Neuroimaging meta-analysis

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OUTLINE

- Motivation
- The BrainMap database.
- Modeling "locations": Meta-analysis of stereotactic coordinates.
- Anatomical atlas: Probabilistic anatomical atlas by modeling of 3D distribution of location conditioned on anatomical label.
- Functional volumes modeling: ...conditioned on behavioral labels.
- Finding related volumes. Indices:
  - Asymmetry: Left/right asymmetric among a set of locations.
  - Novelty: Experiment outliers.
  - SVD: Singular value decomposition.
  - ICA: Independent component analysis.
- Co-activation: Assessing functional connectivity.

MOTIVATION

- Network = node + links.
- Node: Anatomical atlases
  - Usual network analysis is made on regions (to get a well-posed problem with non-singular matrices).
  - Definition of regions necessary.
  - Need of an anatomical atlas as the spatial prior for network analyses.
- Links: Connection between brain regions
  - "Prior knowledge" comes from experts or . . .
  - . . . Exploratory analyses.
  - Need new methods to propose functional connectivity.

THE BRAINMAP DATABASE

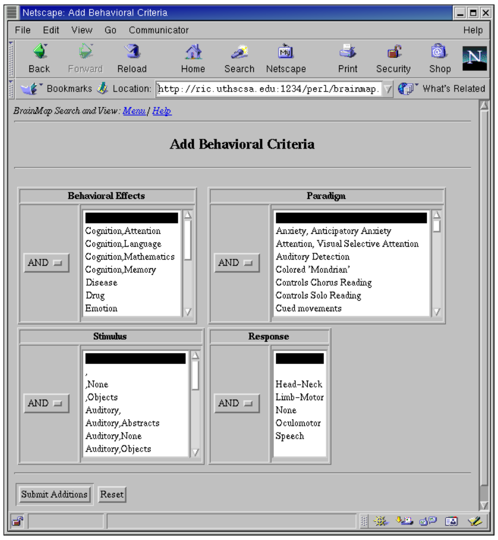


Figure 1: Behavioral criteria query web-page.

- *BrainMap* database: *Research Imaging Center*, San Antonio, Texas, http://ric.uthscsa.edu. (Fox and Lancaster, 1994). Stereotactic coordinates from human functional neuroimaging studies.
- 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- Superseded with the BrainMap DBJ http://www.brainmapdbj.org/.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

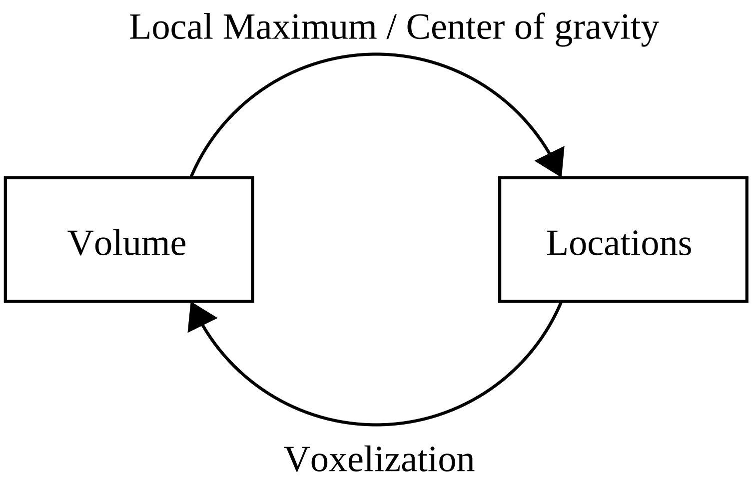


Figure 2: Voxelization.

- 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"

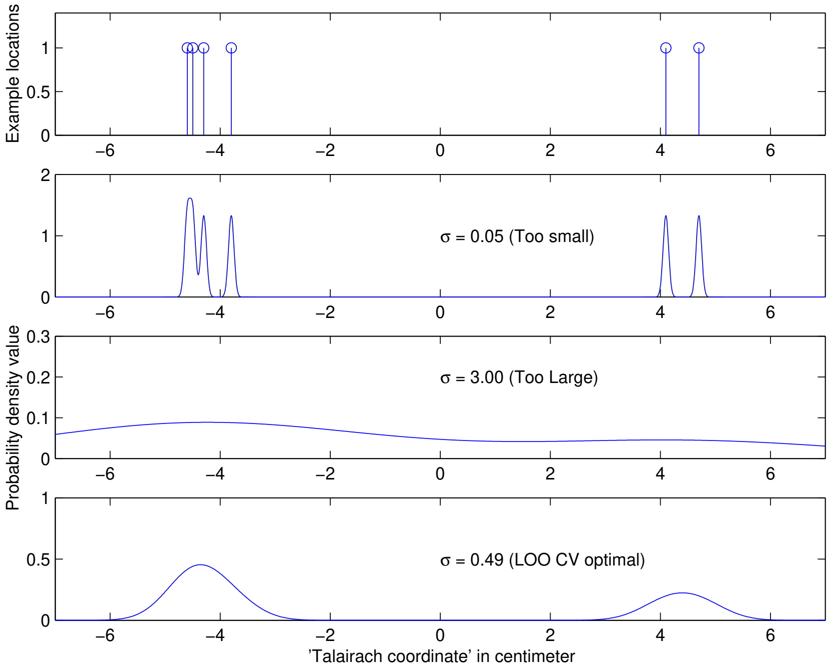


Figure 3: Example of probability density modeling

- 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., 2000).
- "Kernel methods" (kernels centered on each object: $K = N$) with homogeneous Gaussian kernel

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

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

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)

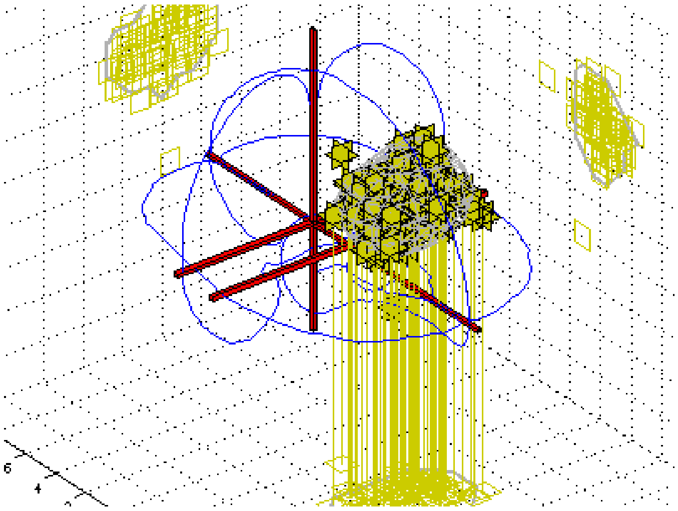


Figure 4: "Precuneus" web-page with Corner Cube visualization. Glyphs are original BrainMap locations.

- Modeling the relation between *3D Talairach Coordinates* (three dimensional continuous value) and *anatomical labels* ("lobar anatomy" text field Brain-Map field).
- Collaborative efforts sometimes better than individual experts, e.g., "consensus models" (Hansen et al., 2001) and artificial information markets (Pennock et al., 2001a; Pennock et al., 2001b).

MODELING OF ANATOMICAL LABELS AND 3D TALAIRACH LABELS

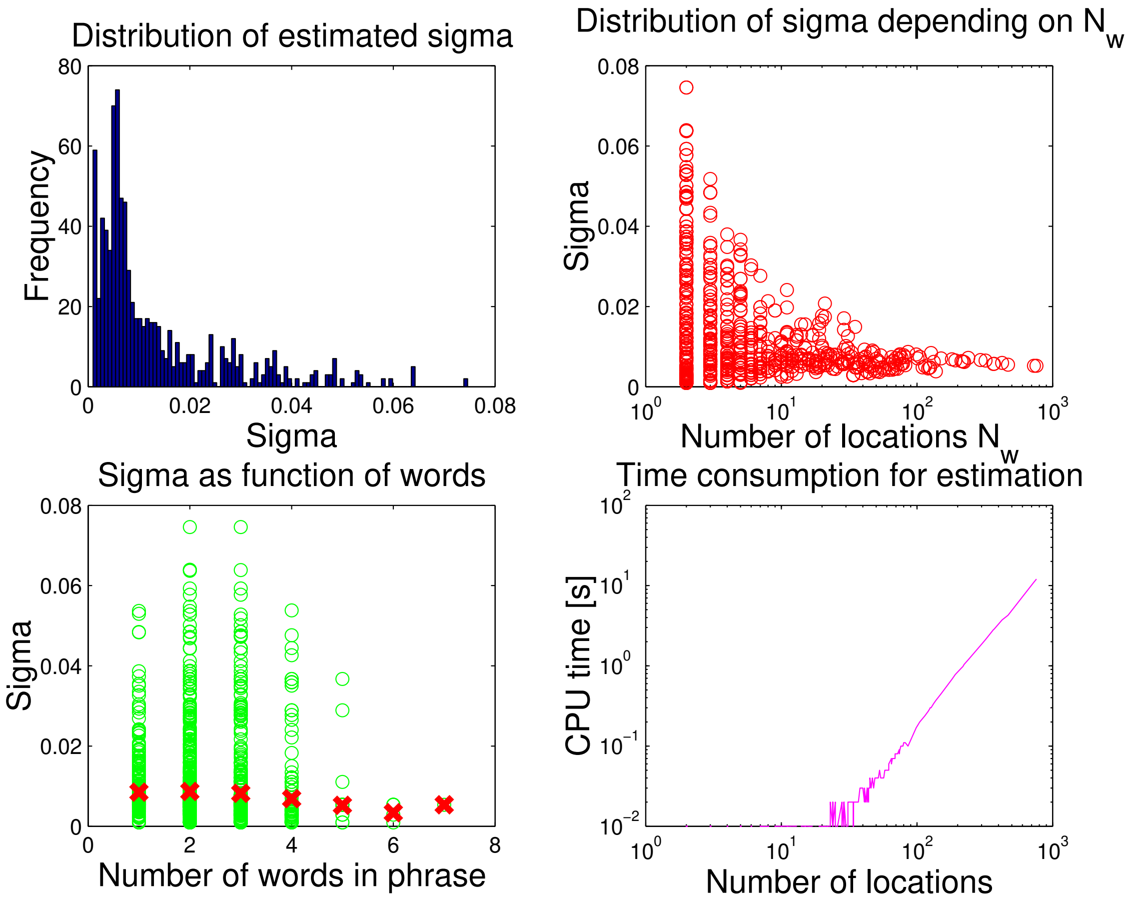


Figure 5: Sigma: width of kernel

- 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.

"FUNCTIONAL VOLUMES MODELING"

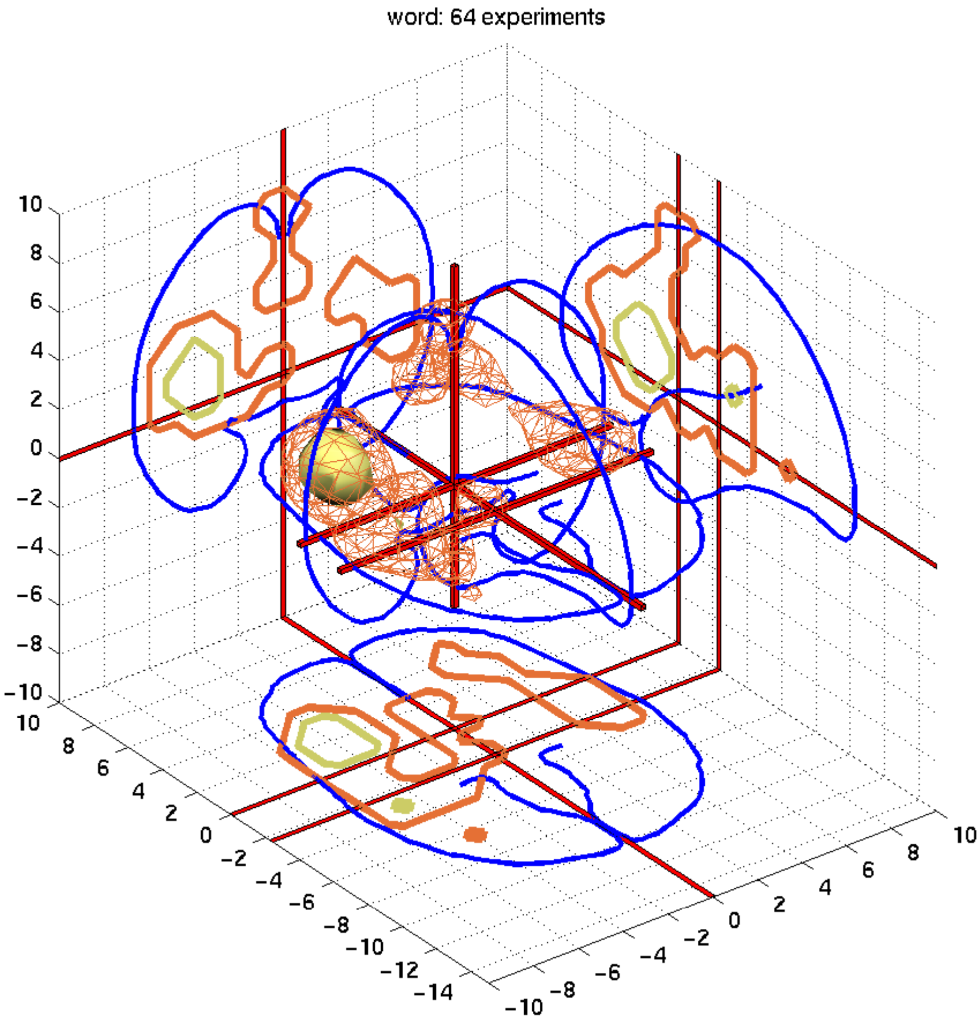


Figure 6: Densities from the word "word".

- "Functional volumes modeling" (Fox et al., 1997; Fox et al., 1999; Fox et al., 2001).
- Virtual brain mapping by conditioning on "behavior", e.g., words from experiment description.
- Functional segmentation. Providing priors for new experiments.

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).
- 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 7: 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

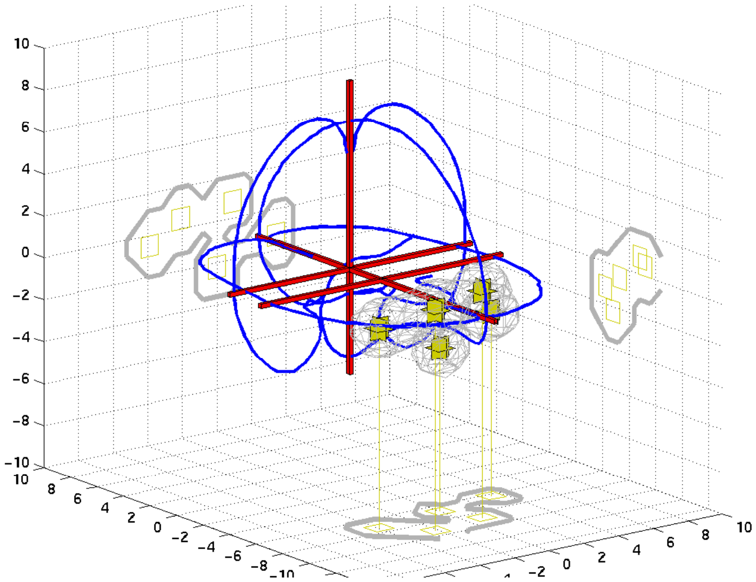


Figure 8: Query volume formed from (Sergent et al., 1992b) — a letter and object (visual) processing paper with the 5 original points and an isosurface in the volume.

(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 9: Result list: All vision experiments.

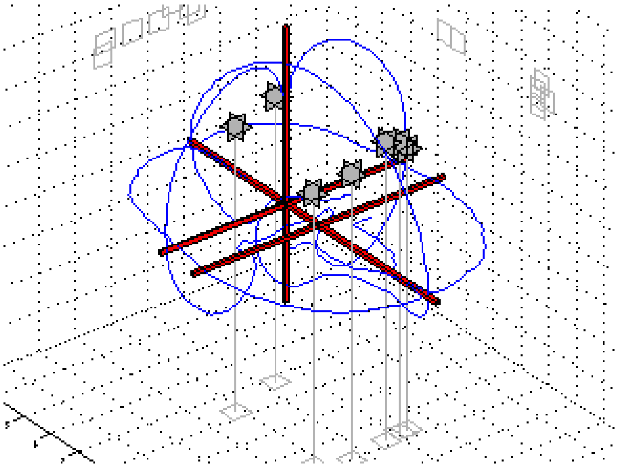
EXAMPLE

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

EXAMPLE: VISUAL MOTION

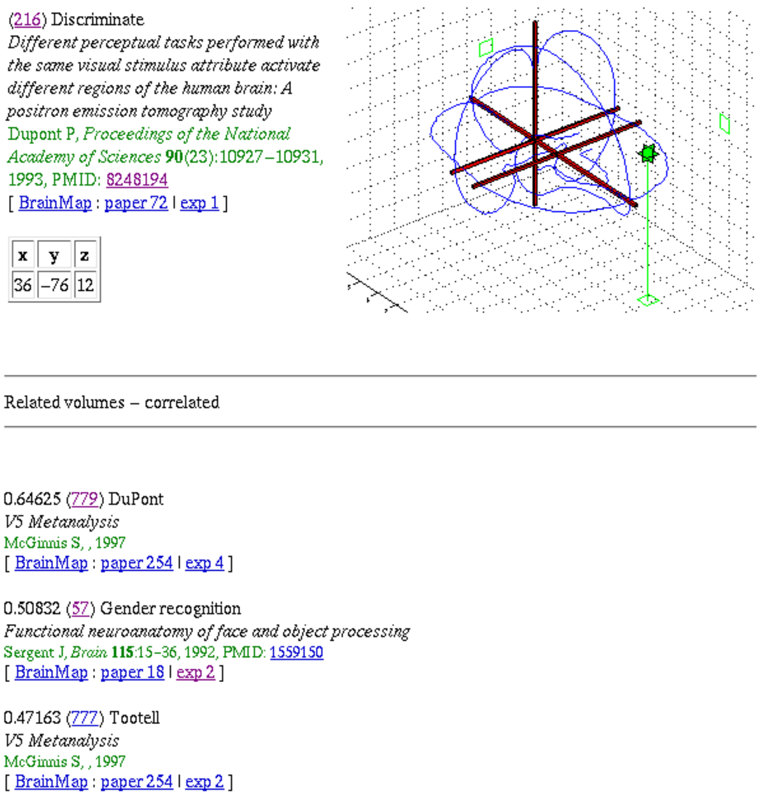


Figure 11: Result web-page.

- Similar volume for a location reported in (Dupont et al., 1993): $(36, -76, 12)$. Among the 10 first:
  - Unpublished meta-analysis of V5 Metanalysis by 'McGinnis S, 1997'.
  - Visual motion studies (McCarthy et al., 1995; Zeki et al., 1993)
  - Other: Gender discrimination from images (Sergent et al., 1992a), 'Semantic processing' (Kosslyn et al., 1995).

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 12: 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: 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 1: 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'

IMAGE-BASED INDICES: SVD

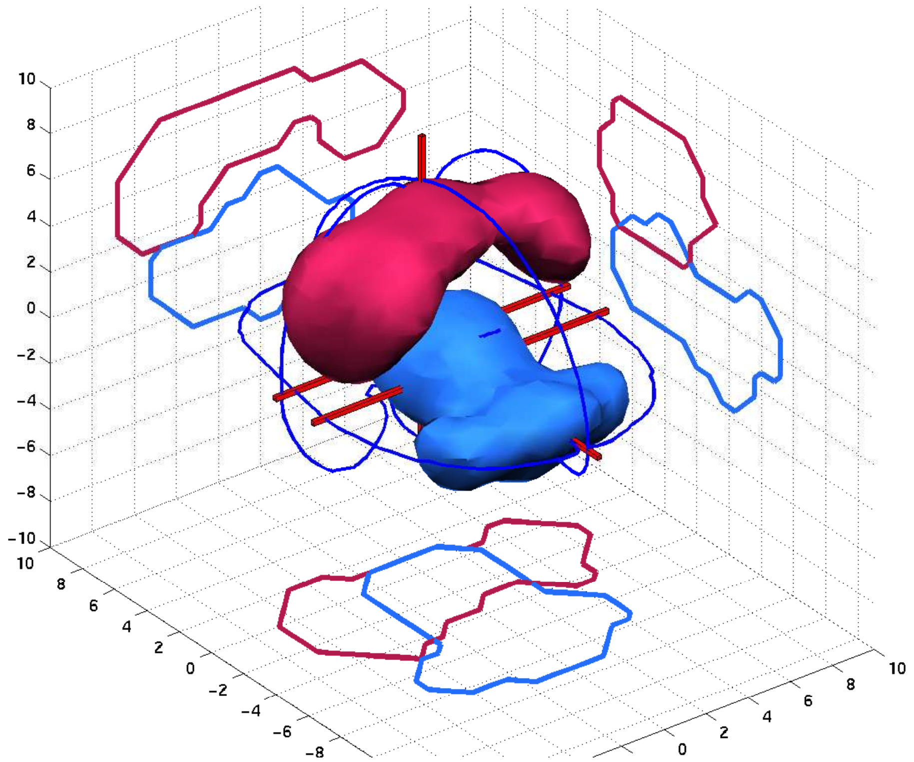


Figure 13: Both ends of the second eigenimage v_2.

- Singular value decomposition of the (experiment $\times$ voxel) data matrix: $\mathbf{ULV}^\mathsf{T} = \mathrm{svd}(\mathbf{X})$, with columns of $\mathbf{V}$ as 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: ICA

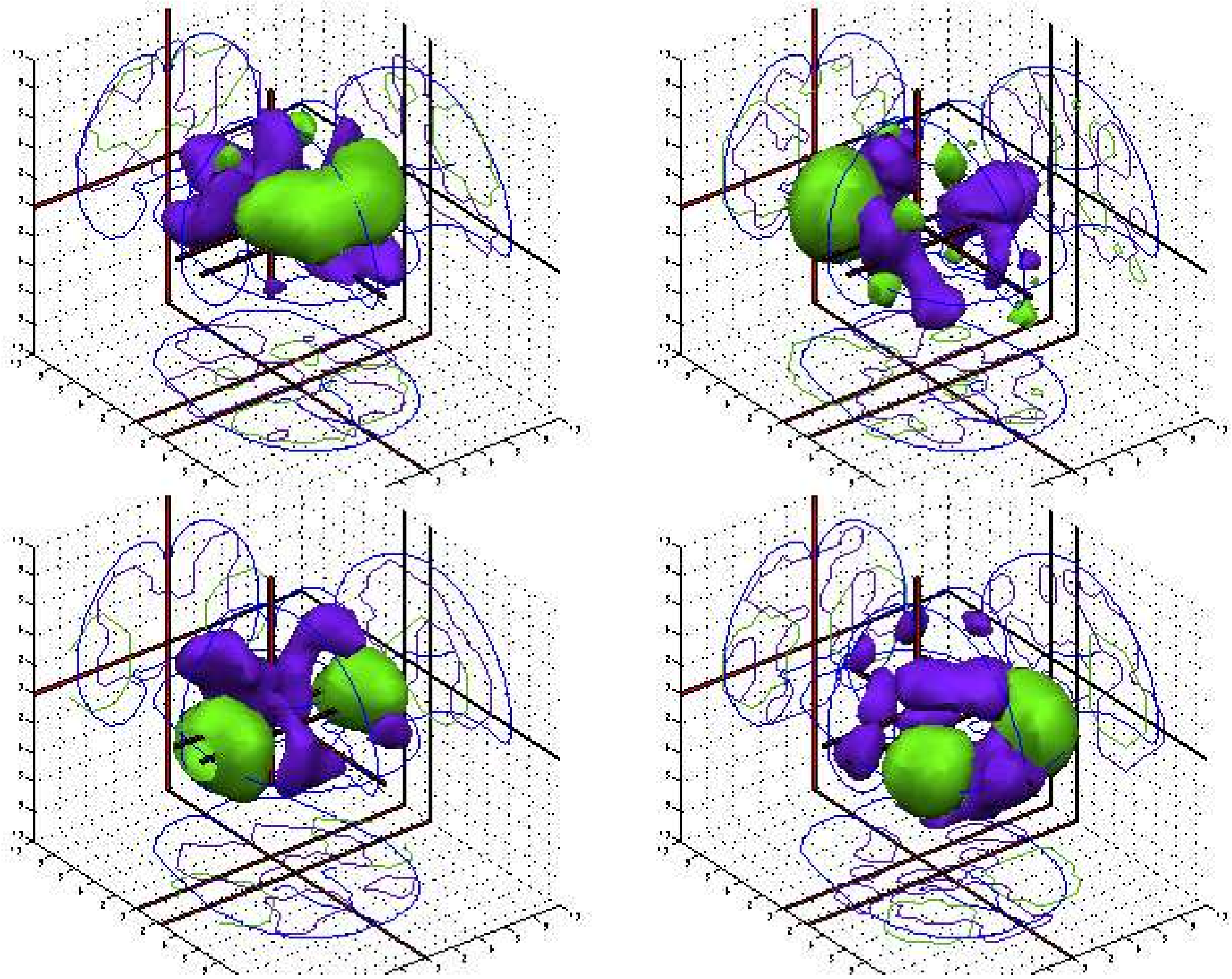


Figure 14: Both ends of the third to sixth source images $\mathbf{s}_3, \ldots, \mathbf{s}_6$.

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

CO-ACTIVATION

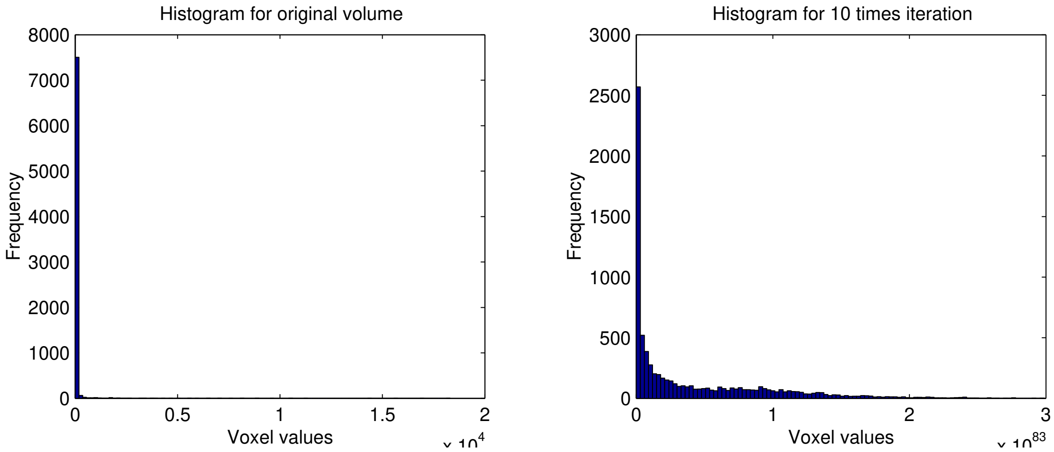


Figure 15: Histogram: Original and after 10 'transitions' iterations.

- Co-activation regarding $\mathbf{P} = \mathbf{X}^\mathsf{T}\mathbf{X}$ as a (voxel $\times$ voxel) 'transition' matrix. Co-activation from area $\mathbf{v}$ to $\mathbf{w}$

$$\mathbf{w} = \mathbf{v}\mathbf{P} \tag{5}$$

- Efficient (memory/computational) multiplication with (voxel $\times$ voxel) matrix

$$\begin{aligned} \mathbf{w} &= \mathbf{v}\mathbf{P} \qquad (6) \\ &= (\mathbf{v}\mathbf{X}^\mathsf{T})\mathbf{X}, \qquad (7) \end{aligned}$$

i.e., one (voxel $\times$ voxel) multiplication transformed to two (experiment $\times$ voxel) multiplications.

CO-ACTIVATION

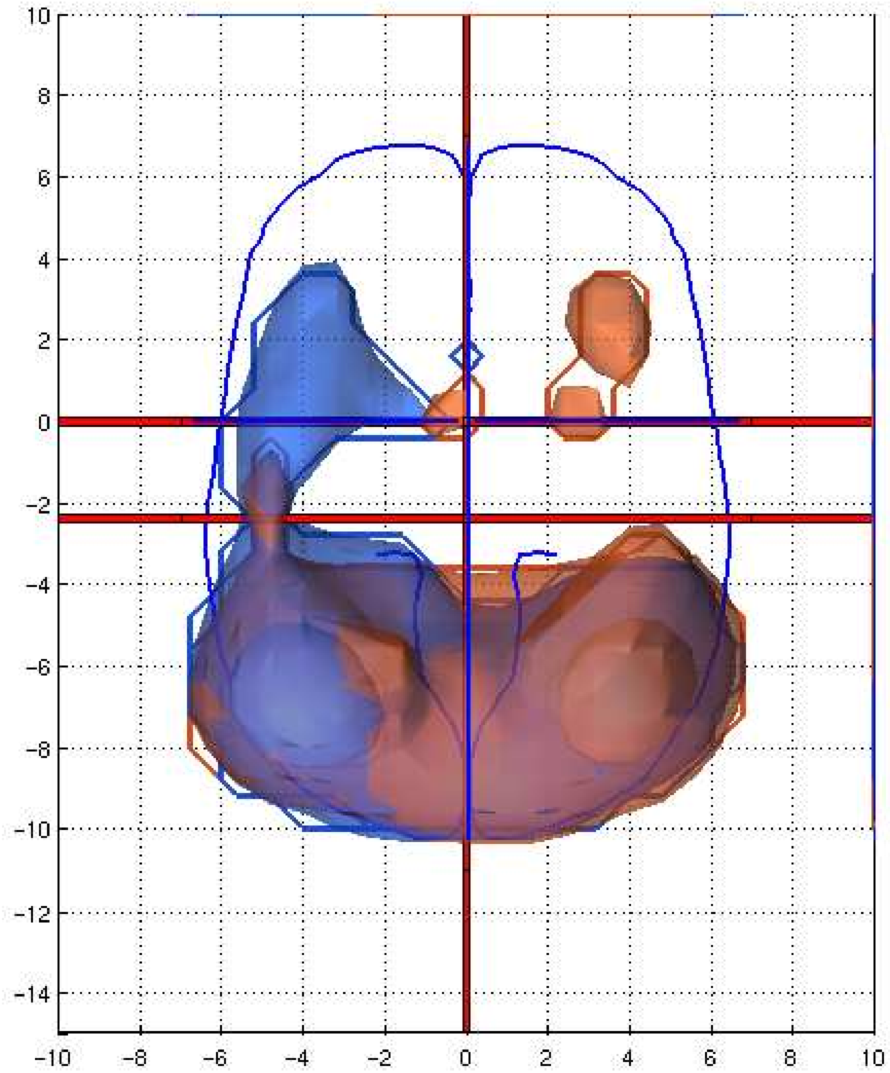


Figure 16: Co-activation with coordinates $(\pm 42, -69, 4)$ corresponding to visual motion with thresholds on 99% and 90% of all voxels.

- 'Activation' added with a Gaussian kernel centered at $(\pm 42, -69, 4)$ corresponding to visual motion.

CO-ACTIVATION

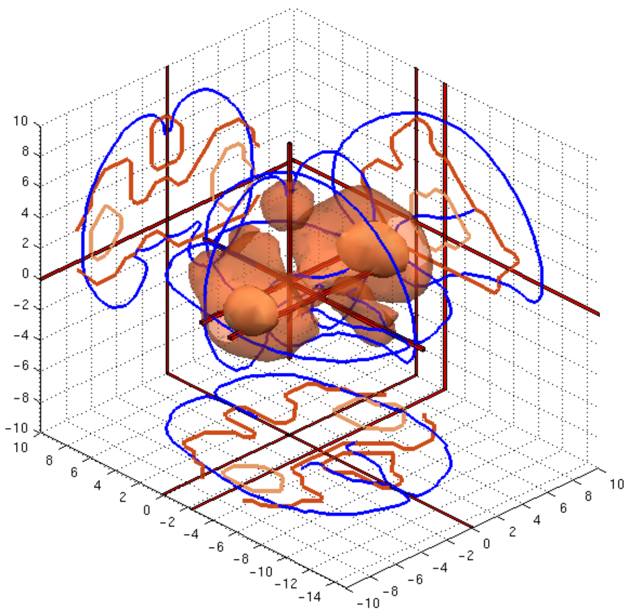


Figure 17: Co-activation with coordinates $(53, -19, 4)$ with thresholds on 99% and 90% of all voxels.

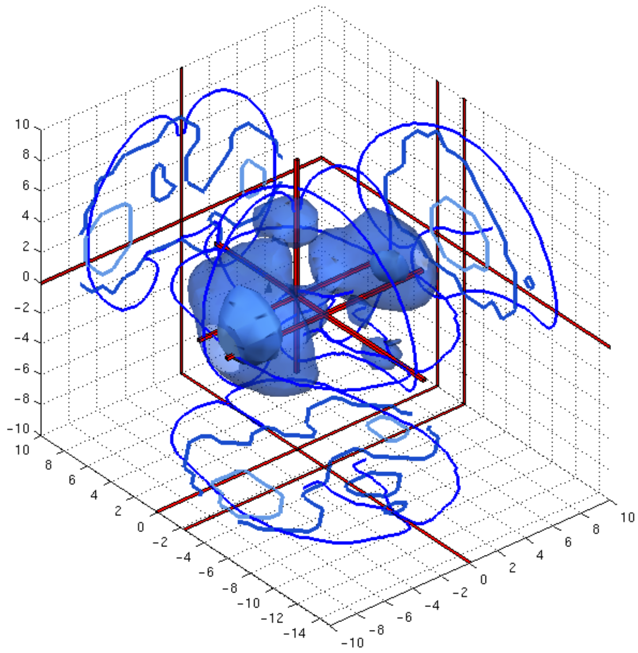


Figure 18: Co-activation with coordinates $(-53, -19, 4)$ with thresholds on 99% and 90% of all voxels.

CONCLUSION

- Modeling 3D Talairach coordinates with kernel density estimators.
- Finding related experiments, functional volumes modeling, anatomical atlases.
- Assessing connectivity with SVD, ICA and through 'co-activation'.
- Results available on the Internet from hendrix.imm.dtu.dk more specifically hendrix.imm.dtu.dk/services/jerne/.

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