Neuroinformatics in Functional Neuroimaging

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OVERSIGT

- Hvad er "Functional neuroimaging"?
- Hvad er "Neuroinformatics"?
- "Kanonisk analyse"
  - Kanonisk ridge analyse. Til singulær kanonisk korrelationsanalyse. Indkapsler andre modeller.
- Link (citation) og term (ord) analyse
  - Forfatter og journal kociteringsanalyser
  - Kontekstfølsomme autoritetter
- Modellering af BrainMap data
  - (Sandsynligheds-) tæthedsmodellering
  - "novelty" (nyhedsværdi).
- Konklusion

HVAD ER "FUNCTIONAL NEUROIMAGING"?

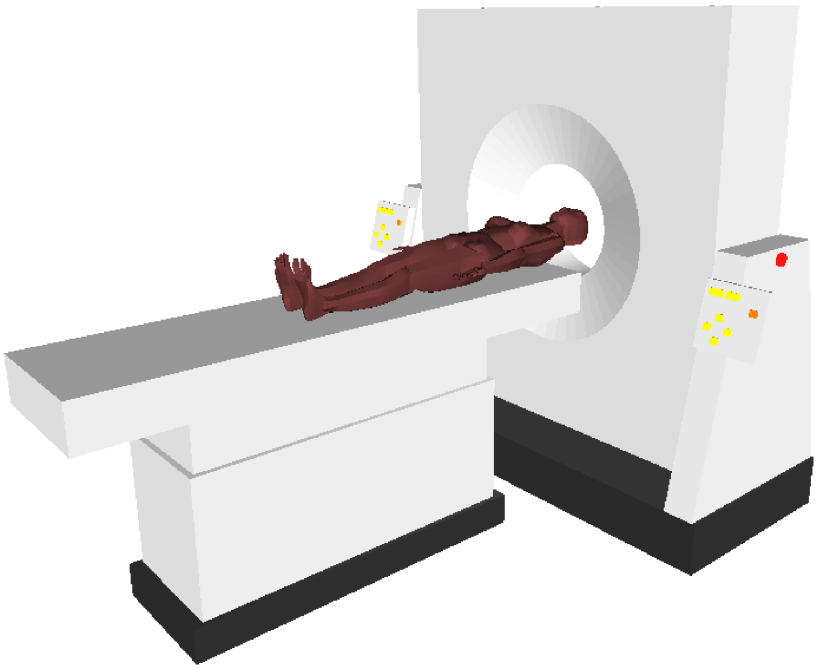


Figure 1: Model af positron emission skanner med en forsøgsperson.

- Functional Neuroimaging = funktionel "hjernebilleddannelse": Billeder af den arbejdende hjerne.
- Hjerneskanning der producerer to- eller tre-dimensionelle billeder/volumener: PET, fMRI. EEG, MEG.
- ...Mens en forsøgsperson udfører en "tanke-opgave": Fast eksperimentelt design (paradigm).

HVAD ER "NEUROINFORMATICS"?

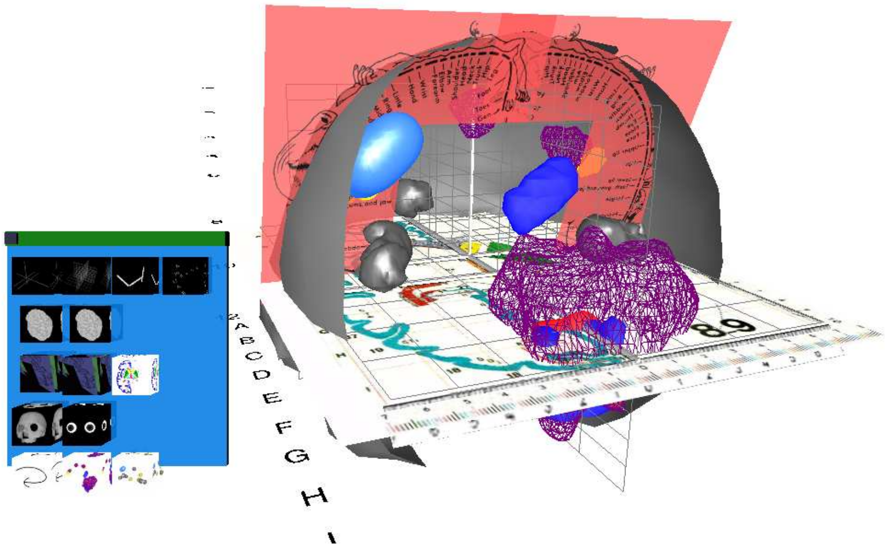


Figure 2: VRML med "summary images" (Ian Law).

- Neuroinformatik = neurovidenskab + informatik
- Præprocessering, e.g., rumlig normalisering til det så-kaldte "Talairach rum".
- Analyse. Resultatet er ofte et billed (summary image) med en eller flere aktiveringsfokus.
  - Tidserie analyse, e.g., 'Smooth FIR".
  - Ikke-superviserede analyse: Klusteranalyse, PCA
  - Kanonisk analyse.
- Meta-analyse. Analyse af publicerede resultater.
  - Få åbne neuroscience databaser (fMRI data center, BrainMap)
  - Meget information i tekst (artikler, web)

"KANONISK ANALYSE"

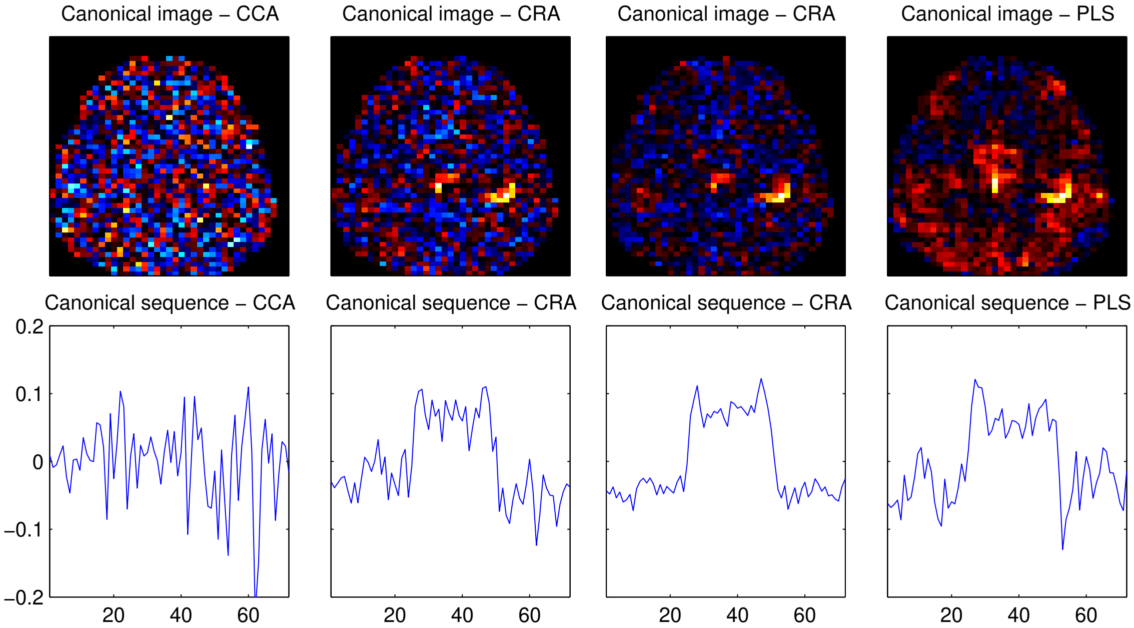


Figure 3: Kanonisk ridge analyse af singulært fMRI data set fra MGH.

- Lineær model mellem to matricer $\mathbf{X}(N \times P)$ og $\mathbf{Y}(N \times Q)$.
- Kanonisk korrelationsanalyse

$$\mathbf{ALB}^{\mathsf{T}} = \mathbf{S}_{\mathbf{xx}}^{-1/2} \mathrm{svd} \left[\mathbf{S}_{\mathbf{xx}}^{-1/2} \mathbf{S}_{\mathbf{xy}} \mathbf{S}_{\mathbf{yy}}^{-1/2} \right] \mathbf{S}_{\mathbf{yy}}^{-1/2}, \quad (1)$$

hvor kovariansen er $\mathbf{S}_{\mathbf{xx}} = N^{-1}\mathbf{X}^{\mathsf{T}}\mathbf{HX}$.

- Kan ikke direkte anvendes til singulær data data de inverse ikke eksisterer.
- Kanonisk ridge analyse (Vinod, 1976)

$$\tilde{\mathbf{S}}_{\mathbf{xx}} = (1 - k_X)\mathbf{S}_{\mathbf{xx}} + k_X \mathbf{I} \quad (2)$$

$$\tilde{\mathbf{S}}_{\mathbf{yy}} = (1 - k_Y)\mathbf{S}_{\mathbf{yy}} + k_Y \mathbf{I}, \quad (3)$$

KANONISK RIDGE ANALYSE

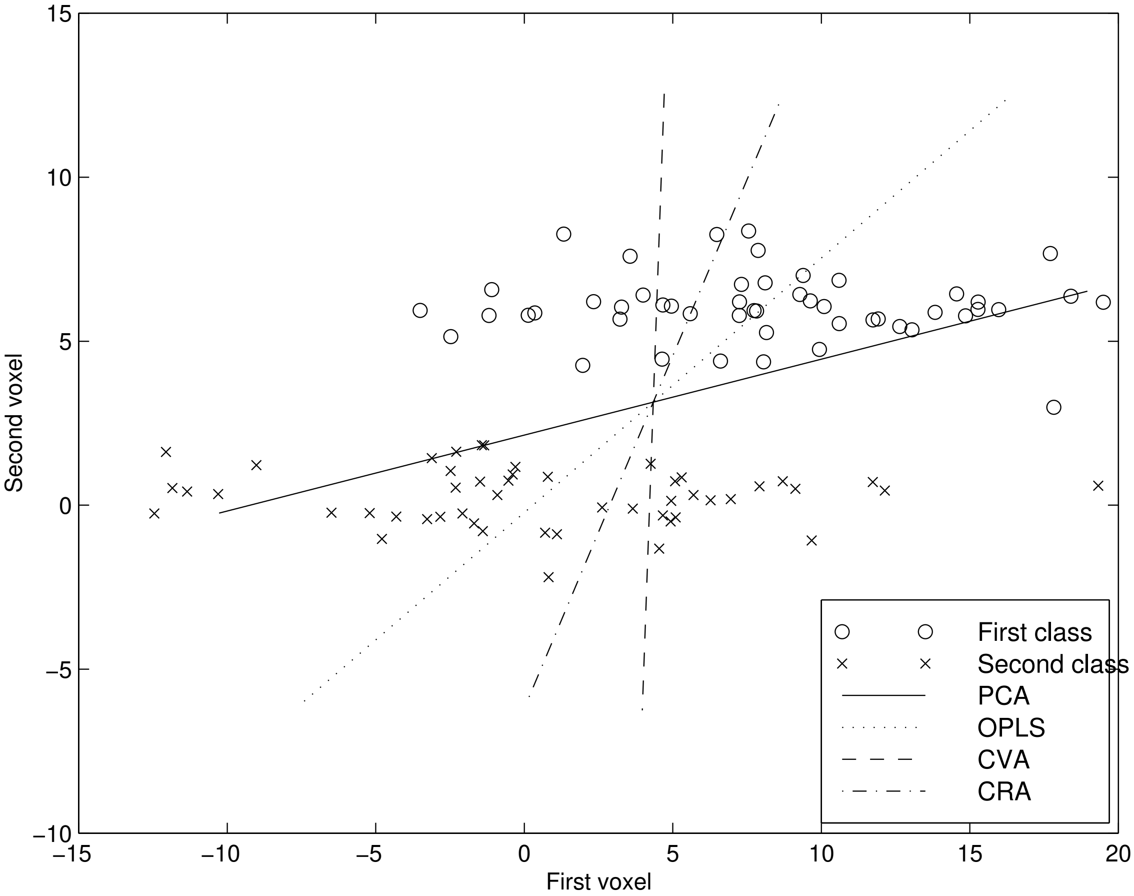


Figure 4: Kanonisk analyse af en to-voxel hjerne.

- En type af "partial least square" with $k_X = k_Y = 1$ (McIntosh et al., 1996).

$$\mathbf{U}\mathbf{L}\mathbf{V}^{\mathsf{T}} = \mathsf{svd}(\mathbf{X}^{\mathsf{T}}\mathbf{Y}). \tag{4}$$

- "Orthonormalized partial least squares" $k_X = 0, k_Y = 1$

$$\left(\mathbf{X}^{\mathsf{T}}\mathbf{X}\right)^{-1/2}\left[\left(\mathbf{X}^{\mathsf{T}}\mathbf{X}\right)^{-1/2}\mathbf{X}^{\mathsf{T}}\mathbf{Y}\right] \tag{5}$$

- Principal component analyse med $\mathbf{Y} = \mathbf{I}$ og $k_X = 1$.

KOMBINERING AF ORD OG LINK ANALYSE

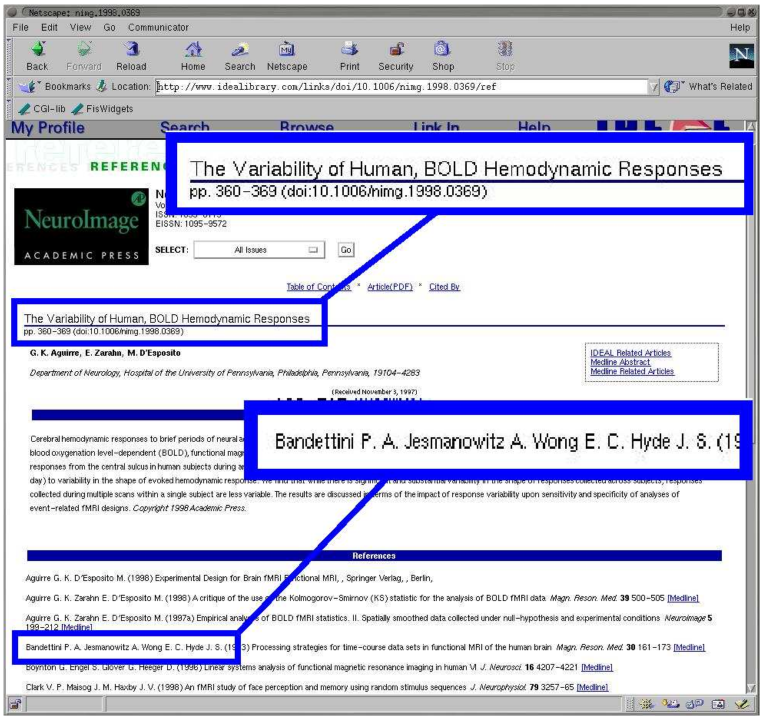


Figure 5: Udtrækning af data for kociteringsanalyse.

- Data fra “NeuroImage”: 325 web-sider med resuméer og citeringer.
- Udtrækning med perl/matlab: Titel (ord i title), navne på citerede forfattere, osv.
- Eksempler på præprocessering: Navne: Efternavn + ét initial. Tidskrifttitler: “3-stemming”, f. eks., “Hum Bra Map”, udtagen for visse præfix “neuropsy-”.
- Matrix eksempler: $\mathbf{X}(N \times P)$: Dokument $\times$ forfatter matrix: “Links”. $\mathbf{Y}(N \times Q)$: Dokument $\times$ ord matrix

CITERINGER SOM ET NETVÆRK

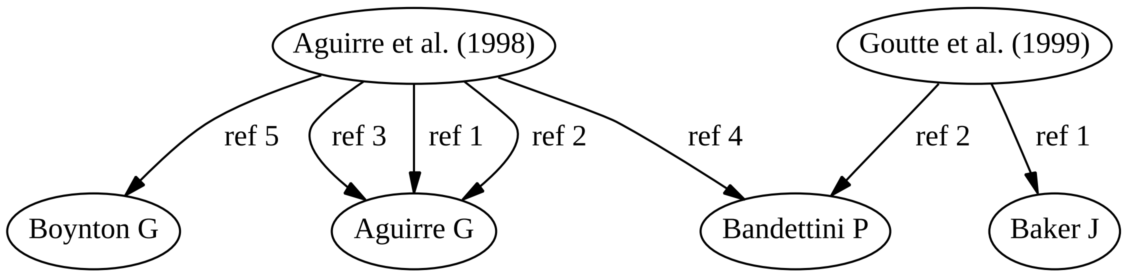


Figure 6: Netværk med artikel der citere forfattere.

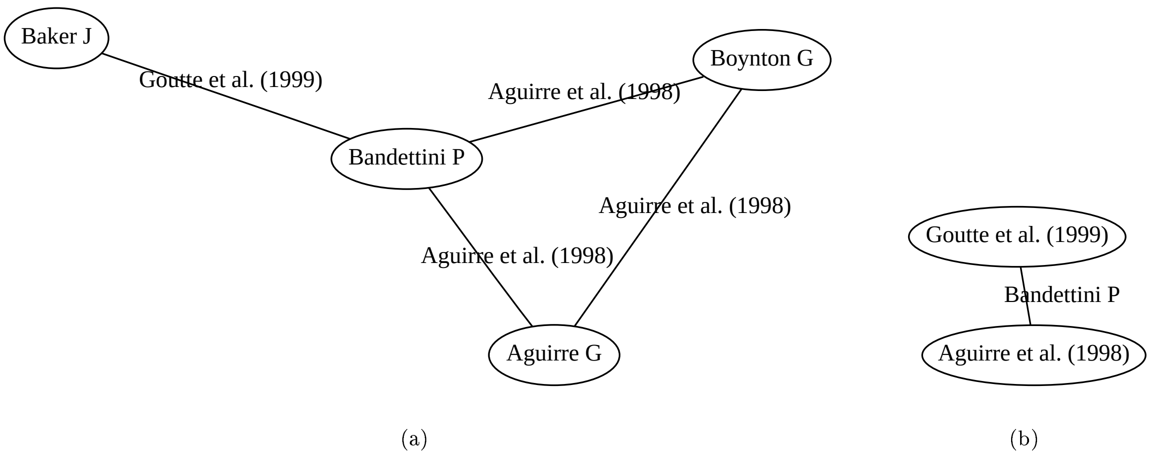


Figure 7: Forfattere og dokumenter som knude punkter

FORFATTERKOCITERINGSANALYSE

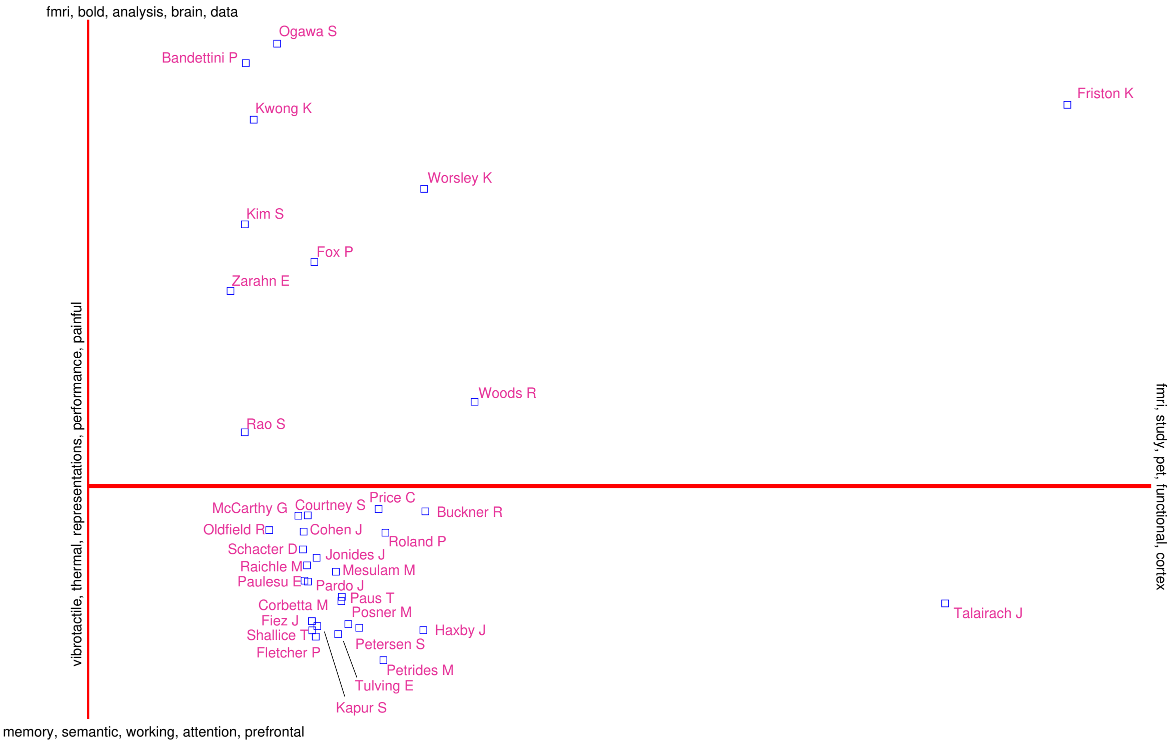


Figure 8: Først og anden principal komponent med de mest citerede forfattere.

- $\mathbf{X}(N \times P)$: Dokument $\times$ citerede fofatter matrix, i.e., listen med citeringer for hver artikel. $N = 325$ dokuments, $P = 11558$ citerede forfattere.
- "Forfatter kociteringsanalyse" (McCain, 1990; White and Griffith, 1981). Klusteranalyse, multidimensionel skalering, her SVD:

$$\mathbf{X} = \mathbf{U}\mathbf{L}\mathbf{V}^{\mathsf{T}}. \tag{6}$$

- Første principale komponent (Kleinberg, 1997): $\mathbf{u}_1$: Hub dokuments (citere mange autoriteter), $\mathbf{v}_1$: Autoritative forfattere (er citeret af mange hubs)

AKSE ANNOTERING

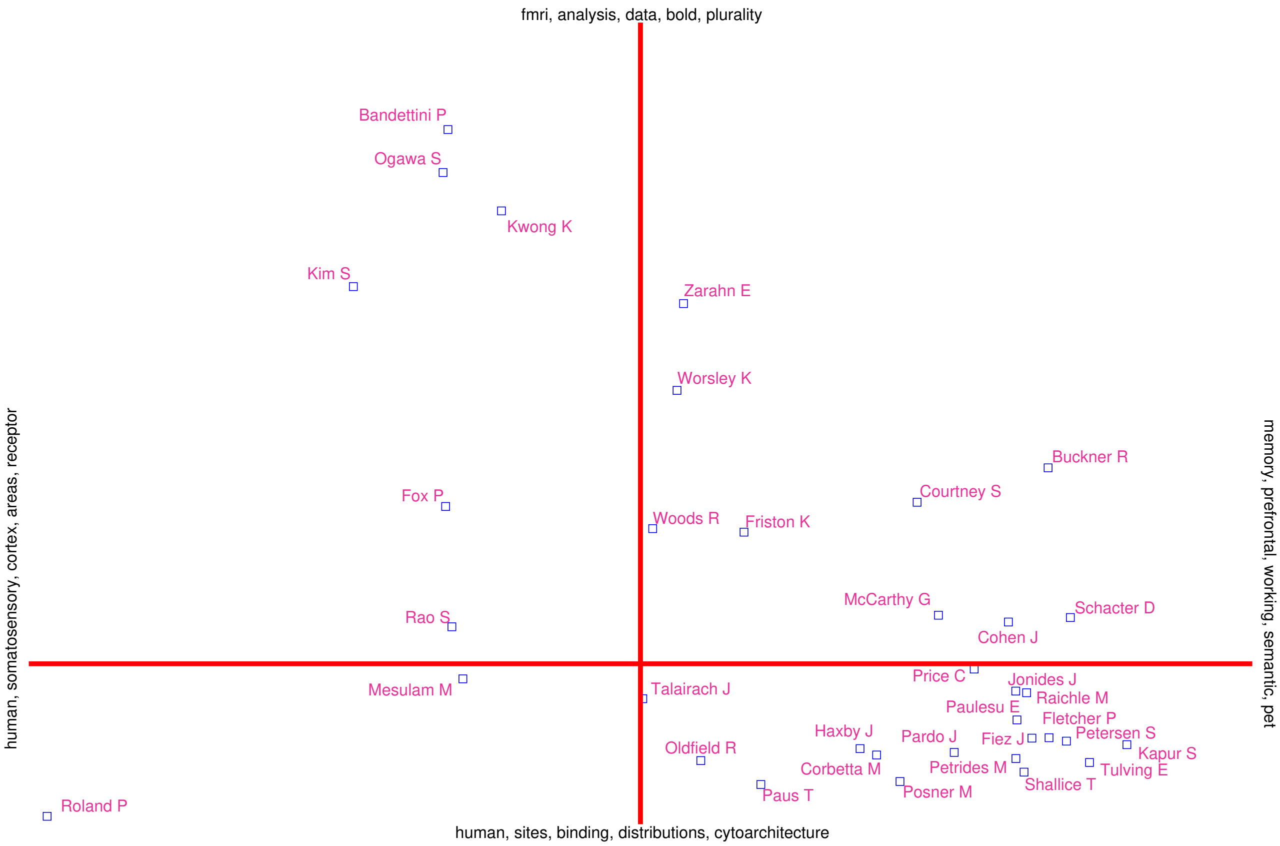


Figure 9: Anden og tredie principale kmponenter med de mest citerede forfattere.

- $\mathbf{Y}(N \times Q)$: Dokument $\times$ ord matrix. Ord fra artikeltitlen.
- Projicér ordene på egenforfatter-rummet

$$\mathbf{Z} = \mathbf{Y}^{\mathsf{T}}\mathbf{U} \qquad (7)$$

- Akse-annoteringen for den i'de egenforfatter er de (fem) største elementer med den højeste score i den i'de kolonne af $\mathbf{Z}$.

IDENTIFICERING AF GRUPPER

1	2	3	4	5	6
Raichle M	Rosen B	Friston K	Haxby J	Woods R	Roland P
Petersen S	Turner R	Frackowiak R	Ungerleider L	Passingham R	Cherry S
Buckner R	Bandettini P	Frith C	Mintun M	Rao S	Mesulam M
Grasby P	Kwong K	Evans A	Petrides M	Brooks D	Toga A
Grady C	Glover G	Talairach J	D'Esposito M	Mazoyer B	Zatorre R
Miezin F	Jezzard P	Worsley K	Gore J	Binder J	Zilles K
Fletcher P	Belliveau J	Tournoux P	Noll D	Fink G	Van Essen D
Horwitz B	Kim S	Mazziotta J	Cohen J	Grafton S	Weinberger D
Posner M	Hyde J	Poline J	Goldman-Rakic P	Deiber M	Arndt S
Maisog J	Ugurbil K	Holmes A	Meyer E	Hammeke T	Gazzaniga M
Wise R	Kennedy D	Fox P	McCarthy G	Frost J	Lancaster J
Houle S	Weisskoff R	Dolan R	Koeppe R	Hallett M	Ledberg A
Fiez J	Cohen M	Liddle P	Aguirre G	Weiller C	Schlaug G
Shallice T	Wong E	Ashburner J	Smith E	Kleinschmidt A	Steinmetz H
Alpert N	Josephs O	Price C	Minoshima S	Sadato N	Eriksson L
Herscovitch P	Menon R	Heather J	Corbetta M	Silbersweig D	Matelli M
Kapur S	Ogawa S	Neelin P	Jonides J	Kawashima R	Pandya D
Tulving E	Williams S	Watson J	Nobre A	Seitz R	Galaburda A
Paulesu E	Brady T	Marrett S	Shulman G	Tzourio N	Meyer J
Rapoport S	Dale A	Phelps M	Paus T	Allison T	Peters T
McIntosh A	Jesmanowicz A	Carson R	Zarahn E	Nixon P	Schleicher A

Figure 10: NMF of dokument citeret forfatter matrix.

- Non-negative matrix factorization (NMF) (Lee and Seung, 2001)
- Grupper i dette data set:
  - fMRI gruppe: Bruce Rosen, Robert Turner; "fMRI", "BOLD", "MRI".
  - Haxby, Glover: "Memory", "prefrontal", "working" modsat "motor", "human", "activation" with Mazziotta and Roland.
  - Metodologi: Karl J. Friston, Keith J. Worsley; "Statistical", "Analysis"

TIDSSKRIFT KOCITATION ANALYSE

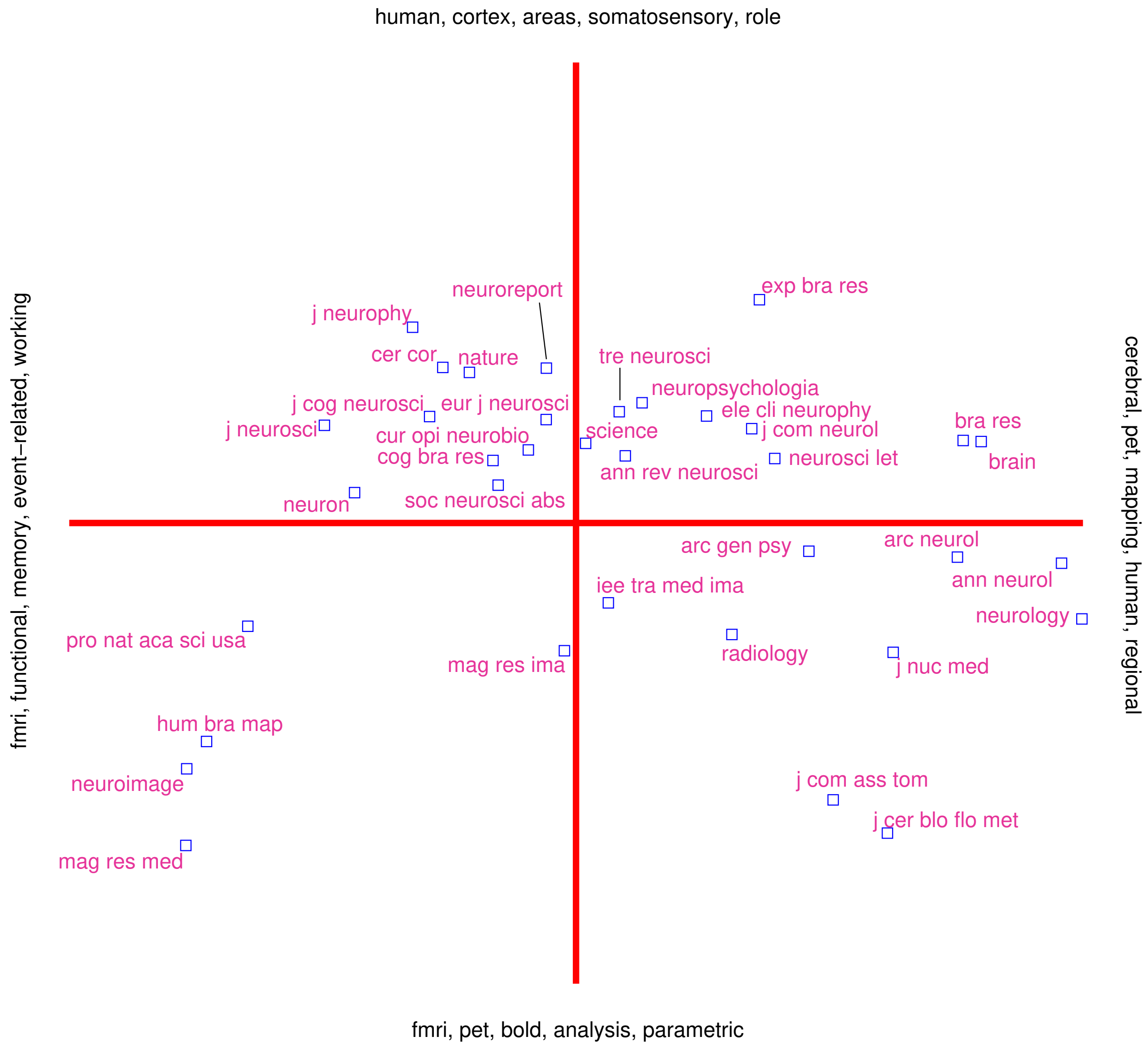


Figure 11: Anden og tredie principale komponent med de mest citerede tidsskrifter fra "NeuroImage".

- $\mathbf{X}(N \times P)$: Dokument $\times$ citeret tidskrift matrix.
- Akser: PET versus fMRI, makroskopisk versus mikroskopisk.

KONTEXTFØLSOMME AUTORITETER

Ikke-kontekst	a(fmri)	b(fmri)
Frackowiak R	Friston K	Friston K
Friston K	Frackowiak R	Frackowiak R
Frith C	Turner R	Turner R
Raichle M	Rosen B	Rosen B
Evans A	Raichle M	Frith C
Talairach J	Frith C	Holmes A
Tournoux P	Holmes A	Raichle M
Worsley K	Bandettini P	Bandettini P
Petersen S	Kwong K	Worsley K
Mazziotta J	Worsley K	Poline J
Holmes A	Poline J	Evans A

- Singular værdi dekomposition af ord matrixen (latent sematisk analyse) (Deerwester et al., 1990):

$$\mathbf{Y} = \mathbf{ULV}^{\mathsf{T}} \tag{8}$$

- Projicér en ord vektor $\mathbf{v}$ på $\mathbf{y}$-rummet med et passende generaliserbart underrum

$$\mathbf{y} = \mathbf{U}f(\mathbf{L})\mathbf{v}^{\mathsf{T}} \tag{9}$$

- Anvendelse af dokument vægtning på forfattere:
  - Enten gennem en ekstra SVD (a):

$$\mathbf{X}^* = \mathbf{y}\mathbf{1}^{\mathsf{T}} \odot \mathbf{X} \tag{10}$$

    ...og SVD med $\mathbf{X}^*$.
  - Eller ved direkte projicering (b):

$$\mathbf{a} = \mathbf{X}^{\mathsf{T}}\mathbf{y} \tag{11}$$

VISUALISERING AF LINKS

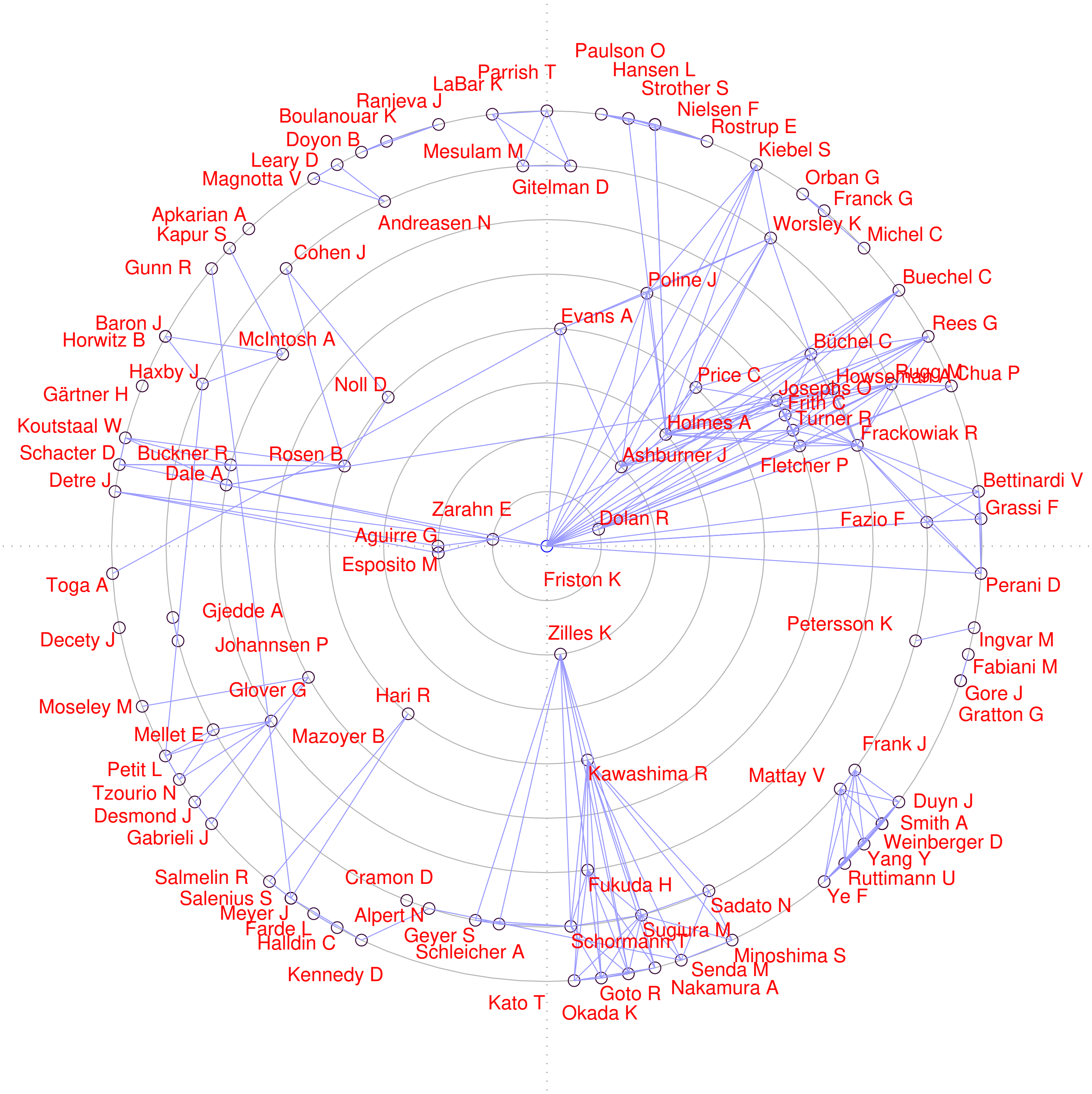


Figure 12: Koforfatterskab bullseyeplot/"targetgram" inspireret af visualisering fra gruppepsykologi. 109 af de mest publiserende forfattere (svarende til tre dokumenter eller mere).

BRAINMAP DATABASEN

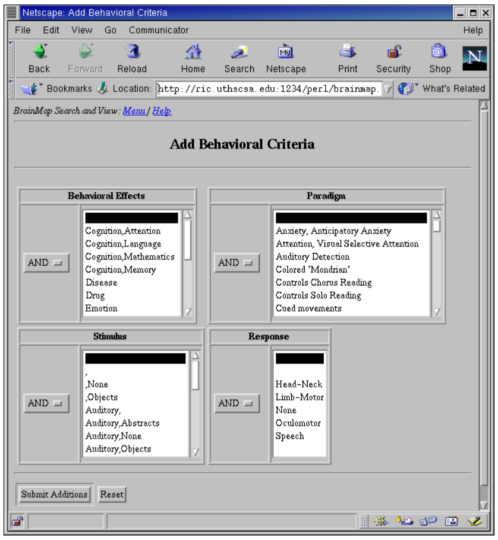


Figure 13: "Behavioral" (adfærds-) kriteria forespøgelse web-page.

- Database med resultater fra funktionelle neuroimaging studier. *Research Imaging Center*, http://ric.uthscsa.edu. (Fox and Lancaster, 1994)
- Består af: Entry + Database + Search and View.
  - "BrainMap Entry". Indtastningsprogram
  - Database. Oracle SQL Relationsdatabase.
  - "BrainMap Search & View".
- 3 forskellige datastrukturer + adfærdsstruktur
  - Paper (225): Bibliografisk information
  - Experiment (771): Beskrivelse af paradigmet
  - Location (7683): Talairach koordinater, anatomiske og Brodmann label.

MODELLERING AF ANATOMISKE LABELS OG 3D TALAIRACH KOORDINATER

- Modellering af forholdet mellem *3D Talairach koordinater* (tre-dimensionelle kontinuerte værdier) og *anatomiske labels* (BrainMap's "lobar anatomy" tekstfelt).
- Novelty detektion: Opdagelse af usædvanlige entry (outliers).

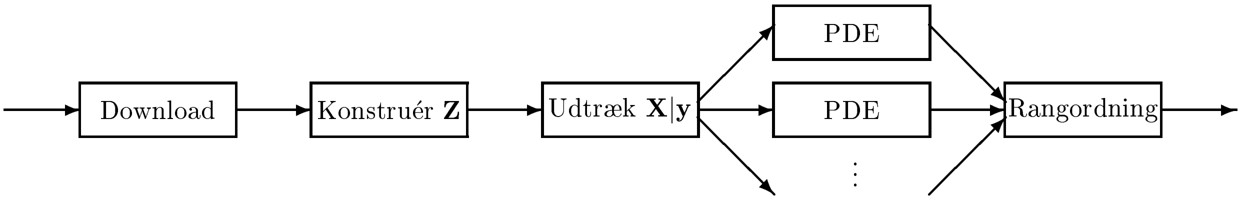


Figure 14: Processeringskema til at finder outliere i BrainMap

- Nedhent BrainMap web-sider med et Perl/Matlab skript
- Konstruér en matrix $\mathbf{Z}(N \times P) = [\mathbf{X}, \mathbf{Y}]$ der indeholder N række svarende til $N = 3935$ *locations*.
- Udtræk undermatrix $\mathbf{X}$ der indeholder Talairach koordinater for en given frase.
- Konstruér tæthedsmodeller for hver undermatrix. submatrix.
- Rangorden *location* afhængig af deres tæthedsværdier.

UDTRÆKNING AF LOCATION DATA

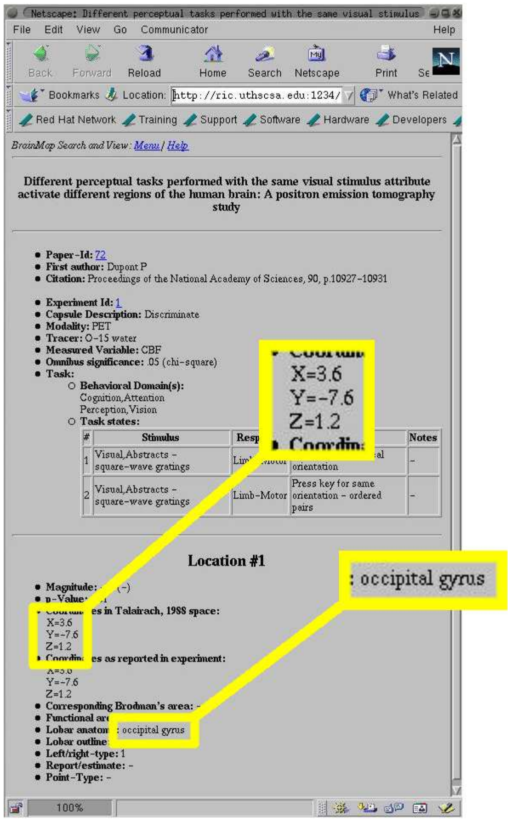
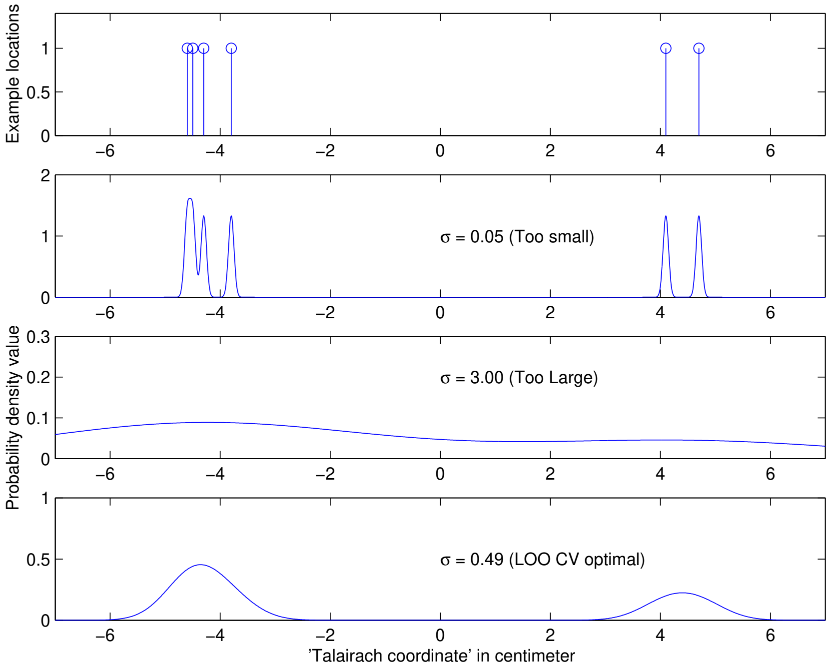


Figure 15: Extraction of data from a "location".

- Udtræk af Talairach koordinate. Eksempel (3.6, -7.6, 1.2).
- Udtrækning af hvert ord og frase fra feltet "Lobar anatomy".
- Eksampel "lateral superior parietal" → {"lateral", "superior", "parietal", "lateral superior", "superior parietal", "lateral superior parietal"}.
- Flere data punkter for hver *location*.

TÆTHEDSMODELLERING



- Anse "locations" genereret fra en fordeling $p(\mathbf{x}|c)$, hvor $\mathbf{x}$ er en koordinat og c er et ord eller en frase.
- Modeller: Simpel parametrisk fordeling, mikstur-modeller, kernemetoder.

$$p(\mathbf{x}) = N^{-1} \sum_{n}^{N} (2\pi\sigma^2)^{-3/2} \exp\left(-\frac{1}{2\sigma^2}(\mathbf{x}-\boldsymbol{\mu}_n)^2\right) \tag{12}$$

- Optimering af kernebredden med "lad-en-ud" krydsvalidering.
- Robust to-trins analyse hvor andet trin ekskluderer 5% af *locations* med laveste tæthed.

PDFS FOR LOCATION LABEL

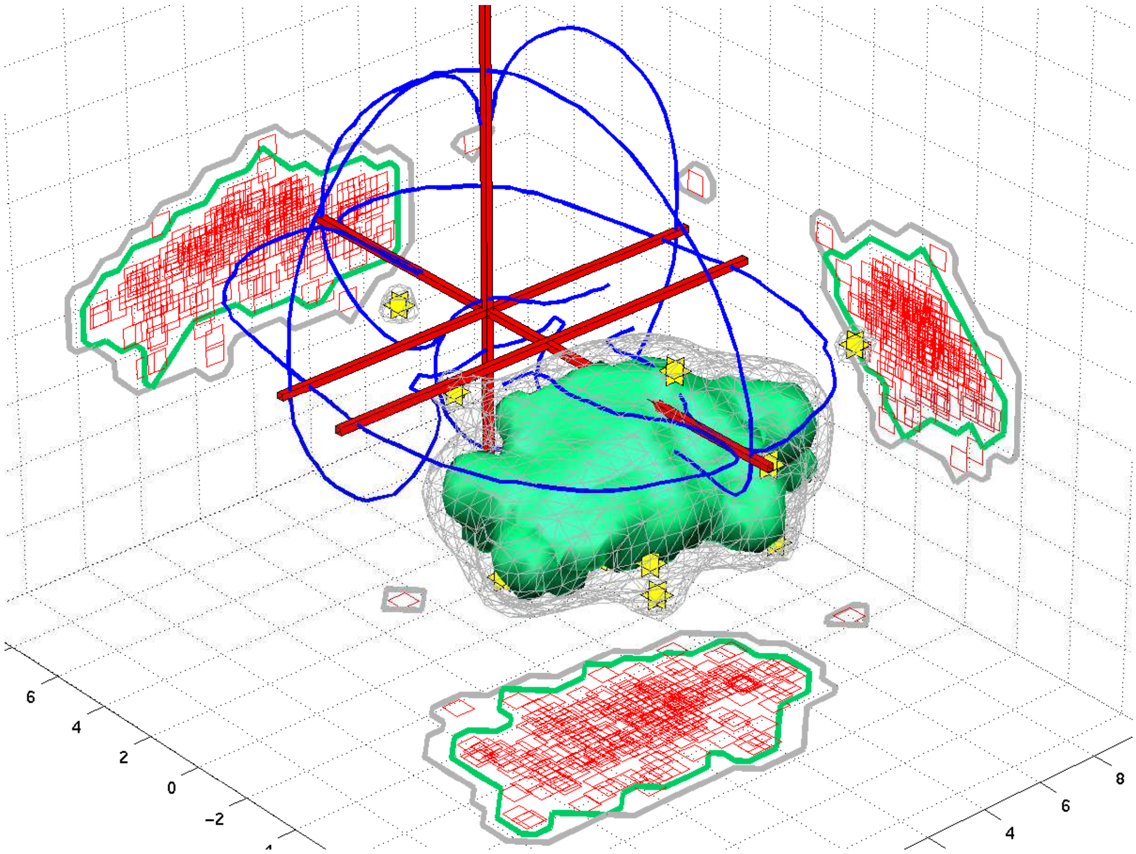
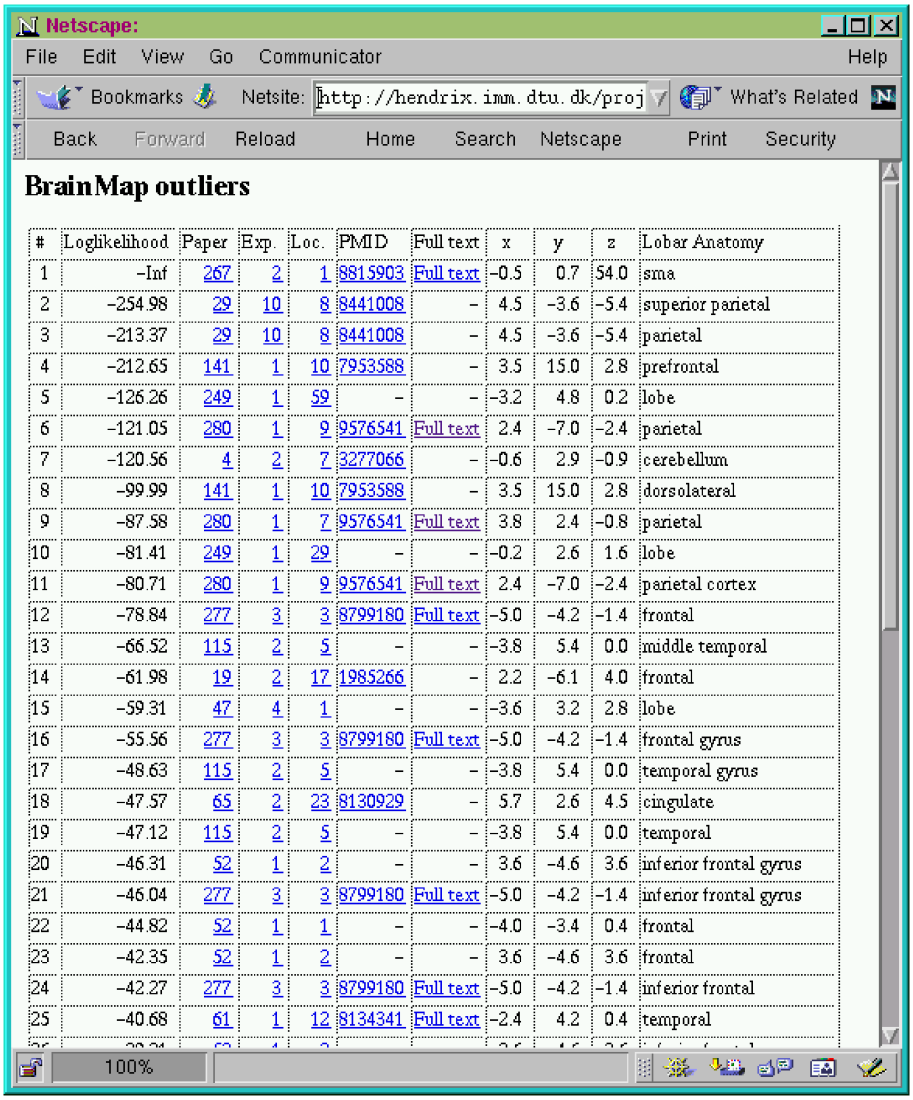


Figure 16: Tætheder for cerebellum (lillehjerne) locations.

- "Corner cube" visualisering. Betingning på anatomiske labler: $p(\mathbf{x}|c = \text{cerebellum})$.
- Gule glyffer: Oprindelige BrainMap locations.
- Grå gitter: Isoflade i første niveau tætheder.
- Grøn flade: Isoflade i andet "robuste" niveau.

RANGORDNING AF OUTLIERE



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

- Automatisk genereret liste med hyperlinks.
- Elementer sorteret efter novelty
- 2. og 3. element: “superior parietal”, “parietal”. Mere information i en frase end i et ord.

"MANUEL" UNDERSØGELSE AF 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. Elementerne er ordnet i henhold til novelty. Anden kolonne er "paper", "experiment" og "location" identifikator fra BrainMap. Tredie til femte kolonne er x, y og z med "reported" koordinater fra BrainMap (ikke de korregerede "Talairach 1988" koordinater.

ORDET "LOBE"

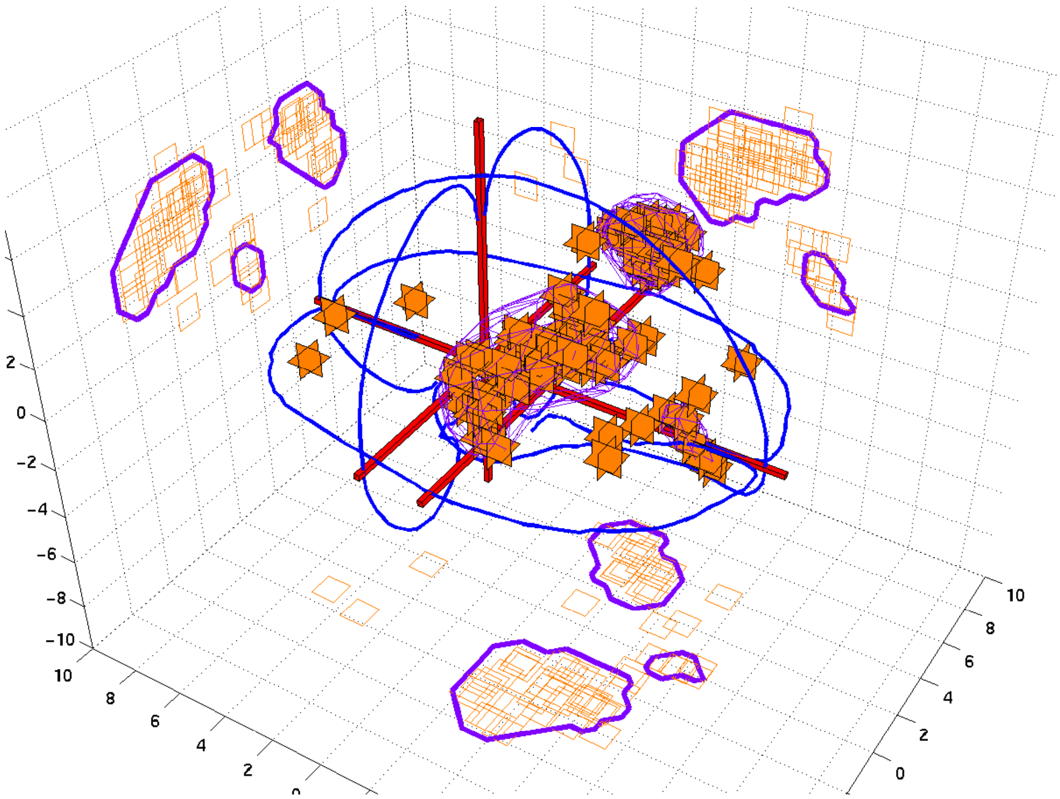


Figure 17: Tæthed af ordet "lobe". Den blå/magenta gittermodel er andet trins tæthed ved $P_{\mathrm{HPD}} = 0.5$ tærskel, og den orange glyf er "lobe" BrainMap locations.

Antal	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 er fokuseret i bestemte områder.

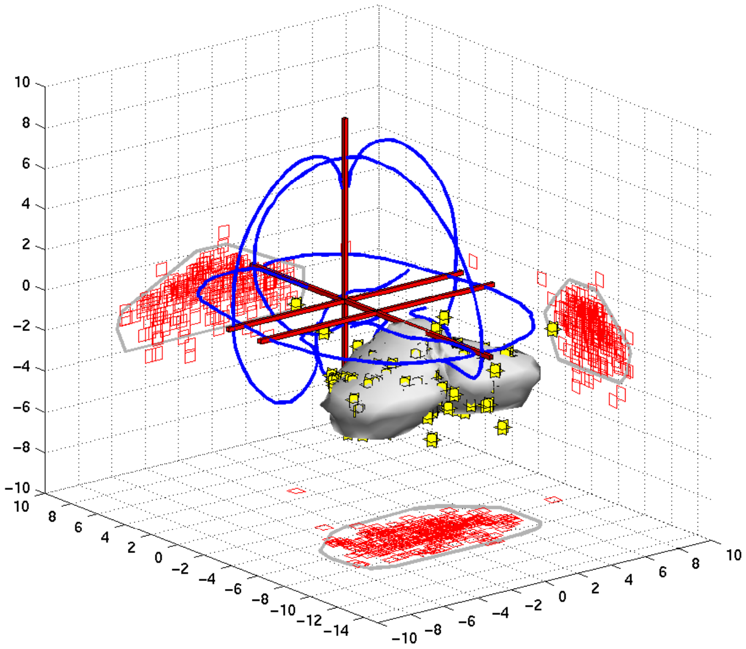


Figure 18: Talairach cerebellum.

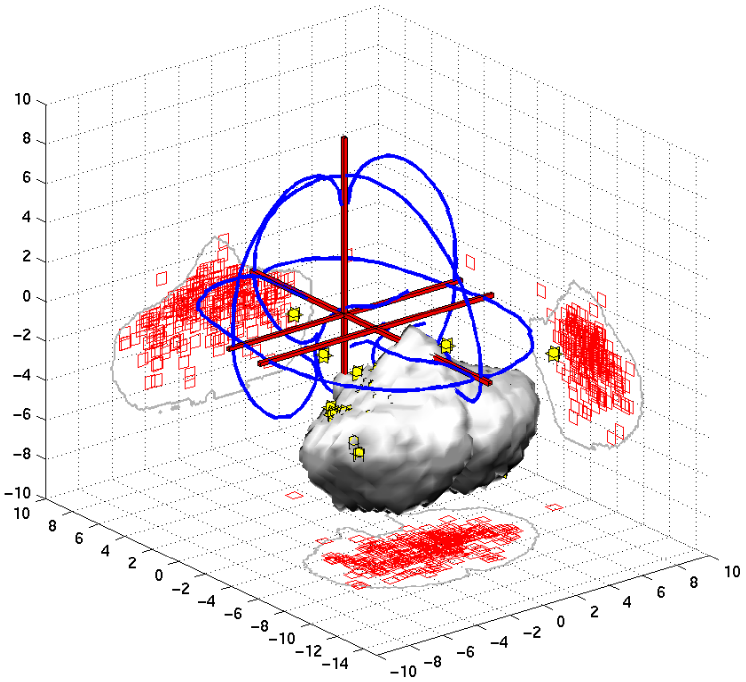


Figure 19: MNI cerebellum.

MODELLERING AF ADFÆRDSDATA OG 3D TALAIRACH KOORDINATER

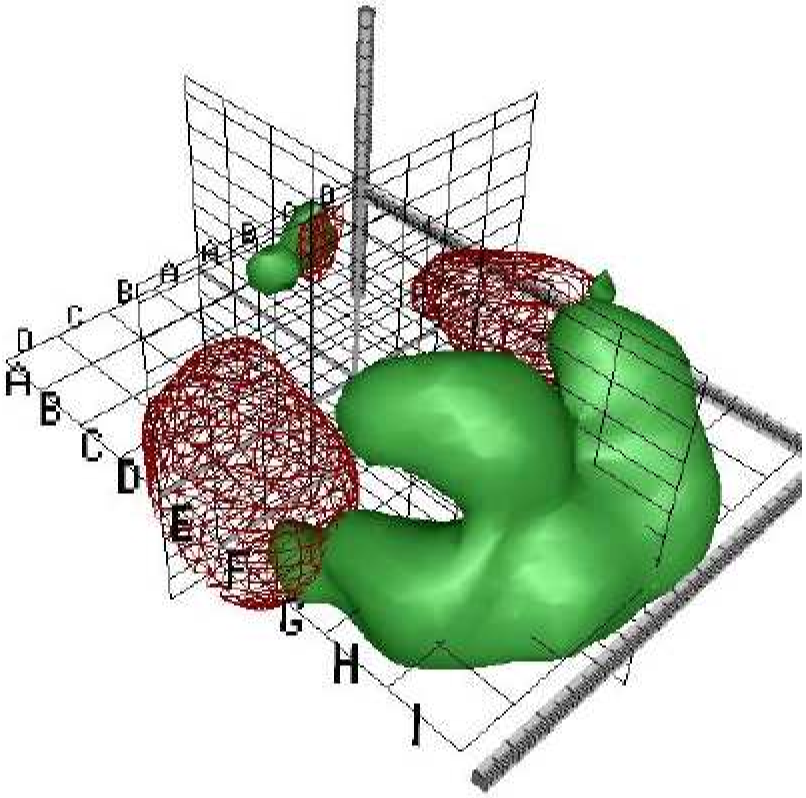


Figure 20: Tætheder fra "Vision" og "Audition" adfærdsparadigm i BrainMap.

- Betingning på adfærd: $p(\mathbf{x}|\text{behavior} = \text{"vision"})$.
- Problem: Adfærdbeskrivelsen er på *experiment* niveau. Resumé og andet et endnu højere niveau. Multiple betingning
- Anvendt for enkeltordslæsning med 154 håndplukket *locations* (Turkeltaub et al., 2001). "Functional volume modeling" (Fox et al., 1997)

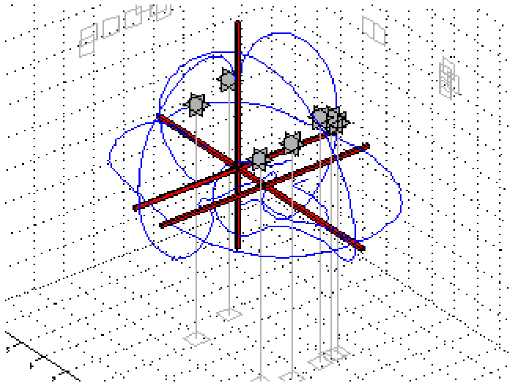
RELATEREDE VOLUMNER

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: Genereret web-sider (Corbetta et al., 1993).

- Konstruering af matrix $\mathbf{X}(N \times P)$ med voxeliserede BrainMap eksperimenter og andre volumner.
- Måling af afstand mellem de N volumner i $\mathbf{X}$, f. eks. med korrelationkoefficienten.
- Rangordning af de $N-1$ volumener for hver volume og rapportering på web-side.

KONKLUSION

- Kanonisk ridge analyse til singulær data
- Kombinering af tekst og link analyse gennem kociteringsanalyse.
  - Identificering af relevante grupper.
  - Kontekstfølsomme authoritetter
- Automatisk ikke-superviseret outlierdetektion i BrainMap.
  - Ingen intervention er nødvendig
  - Finder "interessante" outliers: Indtastningsfejl, fejl i artiklen.
- "Relaterede volumner" er det muligt at finde.
- *Lyngby* Matlab toolbox til modellering af funktionelle hjernebilleder.
- *Brede* Matlab toolbox til håndtering, modellering og visualisering af BrainMap data og lignende.

ERRATA

- Ligning 3.27, side 47

$$\mathbf{U}\mathbf{L}\mathbf{V}^{\mathsf{T}} = \mathsf{svd}\left[\mathbf{H}\mathbf{X}\mathbf{D}^{-1}\right] \qquad (13)$$

  hvor $\mathbf{D}(P \times P)$ er en diagonal matrix med standard afvigelserne for hver variable. Dette er skala transformationen (Mardia et al., 1979, sektion 1.5.1).

- Samme fejl i ligning 3.117, side 67.

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