Modelling Strategies for Functional Magnetic Resonance Imaging

This thesis collects research done on several models for the analysis of functional magnetic resonance neuroimaging (fMRI) data. Several extensions for unsupervised factor analysis type decompositions including explicit delay modelling as well as handling of spatial and temporal smoothness and generalisations to higher order arrays are considered. Additionally, an application of the natural conjugate prior for supervised learning in the general linear model to efficiently incorporate prior information for supervised analysis is presented. Further extensions include methods to model nuisance effects in fMRI data thereby suppressing noise for both supervised and unsupervised analysis techniques.

Long-term global and regional brain volume changes following severe traumatic brain injury: A longitudinal study with clinical correlates

Traumatic brain injury (TBI) results in neurodegenerative changes that progress for months, perhaps even years post-injury. However, there is little information on the spatial distribution and the clinical significance of this late atrophy. In 24 patients who had sustained severe TBI we acquired 3D T1-weighted MRIs about 8 weeks and 12 months post-injury. For comparison, 14 healthy controls with similar distribution of age, gender and education were scanned with a similar time interval. For each subject, longitudinal atrophy was estimated using SIENA, and atrophy occurring before the first scan time point using SIENAX. Regional distribution of atrophy was evaluated using tensor-based morphometry (TBM). At the first scan time point, brain parenchymal volume was reduced by mean 8.4% in patients as compared to controls. During the scan interval, patients exhibited continued atrophy with percent brain volume change (%BVC) ranging between − 0.6% and − 9.4% (mean − 4.0%). %BVC correlated significantly with injury severity, functional status at both scans, and with 1-year outcome. Moreover, %BVC improved prediction of long-term functional status over and above what could be predicted using functional status at not, vert, similar 8 weeks. In patients as compared to controls, TBM (permutation test, FDR 0.05) revealed a large coherent cluster of significant atrophy in the brain stem and cerebellar peduncles extending bilaterally through the thalamus, internal and external capsules, putamen, inferior and superior longitudinal fasciculus, corpus callosum and corona radiata. This indicates that the long-term atrophy is attributable to consequences of traumatic axonal injury. Despite progressive atrophy, remarkable clinical improvement occurred in most patients.
Regional activation of the human medial temporal lobe during intentional encoding of objects and positions

The medial temporal lobe (MTL) consists of several regions thought to be involved in learning and memory. However, the degree of functional specialization among these regions remains unclear. Previous studies have demonstrated effects of both content and processing stage, but findings have been inconsistent. In particular, studies have suggested that the perirhinal cortex is more involved in object processing than spatial processing, while other regions such as the parahippocampal cortex have been implicated in spatial processing. In this study, functional magnetic resonance imaging (fMRI) optimized for the MTL region was used to probe MTL activation during intentional encoding of object identities or positions. A region of interest analysis showed that object encoding evoked stronger activation than position encoding in bilateral perirhinal cortex, temporopolar cortex, parahippocampal cortex, hippocampus and amygdala. Results also indicate an unexpected significant correlation in activation level between anterior and posterior portions in both the left parahippocampal cortex and left hippocampus. Exploratory analysis did not show any regional content effects during preparation and rehearsal stages. These results provide additional evidence for functional specialization within the MTL, but were less clear regarding the specific nature of content specificity in these regions. (C) 2009 Elsevier Inc. All rights reserved.
The effects of age on functional specialization in the human medial temporal lobe

Recent advances in the cognitive neuroscience of ageing have uncovered important links between age-related neurobiological changes and their role in cognitive and behavioural changes. However, the exact nature of this relationship is still unresolved, and studies of regions such as the medial temporal lobe (MTL) have produced conflicting findings. Here, we report the results from a functional Magnetic Resonance Imaging (fMRI) study of the effect of age on functional specialization in the MTL region during intentional encoding and recognition of objects and positions. We applied a region of interest analysis in native space and corrected for the effects of gender and individual differences in cerebral blood flow. Behavioural results demonstrated that performance on both the object and position tasks declined equally with increasing age. Our fMRI results showed that during the encoding and recognition stage, increasing age was associated with a reduction in functional specialization in a number of MTL regions. These findings are discussed in light of theories of the effects of age on functional specialization in the brain.

General information

State: Submitted
Organisations: Image Analysis and Computer Graphics, Department of Informatics and Mathematical Modeling, Aarhus University, Copenhagen University Hospital
Authors: Ramsey, T. (Ekstern), Liptrot, M. (Ekstern), Skimminge, A. J. M. (Intern), Lund, T. (Ekstern), Sidaros, K. (Intern), Christensen, M. S. (Ekstern), Baaré, W. (Ekstern), Paulson, O. B. (Ekstern), Jernigan, T. L. (Ekstern)
Monitoring angiogenesis using magnetic resonance methods
When a tumor reaches a certain size it can no longer rely on passive perfusion for nutrition. The tumor therefore emits signaling molecules which stimulating surrounding vessels to divide and grow towards the tumor, a process known as angiogenesis. Very little angiogenesis is present in healthy adults where it is primarily found in wound healing, pregnancy
and during the menstrual cycle. This thesis focuses on the negative consequences of angiogenesis in cancer. It consists of an initial overview followed by four manuscripts. The overview gives a short introduction to the process of angiogenesis and the involved signaling molecules. Subsequently, a short review of contrast agents and perfusion measurements is given. Finally, methods for monitoring angiogenesis using magnetic resonance imaging are reviewed. A method for monitoring early stages of angiogenesis as well as the effect of anti-angiogenic treatment is presented in the first manuscript. In the second and third manuscript, two separate methods of quantifying perfusion, blood volume and vessel permeability are presented. The methods are used to show that drug delivery to a xenografted tumor is plausible and to show possible vascular maturation in a transgenic mouse model. The last manuscript presents a new method for in vivo cell labeling. This method could find use in studying the metastatic spread of cancer cells throughout the body.

**General information**
State: Published
Organisations: Image Analysis and Computer Graphics, Department of Informatics and Mathematical Modeling
Authors: Holm, D. A. (Intern), Sidaros, K. (Intern), Larsen, R. (Intern)
Number of pages: 130
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**Publication information**
Original language: English
Series: IMM-PHD-2008-199
Main Research Area: Technical/natural sciences
Electronic versions:
phd199_dah.pdf
Source: orbit
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Publication: Research › Ph.D. thesis – Annual report year: 2008

**Investigation of Spatial Normalization Problems for Medial Temporal Lobe Structures**

**General information**
State: Published
Organisations: Department of Informatics and Mathematical Modeling, Cognitive Systems
Authors: Liptrot, M. G. (Intern), Ramsøy, T. Z. (Ekstern), Lund, T. E. (Ekstern), Sidaros, K. (Intern), Christensen, M. S. (Ekstern), Nielsen, F. Å. (Intern), Baare, W. (Ekstern), Jernigan, T. L. (Ekstern)
Publication date: 2006

**Host publication Information**
Title of host publication: NeuroImage special issue: Twelfth Annual Meeting of the Organization for Human Brain Mapping
Publisher: Elsevier
Main Research Area: Technical/natural sciences
Links:
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Source-ID: 191590
Publication: Research - peer-review › Article in proceedings – Annual report year: 2006

**Non-white noise in fMRI: Does modelling have an impact?**
The sources of non-white noise in Blood Oxygenation Level Dependent (BOLD) functional magnetic resonance imaging (fMRI) are many. Familiar sources include low-frequency drift due to hardware imperfections, oscillatory noise due to respiration and cardiac pulsation and residual movement artefacts not accounted for by rigid body registration. These contributions give rise to temporal autocorrelation in the residuals of the fMRI signal and invalidate the statistical analysis as the errors are no longer independent. The low-frequency drift is often removed by high-pass filtering, and other effects are typically modelled as an autoregressive (AR) process. In this paper, we propose an alternative approach: Nuisance Variable Regression (NVR). By inclusion of confounding effects in a general linear model (GLM), we first confirm that the spatial distribution of the various fMRI noise sources is similar to what has already been described in the literature. Subsequently, we demonstrate, using diagnostic statistics, that removal of these contributions reduces first and higher order autocorrelation as well as non-normality in the residuals, thereby improving the validity of the drawn inferences. In addition, we also compare the performance of the NVR method to the whitening approach implemented in SPM2.

**General information**
State: Published
Organisations: Cognitive Systems, Department of Informatics and Mathematical Modeling
Slice profile optimization in arterial spin labeling using presaturation and optimized RF pulses

General information
State: Published
Organisations: Image Analysis and Computer Graphics, Department of Informatics and Mathematical Modeling
Authors: Holm, D. (Intern), Sidaros, K. (Intern)
Pages: 1229-1240
Publication date: 2006
Main Research Area: Technical/natural sciences

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Journal: Magnetic Resonance Imaging
Volume: 24
Issue number: 9
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Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.947 SNIP 1.039 CiteScore 2.38
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.096 SNIP 1.093 CiteScore 2.49
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.009 SNIP 1.063 CiteScore 2.4
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.966 SNIP 0.962 CiteScore 2.32
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.041 SNIP 1.029 CiteScore 2.38
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.119 SNIP 1.008 CiteScore 2.34
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.048 SNIP 1.027
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.003 SNIP 0.901
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.858 SNIP 0.859
Scopus rating (2007): SJR 0.838 SNIP 0.849
Scopus rating (2006): SJR 0.754 SNIP 0.952
ASL: Comparison of presaturation and RF pulse optimization

General information
State: Published
Organisations: Department of Informatics and Mathematical Modeling
Authors: Holm, D. (Intern), Sidaros, K. (Intern)
Number of pages: 1,153
Publication date: 2005

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Title of host publication: Proc. International Society of Magnetic Resonance In Medicine - ISMRM 2005, Miami, Florida, USA
Main Research Area: Technical/natural sciences
Conference: 13th Scientific Meeting & Exhibition of the International Society of Magnetic Resonance In Medicine, Miami, FL, United States, 07/05/2005 - 07/05/2005
Electronic versions:
imm3595.pdf
Links:
http://www2.imm.dtu.dk/pubdb/p.php?3595
Source: orbit
Source-ID: 185788
Publication: Research - peer-review › Article in proceedings – Annual report year: 2005

Effects of Spatial Normalization on Detection of Perirhinal Cortex Activation in Individual Subjects Using fMRI

General information
State: Published
Organisations: Department of Informatics and Mathematical Modeling, Cognitive Systems
Authors: Ramsøy, T. Z. (Ekstern), Lund, T. E. (Ekstern), Liptrot, M. G. (Intern), Sidaros, K. (Intern), Christensen, M. S. (Ekstern), Nielsen, F. Å. (Intern), Paulson, O. B. (Ekstern), Jernigan, T. L. (Ekstern)
Publication date: 2005

Host publication information
Title of host publication: Alzheimer's Assocation International Conference on Prevention of Dementia, 2005 June 18-21, Washington, D.C.
Main Research Area: Technical/natural sciences
Links:
Source: orbit
Source-ID: 185799
Publication: Research - peer-review › Article in proceedings – Annual report year: 2005
Improved Brain Perfusion Quantification using a Saturation Recovery Sequence

**General information**
State: Published
Organisations: Department of Informatics and Mathematical Modeling
Authors: Andersen, I. K. (Intern), Rosenbaum, S. (Ekstern), Sidaros, K. (Intern), Hansson, L. (Ekstern), Larsson, H. B. (Ekstern)
Publication date: 2002

**Host publication information**
Title of host publication: Proc 19th Annual M European Soc Mag Reson Med and Biol
Main Research Area: Technical/natural sciences
Links:
Source: orbit
Source-ID: 58254
Publication: Research - peer-review › Article in proceedings – Annual report year: 2002

Slice profile effects in MR perfusion imaging using pulsed arterial spin labelling

**General information**
State: Published
Organisations: Department of Informatics and Mathematical Modeling
Authors: Sidaros, K. (Intern)
Publication date: 2002

**Publication information**
Original language: English
Main Research Area: Technical/natural sciences
Electronic versions:
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Links:
Source: orbit
Source-ID: 58366
Publication: Research › Ph.D. thesis – Annual report year: 2002

Improved perfusion quantification in FAIR imaging by offset correction

**General information**
State: Published
Organisations: Department of Informatics and Mathematical Modeling, Department of Chemistry
Authors: Sidaros, K. (Intern), Andersen, I. K. (Intern), Gesmar, H. (Intern), Rostrup, E. (Ekstern), Larsson, H. B. W. (Ekstern)
Pages: 193-197
Publication date: 2001
Main Research Area: Technical/natural sciences

**Publication information**
Journal: Magnetic Resonance in Medicine
Volume: 46
Issue number: 1
ISSN (Print): 0740-3194
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Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.52 SJR 1.867 SNIP 1.438
A model system for perfusion quantification using FAIR

Flow-sensitive experiments (FAIR) have been performed on a tube-flow phantom in order to validate quantitative perfusion measurements on humans. A straight-forward correspondence between perfusion and bulk-flow is found. It is shown that the flow phantom model only holds when the slice profiles of the involved RF pulses are taken into account. A small flow-independent off-set may be present in the data. The off-set is explained by the model. Based on the correspondence between the phantom and the in vivo models, it is shown that the lowest flow values that could be measured in the phantom correspond to perfusion values lower than the cortical perfusion in the brain. Thus, the experimental accuracy and the computational methods for quantitative perfusion measurements in vivo can be validated by a tube-flow phantom.
Brain Activation in Normoxic and Hypoxic subjects using Oxygenation and Flow Sensitive MR Imaging

**General information**

State: Published
Organisations: Department of Informatics and Mathematical Modeling, Danish Research Centre for Magnetic Resonance, Copenhagen University Hospital
Authors: Rostrup, E. (Ekstern), Born, P. (Ekstern), Sidaros, K. M. (Intern), Larsson, H. (Ekstern), Paulson, O. (Ekstern)
Number of pages: 161
Publication date: 1999

**Host publication information**

Title of host publication: Magma 8, suppl. 1
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 172658
Publication: Research › Article in proceedings – Annual report year: 1999

The Influence of a Signal Offset on Perfusion Quantification using FAIR

**General information**

State: Published
Organisations: Department of Informatics and Mathematical Modeling, Danish Research Centre for Magnetic Resonance
Authors: Andersen, I. K. (Intern), Sidaros, K. M. (Intern), Gesmar, H. (Ekstern), Larsson, H. (Ekstern), Rostrup, E. (Ekstern)
Publication date: 1999

**Host publication information**

Title of host publication: NeuroImage 9(6)
Main Research Area: Technical/natural sciences
Conference: 5th Int. Conference on the Mapping of the Human Brain, Düsseldorf, 01/01/1999
Source: orbit
Source-ID: 172656
Publication: Research › Article in proceedings – Annual report year: 1999

Zero Perfusion Calibration of FAIR Imaging with Arbitrary Inversion Slice Profiles

**General information**

State: Published
Organisations: Department of Informatics and Mathematical Modeling, Danish Research Centre for Magnetic Resonance
Authors: Sidaros, K. M. (ed.) (Intern), Andersen, I. K. (Intern), Larsson, H. (Ekstern), Gesmar, H. (Ekstern), Rostrup, E. (Ekstern)
Number of pages: 165
Publication date: 1999

**Host publication information**

Title of host publication: Magma 8, suppl. 1
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 172657
Publication: Research › Article in proceedings – Annual report year: 1999

Projects:

Modeling the Effects of Drugs Targetes to Tumor Vasculature using MRI

Department of Informatics and Mathematical Modeling
Period: 01/11/2004 → 05/11/2008
Number of participants: 7
Phd Student: Holm, David Alberg (Intern)
Supervisor: Rowland, Ian (Ekstern)
Sidoros, Karam (Intern)
Main Supervisor: Larsen, Rasmus (Intern)
Examiner: Ersbøll, Bjarne Kjær (Intern)
Larsson, Elna-Marie (Ekstern)
Maxwell, Ross James (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: 1/3 DTU-stip, 2/3 FUR/andet
Project: PhD

Funktionelle hjernebilleder - Modellering og data-analyse
Department of Informatics and Mathematical Modeling
Period: 01/09/2004 → 17/06/2009
Number of participants: 8
Phd Student: Madsen, Kristoffer Hougaard (Intern)
Supervisor: Larsen, Axel (Ekstern)
Lund, Torben E. (Ekstern)
Sidoros, Karam (Intern)
Main Supervisor: Hansen, Lars Kai (Intern)
Examiner: Larsen, Jan (Ekstern)
Adali, Tulay (Ekstern)
Kjær, Troels Wesenberg (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: DTU-lønnet stipendie
Project: PhD

Modellering og digital signalbehandling for MR-baseret måling af blodgennemstrømning
Department of Informatics and Mathematical Modeling
Period: 01/02/1999 → 27/09/2002
Number of participants: 6
Phd Student: Sidoros, Karam (Intern)
Supervisor: Larsson, Henrik B. W. (Ekstern)
Main Supervisor: Hansen, Lars Kai (Intern)
Examiner: Larsen, Jan (Ekstern)
Calamante, Fernando (Ekstern)
Schaumburg, Kjeld (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: DTU-lønnet stipendie
Project: PhD