nielsen, J. (1996). Top ten mistakes in web design. Internet. Alertbox.

Nowinski, W. L., Bryan, R. N., and Raghavan, R. (1997). *The Electronic Clinical Brain Atlas*. Thieme. ISBN 3131076615, [defkat.dk — bibliotek.dk — amazon.com — bn.com — isbn.nu]. CD-ROM.

Nowinski, W. L., Fang, A., and Nguyen, B. T. (1995). Medical imaging 1995: Image display. In Kim, Y., editor, *Schaltenbrand-Wahren/Talairach-Tournoux brain atlas registration*, volume 2431 of *SPIE Proceedings*, pages 126–136, San Diego. The International Society for Optical Engineering. http://spie.org/scripts/abstract.pl?bibcode=1995SPIE%2e2431%2e%2e126N&page=1&qs=spie. ISBN 0819417793, [defkat.dk — bibliotek.dk — amazon.com — bn.com — isbn.nu].

O'Sullivan, B. T., Roland, P. E., and Kawashima, R. (1994). A PET study of somatosensory discrimination in man. Microgeometry versus macrogeometry. *European Journal of Neuroscience*, 6(1):137–148. PMID: 8130929.

Owen, A. M., Milner, B., Petrides, M., and Evans, A. C. (1996). Memory for object features versus memory for object location: A positron-emission tomography study of encoding and retrieval processes. *Proceedings of the National Academy of Sciences USA*, 93(17):9212–9217. PMID: 8799180.

Pardo, J. V., Raichle, M. E., and Fox, P. T. (1991). Localization of a human system for sustained attention by positron emission tomography. *Nature*, 349(6304):61–63. PMID: 1985266.

Park, D. (2000). Minimal XML 1.0.

Pennock, D. M., Lawrence, S., Giles, C. L., and Nielsen, F. Å. (2001a). Extracting collective probabilistic forecasts from web games. In *KDD-2001, The Seventh ACM SIGKDD International Conference on Knowledge Discovery and Data Mining, August 26 - 29, 2001, San Francisco, California, USA*. SIGKDD, Association for Computing Machinery. http://www.neci.nec.com/~lawrence/papers/am-kdd01/am-kdd01.ps.gz.

Pennock, D. M., Lawrence, S., Giles, C. L., and Nielsen, F. Å. (2001b). The real power of artificial markets. *Science*, 291(5506):987–988.

Petersen, S. E., Fox, P. T., Posner, M. I., Mintun, M., and Raichle, M. E. (1988). Positron emission tomographic studies of the cortical anatomy of single-word processing. *Nature*, 331(6157):585–589. PMID: 3277066.

Rehm, K., Schaper, K. A., Strother, S. C., Anderson, J. R., and Rottenberg, D. A. (1997). Visualization tools for comparing functional neuroimaging datasets. *NeuroImage*, 5(4):S390.

Reiman, E. M., Fusselman, M. J., Fox, P. T., and Raichle, M. E. (1989). Neuroanatomical correlates of anticipatory anxiety. *Science*, 243(4894 Part 1):1071–1074. PMID: 2784226.

Rui, Y., Huang, T. S., and Chang, S.-F. (1999). Image retrieval: Current techniques, promising directions, and open issues. *Journal of Visual Communication and Image Representation*, 10(1):39–62. http://www.idealibrary.com/links/doi/10.1006/jvci.1999.0413. ResearchIndex: http://citeseer.nj.nec.com/rui99image.html.

Schaltenbrand, G. and Wahren, W. (1977). *Atlas for Stereotaxy of the Human Brain*. Thieme, Stuttgart, 2nd edition. ISBN 0865770557, [defkat.dk — bibliotek.dk — amazon.com — bn.com — isbn.nu].

Schlösser, R., Hutchinson, M., Joseffer, S., Rusinek, H., Saarimaki, A., Stevenson, J., Dewey, S. L., and Brodie, J. D. (1998). Functional magnetic resonance imaging of human brain activity in a verbal fluency task. *Journal of Neurology, Neurosurgery, and Psychiatry*, 64(4):492–495. PMID: 9576541. http://jnnp.bmjjournals.com/cgi/content/full/64/4/492.

Sergent, J., Zuck, E., Levesque, M., and MacDonald, B. (1992). Positron emission tomography study of letter and object processing: empirical findings and methodological considerations. *Cerebral Cortex*, 2(1):68–80. PMID: 1633409.

Shaywitz, B. A., Pugh, K. R., Constable, R. T., Shaywitz, S. E., Bronen, R. A., Fulbright, R. K., Shankweiler, D. P., Katz, L., Fletcher, J. M., Skudlarski, P., and Gore, J. C. (1995). Localization of semantic processing using functional magnetic resonance imaging. *Human Brain Mapping*, 2:149–158.

Smith, J. R. and Chang, S.-F. (1996a). Searching for images and videos on the world-wide web. Technical Report 459-96-25, Department of Electrical Engineering and Center for Image Technology for New Media, Columbia University, New York.

Smith, J. R. and Chang, S.-F. (1996b). VisualSEEk: a fully automated content-based image query system. *ACM Multimedia*, pages 87–98.

Tulving, E., Kapur, S., Markowitsch, H. J., Craik, F. I. M., Habib, R., and Houle, S. (1994). Neuroanatomical correlates of retrieval in episodic memory: Auditory sentence recognition. *Proceedings of the National Academy of Sciences of the USA*, 91:2012–2015.

Turkeltaub, P., Eden, G. F., Jones, K. M., and Zeffiro, T. A. (2001). A novel meta-analysis technique applied to single word reading. *NeuroImage*, 13(6 (part 2)):S272. http://www.apnet.com/www/journal/hbm2001/10478.html.

Turkeltaub, P. E., Eden, G. F., Jones, K. M., and Zeffiro, T. A. (2002). Meta-analysis of the functional neuroanatomy of single-word reading: method and validation. *NeuroImage*, 16(3 part 1):765–780. PMID: 12169260. http://www.idealibrary.com/retrieve/doi/10.1006/nimg.2002.1131.