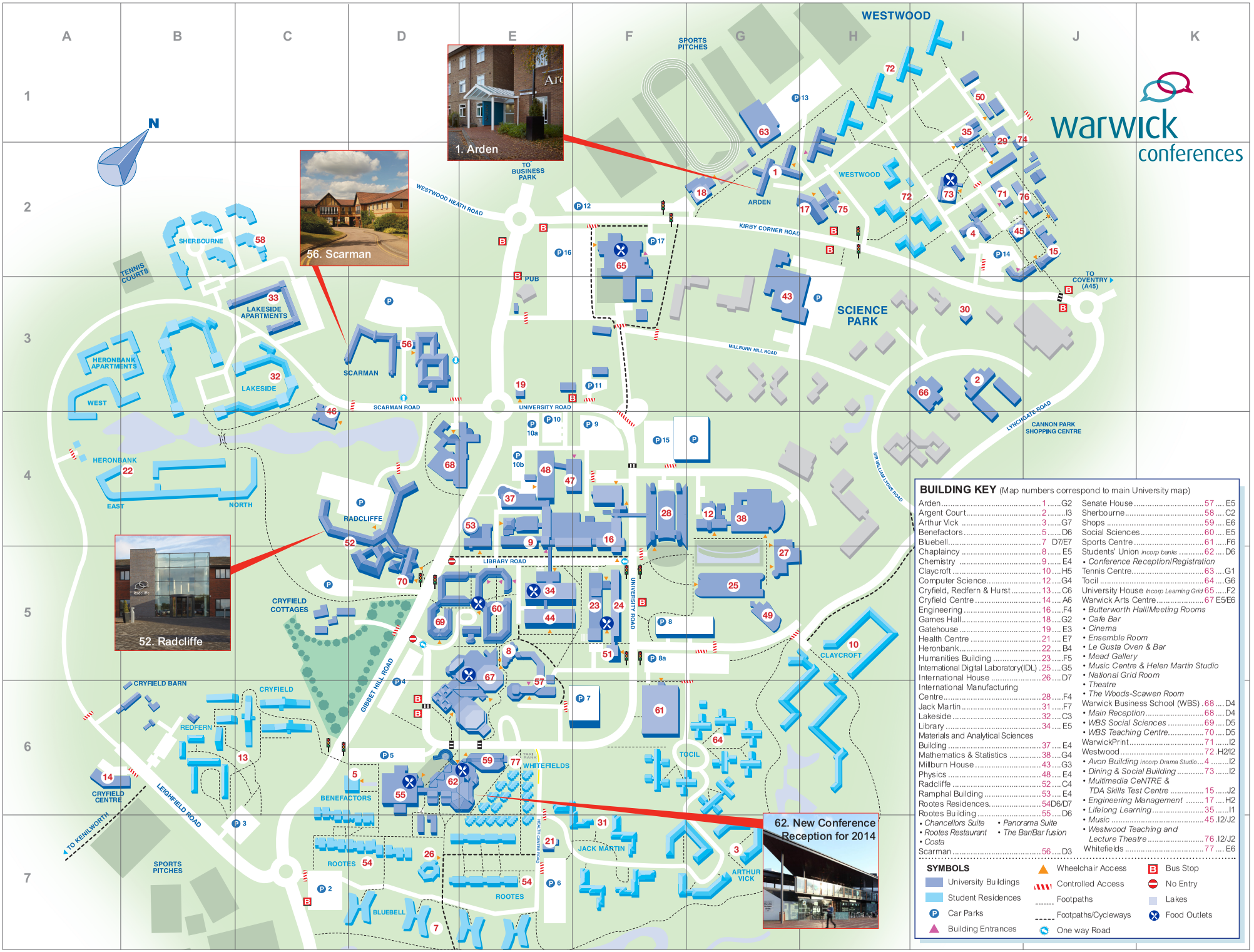
Statistical Challenges in Neuroscience
3rd – 5th September 2014

Contents



BUILDING KEY (Map numbers correspond to main University map)

Arden	1 G2	Senate House	57 E5
Argent Court	2 I3	Sherbourne	58 C2
Arthur Vick	3 G7	Shops	59 E6
Benefactors	5 D6	Social Sciences	60 E5
Bluebell	7 D7/E7	Sports Centre	61 F6
Chaplaincy	8 E5	Students' Union *incorp banks*	62 D6
Chemistry	9 E4	• *Conference Reception/Registration*	
Claycroft	10 H5	Tennis Centre	63 G1
Computer Science	12 G4	Tocil	64 G6
Cryfield, Redfern & Hurst	13 C6	University House *Incorp Learning Grid*	65 F2
Cryfield Centre	14 A6	Warwick Arts Centre	67 E5/E6
Engineering	16 F4	• *Butterworth Hall/Meeting Rooms*	
Games Hall	18 G2	• *Cafe Bar*	
Gatehouse	19 E3	• *Cinema*	
Health Centre	21 E7	• *Ensemble Room*	
Heronbank	22 B4	• *Le Gusta Oven & Bar*	
Humanities Building	23 F5	• *Mead Gallery*	
International Digital Laboratory(IDL)	25 G5	• *Music Centre & Helen Martin Studio*	
International House	26 D7	• *National Grid Room*	
International Manufacturing Centre	28 F4	• *Theatre*	
Jack Martin	31 F7	• *The Woods-Scawen Room*	
Lakeside	32 C3	Warwick Business School (WBS)	68 D4
Library	34 E5	• *Main Reception*	68 D4
Materials and Analytical Sciences Building	37 E4	• *WBS Social Sciences*	69 D5
Mathematics & Statistics	38 G4	• *WBS Teaching Centre*	70 D5
Millburn House	43 G3	WarwickPrint	71 I2
Physics	48 E4	Westwood	72 H2/I2
Radcliffe	52 C4	• *Avon Building Incorp Drama Studio*	4 I2
Ramphal Building	53 E4	• *Dining & Social Building*	73 I2
Rootes Residences	54 D6/D7	• *Multimedia CeNTRE & TDA Skills Test Centre*	15 J2
Rootes Building	55 D6	• *Engineering Management*	17 H2
• *Chancellors Suite* • *Panorama Suite* • *Rootes Restaurant* • *The Bar|Bar fusion* • *Costa*		• *Lifelong Learning*	35 I1
Scarman	56 D3	• *Music*	45 I2/J2
		• *Westwood Teaching and Lecture Theatre*	76 I2/J2
		Whitefields	77 E6

SYMBOLS

- University Buildings
- Student Residences
- Car Parks
- Building Entrances
- Wheelchair Access
- Controlled Access
- Footpaths
- Footpaths/Cycleways
- One way Road
- Bus Stop
- No Entry
- Lakes
- Food Outlets

Administrative Details

Workshop Registration

Registration on Wednesday will take place in the lobby of the Mathematics & Statistics Building (Map Key 38), between 8am and 10am.

Getting Here

Information on getting to the University of Warwick from Coventry, as well as from other directions locally and further afield, can be found at `http://www.warwick.ac.uk/about/visiting/`

Accommodation

Accommodation is in en-suite rooms on campus in either the Arthur Vick (Map Key 3) or Radcliffe House (Map Key 52) buildings. Keys and directions can be collected from the reception of the Rootes Social Building (Map Key 54) for rooms in Arthur Vick and from the reception of Radcliffe House for rooms in that building. All rooms have linen and toiletries. Rooms will be available after 15:00 for check in. All bedrooms must be vacated by 9:30am on your day of departure.

Car Parking

Workshop participants are invited to use conference car park 7, 8, 8a or 15. Car parking is free of charge during the workshop in the conference car parks. See the *Delegate Joining Instructions for further details.*

Internet Access

Campus: Wireless access is most easily available via eduroam — `http://www.eduroam.org/`. Speak to one of the organisers for details of other options.

Accommodation: *Wired* internet access should also be available in all bedrooms. Details of how to log onto the system will be displayed in each individual bedroom, but participants will need to bring their own Ethernet cable. Ethernet cables can be purchased from Costcutter on campus (Map Key 59).

Start.Warwick

The Start.Warwick app, available for iPads, iPhones and Android devices from `http://www2.warwick.ac.uk/insite/news/intnews2/start_warwick_app`, provides useful information on travel and an interactive map of the campus amongst other things.

Facilities

Supermarkets:	Costcutter (Map Key 59)
	Tesco (Map Grid Reference J4)
Food & Drink:	Dirty Duck (Map Key 62)
	Terrace Bar (Map Key 62)
	Varsity (Map Grid Reference E3)
Coffee Shops:	Curiositea (Map Key 62)
	Costa (Map Key 56)
	Arts Centre (Map Key 67)
Cinema:	Map Key 67
Theatre:	Map Key 67
Sports Centre:	Map Key 61
Health Centre:	Map Key 21
Pharmacy:	Map Key 62

Help, Information & Telephone Numbers

Department

Department of Statistics
University of Warwick
Gibbet Hill Road
Coventry
CV4 7AL

Telephone:	024 7657 4812
Fax:	024 7652 4532
Map Key:	**38**

Emergency Numbers

Emergency:	Internal - 22222; External - 024 7652 2222
Security:	Internal - 22083; External - 024 7652 2083
Organiser:	Internal - 50919; External - 024 7615 0919 (Adam Johansen)

Transport

Swift Taxis (Coventry):	024 7676 7676
Trinity Street Taxis:	024 7699 9999
National Rail Enquiries:	08457 484 950

Delegate Joining Instructions
Warwick Conferences' Conference Park

We are delighted that you will be joining us at the University of Warwick. We hope that the information provided in this document will help you get the most from your event. Please bring these instructions with you as you will find them useful whilst you are on campus.

The Conference Park is on the main campus of the University of Warwick located on the outskirts of Coventry, which is accessible by road, rail and air. You can download further information from the website at www.warwickconferences.com, following the link 'how to find us'. A further link can be found for any relevant traffic information
http://www.warwickconferences.com/delegates/delegates-conference-park

The Conference Park is the name given to the facilities provided by Warwick Conferences on the main University campus.

Getting here:

University and local roadworks 2014

- The University in conjunction with the local areas are working on a major development to improve the roads in and around the University.
- Specifically aiming to improve the safety and capacity of our roads and the appearance and accessibility of major areas of campus.
- This all starts this summer with major changes to Gibbet Hill Road, starting on 23 June 2014 and due to end in October 2014, with sections of the road closed at times.
- We recommend that you allow approximately an additional 30 minutes for your journey (and more at standard rush hour times) as there may well be congestion around campus. On approach to campus, please be aware of diversion signage and follow as directed.
- Once you're on campus, please pay close attention to signage – diversions and traffic management will change on a daily basis depending on what work is being carried out - staff will be located at car parks and other key areas to assist and advise.

Which direction to approach from:

- For the Conference Park please head for Westwood Heath/Kirby Corner Road. If your journey currently brings you along the A46 then you will need to carry along onto the A45 (there will be diversion signs to the A45).

Where to park:

If you're arriving at Central Campus including:

- Conference Park Reception
- Rootes Building
- Warwick Arts Centre
- Ramphal Building

Please use car parks 7, 8, 8a and 15

Car parking:

Once you arrive on campus please look out for the blue Warwick Conferences signage to direct you to the car parks and conference venues.
Complimentary car parking is available for conference delegates in the allocated car parks on campus (7, 8, 8a and 15). On entering the car park, you will be provided with a pass for these car parks and this should be placed in the window of your vehicle, if arriving after 19.00hrs and some weekends it may be necessary for you to collect a pass from the Conference Reception in the Student Union Building.
Disabled parking spaces are available close to the entrance of main buildings.

As a University campus, from time to time these car parks become full and when this happens alternative parking will be available, which you will be directed to. We advise that you allow sufficient time, for up to a ten minute walk to get to your destination on the Conference Park from the car parks. Some of the car parks are not adjacent to the registration and accommodation areas, it is therefore advisable once you have parked, for you to take your luggage to Conference Reception where you will be able to leave it with the team in the left luggage facility.
Your Event Organiser can provide further information regarding car parking arrangements.

Accommodation:

Please check with your Event Organiser as to which type of accommodation has been reserved for your event and what facilities are available.

Conference Reception:

Located within the Students Union Building. The Reception team are available to answer your queries between 07:00 – 23:00. Here you can also:

- Find out general information
- Arrange for secure luggage storage
- Validate your car parking token
- Collect information on how to connect to the wifi around campus
- Ask about any lost property
- Request additional bedroom supplies such as pillows, blankets, clock radio, bath mat or a bedside lamp

Keys:

You will be provided with one key or key card which will access your room and entry door to the residence. Keys can be left at Conference Reception, Rootes Restaurant (in Rootes Building) or one of the boxes situated in the entrance halls of each residence on the day of your departure.

Bedroom check in/out:

Bedroom keys will be available from 15:00 to 23:00 at Conference Reception. If you plan to arrive after 22.45, please contact Conference Reception to arrange late key collection (wcpreception@warwick.ac.uk). Rooms need to be vacated by 09:30 on your day of departure and all luggage and belongings to be removed at that time. Please inform Conference Reception on arrival, of any difficulties you may have in the unlikely event of an evacuation from your accommodation (e.g. hearing or mobility difficulties).

Disability services:

The University of Warwick aims to be accessible and welcoming to everyone and we are committed to making your visit as easy and enjoyable as possible. If you have any particular requirements that we should be aware of, hen please discuss these with your Event Organiser.

Internet access across campus:

If you would like to access the wifi network then please ask at Conference Reception or any of the Information Points around campus (e.g. Rootes Building and Warwick Arts Centre) for details. Alternatively log onto your device and go to your web / wireless browser:

1. Connect your device to the **'Warwick Guest'** wireless network.
2. Upon your first attempt to access online content with the web browser, you will be redirected to the Warwick Guest Wireless web page (most Apple devices will automatically perform this step).
3. If you already have a valid Warwick Guest account, please login with those credentials, otherwise please continue to create yourself a Warwick Guest account. N.B. This is **NOT** the same account used on the 'conferences' wireless network.
4. Click the link within the sentence 'Click here to create an account' and select 'Attending a conference'.
5. Please provide your details, including a valid mobile phone number, to which you generated guest login will be sent.
6. Follow the web links to return to the Warwick Guest Wireless webpage and login.
7. If you do not have a mobile phone, choose the option 'Click here to register if you do not have a mobile phone' at the bottom of the page to have your login details sent to your email address.

Food and Drink:

All meals are provided in Rootes Restaurant located on the first floor of Rootes Building for all delegates (unless your programme indicates otherwise). The restaurant offers an assisted style service of breakfast, lunch and dinner including a range of hot and cold drinks. Your Event Organiser will be able to advise you regarding the specific arrangements for your event. Please have with you your conference badge or room key to gain access to the restaurant. If you have any special dietary requirements then please inform your Event Organiser.

The bar is located on the first floor of Rootes Building and is the ideal place to network and relax after a day's session. There are also alternative bars in Warwick Arts Centre and Students Union building (check opening times locally)
Payment for all sundry items is by cash or credit card payment only.

Shops, Banks, Cafés and Bars on campus:

The campus has many facilities available to all delegates, for all information and opening times please see the website: http://www.warwickretail.com . Warwick Arts Centre cinema offer discounted cinema tickets at £5.50, these can be purchased from the box office and proof of delegate status is required (not applicable for Met Opera Live or NT Live screening).

Sports facilities:

Delegates have use of some of the comprehensive sports facilities including swimming and fitness suite free of charge. Other facilities are available for a nominal charge which will need to be booked in advance. Details and opening times are available at Reception or by visiting the website below. Delegates need to present their bedroom key at the reception to gain access. See www2.warwick.ac.uk/services/sport for more information.

For more information:

You can also refer to our Frequently Asked Questions document (FAQ's) which can be obtained from your Event Organiser or our website: http://www.warwickconferences.com/delegates/delegates-conference-park

Timetable

	Wed 3 Sept	Th 4 Sept	Fri 5 Sept
08:00 - 09:00	Registration		
09:00 - 10:00	M. Girolami 9-10am	J.F. Cardoso 9-10am	A. Hyvärinen 9-10am
10:00 - 11:00	Coffee	Coffee	Coffee
11:00 - 12:00	R. Sirovich M. Hanke L. Carneiro da Costa S. Olhede 10.20-12noon	J. Polzehl S. Allasonniere W. Penny L. Sacerdote 10.20-12noon	I. Gannaz C. Williams L. Theis 10.45-12noon
12:00 - 13:00	Lunch 12.15–1.15pm (Rootes Restaurant)	Lunch 12.15–1.15pm (Rootes Restaurant)	Lunch 12.15–1.15pm (Rootes Restaurant)
13:00 - 14:00	J.D. Victor 1.30-2.30pm	T. Johnson 1.30-2.30pm	P. Ciuciu F. Forbes 1.30-2.45pm
14:00 - 15:00			
15:00 - 16:00	J. Danizeau I. Dryden C. Oates R. Engbert 2.50-4.30pm	A. Sorrentino A. Gramfort J. Aston K. Tabelow 2.50-4.30pm	
16:00 - 17:00	Coffee	Coffee	
17:00 - 18:00	R. Wilkinson 5-6pm	E. Wagenmakers 5-6pm	
18:00 - 19:00	Dinner 6.30–7.30pm (Rootes Restaurant)		
19:00 - 20:00	Posters 7.30–9.00pm (Atrium)	Conference Dinner 7.30pm (Chancellor's Suite)	
20:00 - 21:00			

All activities will take place in the Mathematics & Statistics Building (Map Key 38), with talks in room MS.04 (signposted from lobby), unless otherwise stated.
Keynote *talks appear in blue.*

Talk Abstracts

Statistics on neuro-anatomical configurations: models and estimations
Stephanie Allassonniere (Polytechnique) & ***Stanley Durrleman***

Structural neuroimaging enables the investigation of the anatomical basis of neurologic diseases. Morphological alterations of the cortical or sub-cortical structures occur years before the onset of neurodegenerative diseases. Alterations of structural connectivity during brain development may lead to psychiatric diseases, such as autism. However, such effects could be found only by the automatic processing of large data sets, and therefore by the mean of statistical methods, due to the huge variability of brain structure among individuals. In contrast to usual methods that analyze the differences in image intensity at homologous positions, we investigate differences in brain structures through deformations. Deformations are used to map anatomical configurations, which can be made of the images themselves or any geometric objects segmented from them. The parameters of such deformations give the relative position of a given anatomical configuration on a Riemannian manifold with respect to a reference anatomy called template. We propose to estimate jointly one or several template(s) and the variance of the deformation parameters modeling the geometric distribution of anatomies within the group under study. These estimations are performed in the framework of a Bayesian Mixed Effects (BME) model. Due to the inherent complexity of the deformation model, approximations need to be made. We propose two algorithms to get the Maximum A Posteriori Estimator. In the first place, we use a deterministic approximation of the Expectation-Minimization (EM) algorithm. We also introduce a stochastic version of this EM where the simulation step is optimized using the Anisotropic Metropolis Adjusted Langevin Algorithm (AMALA), which benefits from better theoretical properties. We will illustrate our approach in real case studies, and show how it could not only lead to high classification between disease and non-diseases state, but also could display the most discriminative features in an interpretable way.

Statistical Analysis in Positron Emission Tomography Neuroreceptor Studies
John Aston (University of Cambridge)

Neuroreceptor studies using Positron Emission Tomography (PET) allow the quantification of brain neurochemical changes in-vivo, particularly in the presence of pharmacological challenges. PET is collected both spatially and temporally and it is of interest to try to combine information from both domains. The temporal models that are used in PET analysis are typically non-linear and the data has a low signal-to-noise ratio, particularly when considered voxel-by-voxel. Functional Data Analysis (FDA) is the statistical study of curves and surfaces, and is a natural way of considering PET time activity curves. Recent advances in FDA have allowed improvements in quantification of PET in two different ways. Firstly, model estimates can be improved using FDA as a preprocessing step, while secondly, a model-free approach to multiple deconvolution problems can be directly carried out using FDA. This opens up new possibilities to both model evaluation and outcome testing between patient and control groups in PET Neuroreceptor experiments. [Joint work with Ci-Ren Jiang (Academia Sinica) and Jane-Ling Wang (UC Davis)]

Independent Component Analysis: the basics and some fresh insights
Jean-Francois Cardoso (ENST)

Independent component analysis (ICA) is a framework for processing multi-sensor data based on a simple but powerful idea: if several different linear mixtures of inde-

pendent components can be measured at the output of several sensors, it is possible to recover those components without external knowledge of the mixture coefficients, by resorting only to the property of statistical independence of the underlying components. Various ICA algorithms have been applied with success in many fields, including neuroscience. The success of ICA depends on our ability to implement statistical models for the components which are rich enough to capture the salient features of the component distribution yet simple enough to yield robust and fast algorithms. The talk will discuss the most commonly used models which rely on non Gaussianity, sparsity, non stationarity or spectral diversity. I will show how those models correspond to various versions of mutual information and how this is unified in an information-geometric view. I will also discuss how those models can be enhanced to deal with specific situations: noisy models, partial mixtures information, correlated or multi-dimensional components.

Searching Multiregression Dynamic Models of fMRI Networks using Integer Programming
Lilia Carolina Carneiro da Costa

In this work we estimate the effective connectivity for resting-state and steady-state task-based functional Magnetic Resonance Imaging (fMRI) data, using a class of Dynamic Bayesian Network (DBN) models, called the Multiregression Dynamic Model (MDM). Several models have been developed in order to define and detect a causal flow from one variable to other, especially in the area of machine learning (e.g. Spirtes et al., 2000 and Pearl, 2000). The MDM models embody a particular pattern of causal relationships which, unlike the Bayesian Network (BN), expresses the dynamic message passing as well as the potential connectivity between different areas in the brain.

One of the advantages of this class is that, in contrast to many other DBNs, the hypothesized relationships accommodate conditional conjugate inference. We demonstrate how straightforward it is to search over all possible connectivity networks with dynamically changing intensity of transmission to find the MAP model within this class. This search method is made feasible by using a novel application of an Integer Programming algorithm. The efficacy of applying this particular class of dynamic models to this domain is shown and more specifically the computational efficiency of a corresponding search of 11-node DAG model space. Also, due to a factorization of the marginal likelihood, the search over all possible directed (acyclic or cyclic) graphical structures is even faster and we demonstrate this here.

Multi-subject Bayesian Joint Detection and Estimation in functional MRI
Philippe Ciuciu (CEA)

Modern cognitive experiments in functional Magnetic Resonance Imaging (fMRI) rely on a cohort of subjects sampled from a population of interest to study characteristics of the healthy brain or to identify biomarkers on a specific pathology (e.g., Alzheimer's disease) or disorder (e.g., aging). Group-level studies usually proceed in two steps by making random-effect analysis on top of intra-subject analyses, to localize activated regions in response to stimulations or to estimate brain dynamics. Here, we focus on improving the accuracy of group-level inference of the hemodynamic response function (HRF). We rest on an existing Joint Detection-Estimation (JDE) framework we formerly developed (Makni et al, 2005, 2008; Vincent et al, 2010). The latter aims at detecting evoked activity and estimating HRF shapes jointly. So far, region-specific group-level HRFs have been captured by averaging intra-subject HRF profiles. Here, our approach extends the JDE formalism to the multi-subject context by proposing a hierarchical Bayesian modeling that includes an additional layer for describing

the link between subject-specific and group-level HRFs. This extension outperforms the original approach both on artificial and real multi-subject datasets. It allows us to probe the effect of aging in different cognitive circuits by comparing HRF profiles of young and elderly participants to the same localizer paradigm.

Dynamic Causal Modelling of brain-behaviour relationships
Jean Daunizeau (ICM Paris)

Dynamic Causal Modelling (DCM) of neuroimaging data has become a standard tool for identifying the structure and flexibility of brain networks that respond to the experimental manipulation (e.g., sensory stimuli or task demands). DCM, however, does not explain how distributed brain responses are causally involved in the production of behaviour (e.g. choices, reaction times). In this work, we propose to merge DCM with neuroimaging decoding approaches, with the aim of identifying a neural transfer function that would map experimental inputs to their behavioural response, through activity in the underlying large-scale brain dynamics. In brief, our approach provides a neuro-computational decomposition of behavioural responses, in terms of the contribution of brain regions and their functional connections to the input-output transform. In turn, it provides a direct quantification of the behavioural relevance of effective connectivity. In this view, neuroimaging data serves to identify key parameters (e.g. synaptic weights and their modulation) that control the "transfer function" from experimental inputs to behavioural outputs. This can serve to predict behavioural deficits induced by specific anatomical lesions, as well as behavioural recovery potentials that derive from brain plasticity. We will first recall the basics of the DCM framework and expose its behavioural extension. We will then evaluate the capabilities and limits of the approach using both Monte-Carlo simulations and empirical data.

Sparse Paradign Free Mapping
Ian Dryden (University of Nottingham)

Paradigm Free Mapping (PFM) is a method for detecting brain activations in functional Magnetic Resonance Imaging (FMRI) without specifying prior information on the timing of the events. The PFM method involves a ridge regression estimator for signal deconvolution and a baseline signal period for statistical inference. A sparse version of PFM uses the Dantzig Selector and a new approach called Penalized Euclidean Distance regression. These methods obtain high detection rates of activation, comparable to a model-based analysis, but requiring no information on the timing of the events or a baseline period. The practical operation of sparse PFM was assessed with single-trial fMRI high-field 7T data, where all task-related events as well as several resting state networks were detected. The work is joint with Cesar Caballero Gaudes, Natalia Petridou, Susan Francis and Penny Gowland.

Spatial statistics and attentional dynamics in scene viewing
Ralf Engbert (University of Postdam)

In humans and in foveated animals visual acuity is highly concentrated at the center of gaze, so that choosing where to look next is an important example of online, rapid decision making. Computational neuroscientists have developed biologically-inspired models of visual attention, termed saliency maps, which successfully predict where people fixate on average. Using point process theory for spatial statistics, we show that scanpaths contain, however, important statistical structure, such as spatial clustering on top of distributions of gaze positions. Here we develop a dynamical model of saccadic selection that accurately predicts the distribution of gaze positions as well

as spatial clustering along individual scanpaths. Our model relies on, first, activation dynamics via spatially-limited (foveated) access to saliency information, and, second, a leaky memory process controlling the re-inspection of target regions. This theoretical framework models a form of context-dependent decision-making, linking neural dynamics of attention to behavioral gaze data.

Physiologically informed Bayesian analysis of ASL functional MRI data using MCMC
Florence Forbes (INRIA Grenoble)

ASL fMRI data provides a quantitative measurement of blood perfusion. In contrast to Blood Oxygenation Level Dependent signal, the ASL signal is a direct and closer to neuronal activity measurement. However, ASL data has a lower signal to noise ratio (SNR) and poorer resolution, both in time and space. In this work, we thus aim at taking advantage of the physiological link between the hemodynamic (venous) and perfusion (arterial) components in the ASL signal to improve the estimation of the impulse responses of the neurovascular system. In a Bayesian framework, a linearization of this link is injected as prior information to temporally regularize the regionwise estimation of the perfusion response function while enabling the joint detection of brain activity elicited by stimuli delivered along a fast event-related paradigm. All the parameters of interest in space and time as well as hyperparameter are computed in the posterior mean sense after convergence of a hybrid MetropolisGibbs sampler. In this way, we aim at providing clinically relevant perfusion characteristics for the analysis of ASL data in low SNR conditions. This work has been done by Aina Frau (PhD student) and Thomas Vincent (postdoc fellow) under the joint supervision of Florence Forbes (INRIA Grenoble) and Philippe Ciuciu (CEA &INRIA Saclay).

Estimation of the fractal connectivity
Irne Gannaz (INSA Lyon)

A challenge in imaging neuroscience is to characterize the brain organization, trough the integration of interactions between segregated areas. One way to estimate the functional connectivity consists in estimating correlations of pairs of measurements of neuronal activity. The aim of the present work is to take into account the long range dependence properties of the recordings. Fractal connectivity can statistically be defined as the spectral correlations between long memory processes over a range of low frequency scales. It can be seen as the asymptotic limit of Fourier and wavelets correlation at low frequencies. Fractal connectivity thus corresponds to the "structural" or long-term covariation between the processes. We first introduce a semi-parametric multivariate model, defining the fractal connectivity for a large class of multivariate time series. This model includes the multivariate Brownian motion and fractionally integrated processes. We propose an estimation of the long-dependence parameters and of the fractal connectivity, based on the Whittle approximation and on a wavelet representation of the time series. The theoretical properties of the estimation show the asymptotic optimality. A simulation study confirms the satisfying behaviour of the procedure on finite samples. Finally we propose an application to the estimation of a human brain functional network based on MEG data sets. Our study highlights the benefit of the multivariate analysis, namely improved efficiency of estimation of dependence parameters and of long term correlations.

Hierarch Bayesian Inference of Mixed Modality Brain Imaging for Clinical Diagnostics
Mark Girolami (University of Warwick)

The promise of brain imaging as a general clinical diagnostic remains just that. This talk will present a recent study assessing the statistical importance of fusing a range of diverse imaging modalities in assessing early onset of Parkinsonian type diseases. A hierarchic Bayesian structure to integrate and assess the importance of various modalities is developed and the issues related to efficient inference this model are investigated. This is an ongoing study with clinical neurologists.

How much stats does it take to look at the brain at a millisecond time-scale with MEG and EEG?

Alexandre Gramfort (Telecom Paristech)

Electroencephalography (EEG) and Magnetoencephalography (MEG) are noninvasive techniques that allow to image the active brain at a millisecond time scale. Yet to do so, challenging computational and statistical problems need to be solved. In this talk I will first review the physics behind MEG/EEG measurements before diving into two statistical problems: the estimation of the noise covariance used for prewhitening and then the localization of active sources in the brain. The later problem is a high dimensional regression problem where the target variables are multivariate time series. I will detail recent contributions using sparsity promoting regularizations and time-frequency representations.

Observing the brain in the wild – in need for large scale collaborations to move forward

Michael Hanke (University of Magdeburg)

Prolonged complex naturalistic stimulation is arguably more likely to elicit brain responses that are representative of naturally occurring brain states and dynamics than artificial, highly controlled experiments with a limited number of simplified conditions. If we want to know how the brain works, we need to study it while it does what it can do best: process vast amounts of multi-sensory input, effortlessly determine what is important, and trigger the right actions. The catch is, of course, that without properly designed experiments many of the standard statistical analysis approaches are no longer applicable as they often rely on multiple repetitions, or assumptions of particular distributions. Solutions to this problem are more flexible analysis strategies that can handle complexity in a single dataset, or large amounts of data that enable aggregation across the enormous variety of brain processes. I claim that current neuroimaging research reality hinders progress on both aspects. While there is a lot of neuroscientific data being collected only a minuscule portion of it is accessible for any kind of aggregation or meta-analysis. This situation seriously inhibits inter-disciplinary contributions – a potent source of novel approaches to look at brain data – as scientists from other disciplines (statistics, engineering, machine learning, data mining) cannot easily access neuroimaging datasets that are both relevant to their field and have the potential to move neuroimaging research forward. In order to explore this potential, we have started an experiment on a de-centralized, distributed collaboration on neuroimaging data analysis. The concept of this project is to provide a rich and unique dataset to encourage scientists with various backgrounds to infer as much as possible about the nature of the processes in the human brain. Anybody can participate without a formal agenda or consortium. We published a dataset that has the potential to garner the attention of researchers working in diverse fields of science, within and outside the neuroimaging domain. It is a large (more than 300 GB of raw and readily pre-processed data), state-of-the-art high-resolution, ultra-highfield 7-Tesla fMRI dataset with simultaneous physiological measurements recorded during a 2-hour quasi natural stimulation via a Hollywood audio-movie. As such, this dataset may be the largest consecutive sample of

natural language processing that is publicly available today. Functional brain response data for 20 participants are accompanied by a multitude of structural/anatomical data (sub-millimeter T1w and T2w, DTI, SWI, angiography) and a dedicated measurement of technical noise during the functional scans. All data are released into the public domain in standard open-source data formats, and a reference implementation for data access is made available to streamline workflows for scientists without prior experience with neuroimaging data. An effort was made to describe the dataset in enough detail so that it will be usable for scientists without strict neuroimaging training. The dataset is publicly available since January 2014 at `http://www.studyforrest.org` A detailed data description was published in Hanke, M., Baumgartner, F.J., Ibe, P., Kaule, F.R., Pollmann, S., Speck, O., Zinke, W. & Stadler, J. (in press). A high-resolution 7-Tesla fMRI dataset from complex natural stimulation with an audio movie. Nature Scientific Data. In my presentation I will report on the progress of this experiment. I will give an overview of data use, published and preliminary results, as well as challenges imposed by the complex nature of these data. Moreover, I will discuss what we have learnt from attempting to engage in inter-disciplinary mass-collaboration in this uni-lateral fashion.

Natural Image Statistics
Aapo Hyvärinen (University of Helsinki)

A fundamental question in visual neuroscience is to understand the principles that determine the various stages of visual processing in the brain. That is: Why are the receptive fields and response properties of visual neurons as they are? A modern approach to this problem emphasizes the importance of adaptation to the statistics of ecologically valid input (natural images). The problem is closely related to the engineering problem of finding a good low-level representation of images. In this talk I will review work on natural image statistics and the obtained functional explanations of the properties of visual neurons. The models start with sparse coding or independent component analysis, proceed to non-Gaussian two-layer models, and finally arrive multi-layer models related to the fashionable "deep learning".

Bayesian Methods in Neuroimaging
Timothy D. Johnson (University of Michigan)

Bayesian methods have a long and intimate history with image analysis dating back at least to the seminal paper by Geman and Geman (1984) and perhaps even a decade earlier with Besag (1974). Two primary advantages of Bayesian methods over frequentist or MLE methods for image analyses are the ease at which prior information can be incorporated into the models and the ease at which spatial and temporal correlation can be handled. The primary disadvantages are computational cost and the lack of general software packages that can handle the massive image data currently being collected. In this talk I will present several examples of Bayesian image analyses and highlight their benefits. I will then discuss several recent advances in Bayesian computation that show promise in breaking the computational bottleneck, including recent Monte Carlo simulations methods and approximation methods of the joint posterior.

Deep neural nets elucidate hierarchical visual processing
Patrick Mineault (McGill)

Neurons in intermediate and high-level visual areas hierarchically re-encode the visual input to ever more abstract representations which support high-level behaviours (DiCarlo & Cox 2007). Systems identification can help us understand this process by

identifying the computations supported performed by these neurons. When low-level stages in a hierarchical computation are well-understood, we can estimate relationship between a neuron and its most proximal input - the previous area in the hierarchy (Cadieu et al. 2008; Mineault et al. 2012). When low-level stages are poorly characterized, however, systems identification becomes more challenging. To address this, we used deep feedforward neural networks (Bengio et al. 2006) find to a nonlinear hierarchical transformation of the input which linearizes the relationship between the input and the output of a set of neurons. We choose a convolutional transformation followed by a nonlinearity to approximate the local receptive fields and spiking nonlinearities of neurons. We show in simulations and with recorded neural data that it is possible to learn, via stochastic gradient descent, an effective representation of the input in a standard systems identification paradigm (Marmarelis & Marmarelis 1976) - e.g. a simple-cell-like representation from the output of complex cells. By stacking multiple layers of this transformation, we can learn ever more complex representations of the input in a greedy fashion. In an application to a neural dataset of V2 neurons (David et al. 2010), we show that the proposed method is much more effective than shallow methods in predicting responses to a validation dataset, and that it recovers a number of suspected receptive field properties of V2 neurons. Since the proposed method can be extended to arbitrary depth, it holds promise in characterizing neural computations at the highest levels of the visual system.

Towards a Multi-Subject Analysis of Neural Connectivity
Chris Oates (Warwick)

Directed acyclic graphs (DAGs) and associated probability models are widely used to model neural connectivity and communication channels. In many experiments, data are collected from multiple subjects whose DAGs may differ but are likely to share many features. The first exact algorithm for estimation of multiple related DAGs was recently proposed by Oates, Smith, Mukherjee and Cussens (2014). This talk will showcase examples and discuss implications of the methodology as applied to the analysis of fMRI data from a multi-subject experiment. In addition to joint learning of subject-specific DAGs, we simultaneously estimate relationships between the subjects themselves. Elicitation of hyperparameters requires care and we illustrate how this may proceed retrospectively based on technical replicate data.
Refs:

Oates CJ, Costa L, Nichols T (2014) Towards a Multi-Subject Analysis of Neural Connectivity. Neural Computation (to appear). [arxiv:1404.1239]

Oates CJ, Smith JQ, Mukherjee S, Cussens J (2014) Exact Estimation of Multiple Directed Acyclic Graphs. In Submission. [arxiv:1404.1238]

Multivariate time series in electroencephalography
Sofia Olhede (UCL)

Electroencephalography recordings are measurements of the electrical activity of the brain, taken at the scalp. Generally multiple such series are recorded and the behaviour of these series in response to sensory stimulation is studied. Because the subjects under observation are subjected to different stimulus intensities and modalities, the observations are inherently nonstationary. One of the most important tasks as an applied statistician is to balance the usage of degrees of freedom, especially in heterogeneous populations. I will discuss how time-frequency methods can be used to extract important time-localised information, and the importance of correct normalisation (within and across subjects) in this setting.

Finding the right spot - Background correction in ratiometric calcium imaging using independent background measurements

Marlene Pacharra (Leibniz Institute) Vanessa Hausherr, Ramona Lehmann, Julia Sisnaiske, and Christoph van Thriel

In neuroscience, imaging of transient calcium responses to a range of stimuli (e.g. neurotransmitters, chemicals) in neuronal cells is an important tool to assess cell functionality. After loading fluorescent Ca2+ indicators into living cells ratiometric measurements are used to quantitatively determine the intracellular calcium concentration during stimulation. Without a valid estimation of background fluorescence, the amplitudes of these measured calcium transients cannot be compared across experiments. In order to control for such sample-based differences, a standard approach is the use of an independent background measurement of a cell-free region that is subsequently subtracted from the fluorescence intensity in all the Regions of Interest (ROIs, cells). We investigated across three different cell types from mice (neuronal progenitor cells, primary cortical neurons, trigeminal ganglion neurons) and three biological replicates, if location ($<$ 1 m vs. $>$ 10 m from a cell) and size of the cell-free control area (46 m2 vs. 200 m2), in which the background measurement is made, affects background-corrected calcium amplitudes. We hypothesized that if (a) the background measurement area is close to a cell and (b) the background measurement area is large, the background-corrected amplitudes should be larger since the noisy background can be better eliminated. Depending on location, cell type and replicate, size of background measurement area influenced background-corrected amplitudes differently sometimes resulting in substantially smaller or larger background-corrected amplitudes. Across all cell types, background-corrected amplitudes were larger, if the background measurement was made close to a cell as opposed to further away from a cell. Background correction based on a single independent background measurement is implemented in many software applications for calcium imaging. Results obtained using this approach should be treated carefully. If amplitudes are to be compared across experiments our results suggest that experimenters should control size and location of the background measurement area.

Population Level Models of Dynamical Systems

Will Penny (UCL)

In this talk I will describe two multivariate dynamical systems models of use to imaging neuroscience. The first operates at a fast time scale and describes the evolution of event-related activity underlying working memory, as measured using MEG. The system is modelled by describing the underlying neuronal sources using a phase/amplitude representation. The second operates at a slow time scale and describes the evolution of gray-matter densities underlying normal ageing and dementia, as measured using MRI. For both approaches we use a mixed effects generative model in which subject-specific dynamics are sampled from a population level model. This approach helps avoid the local minima previously encountered in single-subject dynamical models of MEG. It also allows the use of sparsely sampled time series at the individual subject level, which is especially important for longitudinal MRI as we have many subjects, but each is scanned at only a few time points. Statistical inference is implemented using gradient-based MCMC and we improve the efficiency of model estimation by computing gradients using an adjoint method. The broader vision of this work is that aberrant synaptic plasticity operating at the short time scales of memory encoding leads to the molecular and systems level changes underlying neurodegenerative disease at longer time scales.

Quantification of noise in MR experiments
Joerg Polzehl (Weierstrass Institute Berlin)

We present a novel method for local estimation of the noise level in magnetic resonance images in the presence of a signal. The procedure uses a multi-scale approach to adaptively infer on local neighbourhoods with similar data distribution. It exploits a maximum-likelihood estimator for the local noise level. Information assessed by this method is essential in a correct modelling in diffusion magnetic resonance experiments as well as in adequate preprocessing. The validity of the method is evaluated on repeated diffusion data of a phantom and simulated data. The results are compared to other noise estimation methods. We illustrate the gain from using the method in data enhancement and modelling of a high-resolution diffusion dataset.

Partial volume estimation in brain MRI - revisiting the mixel model
Alexis Roche (EPFL)

Conventional magnetic resonance imaging (MRI) based brain morphometry methods rest upon image tissue classification models that ignore, or do not fully account for the mixing of several tissues within voxels, a problem known as partial voluming, which may lead to inaccurate estimation of both local tissue concentrations and regional tissue volumes, and may impede challenging applications such as detection of focal atrophy patterns relating to early-stage progression of particular forms of dementia. While it was shown two decades ago that maximum likelihood partial volume estimation from single channel MR images is an ill-posed problem [1], the neuroimaging community has mainly resorted to finite Gaussian mixture modeling approaches for tissue classification (possibly using Markov random field priors), thereby resolving ill-posedness at the expense of neglecting partial volume effects. Owing to the necessity to incorporate strong prior knowledge for the estimation of plausible tissue concentration maps, we propose to regularize the partial volume maximum likelihood estimation problem using a Bayesian approach that assigns priors on both voxelwise tissue concentrations and image appearance parameters. We further demonstrate an associated maximum a posteriori (MAP) tracking algorithm that essentially uses sequential quadratic programming and works reasonably fast compared to conventional tissue classification methods. Our initial experiments show that global and local brain atrophy measures estimated using the proposed algorithm correlate more with age and disease than using conventional finite mixture modeling approaches or ad-hoc methods such as the fuzzy c-mean algorithm. [1] Choi et al, IEEE Trans. Medical Imaging 10(3), 1991.

On Firing Rate Estimation for Dependent Interspike Intervals
Laura Sacerdote (University of Turin)

Time-varying external inputs determine time dependent neuronal instantaneous firing rate but time dependent instantaneous firing rate may be determined also by dependences between successive inter-spike intervals (ISIs). We show that in this second case, the instantaneous firing rate does not enlighten existence of the ISIs dependencies. Hence the conditional firing rate should be introduced. Existing estimators for the conditional firing rate request the knowledge of the ISIs distribution, a fact rarely verified for observed data. We propose a non-parametric estimator for the conditional instantaneous firing rate for Markov, stationary and ergodic ISIs. An algorithm to check the reliability of the proposed estimator is introduced and its consistency properties are proved. The method is applied to data obtained from a stochastic two compartment model and to experimental data.

Mutual Information: estimation and application to neural data
Roberta Sirovich (University of Turin)

In the past few decades there has been a strong increase in the popularity of information–theoretic analysis of neural data. Information quantities have been used in several directions, such as learning about the signal from the output spike train, but also to quantify dependencies among the involved units. In particular we are interested in using mutual information, a measure of the linear and non linear dependencies among random variables. This approach seems to be very promising in many applications in neurosciences. From a statistical point of view, the direct estimation of mutual information presents problems that increase with the dimension of the problem. In [1] we proposed a new non-parametric estimator that exploits the link between mutual information and the entropy of a suitably transformed sample. After illustrating some features of the new statistical procedure, we discuss some possible applications in neuroscience. [1] Giraudo MT, Sacerdote L, Sirovich R (2013) Non-parametric Estimation of Mutual Information through the Entropy of the Linkage, Entropy 15(12), 5154-5177.

Sequential Monte Carlo samplers for a conditionally linear problem in magneto/electro-encephalography
Alberto Sorrentino (University of Genoa)

Magneto/Electro-encephalography (M/EEG) are powerful tools that record the magnetic field / electric potential generated by brain activity, with a millisecond-by-millisecond resolution. However, estimation of the spatio-temporal distribution of neural currents from MEEG data is an ill-posed problem, due to the non-identifiability of the model. We adopt the Bayesian approach and make use of a multi-dipole model, where the neural current is approximated with a small set of point-like currents (current dipoles), each one characterized by a location and a dipole moment. We consider the problem of estimating the number of dipoles and their parameters either from a single spatial distribution of M/EEG data, or from a time-series, under the assumption that the number of sources and their locations do not change in time. We exploit the linearity with respect to the dipole moment, and set up a variable dimension model and a Sequential Monte Carlo sampler (SMC, Del Moral et al., 2006) to approximate the marginal posterior distribution for the non-linear variables, while the conditionally Gaussian posterior for the dipole moments is computed analytically. As the only time-varying variables are the linear ones, the computational cost of the algorithm does not depend on the length of the time-series. We apply the method to both synthetic and experimental data to show that it can effectively recover neural sources with high accuracy. A comparison with a full SMC (Sorrentino et al., 2014), sampling the whole posterior distribution, shows that exploitation of the linear substructure leads indeed to a reduced Monte Carlo variance of the estimators. Del Moral et al. (2006) Journal of the Royal Statistical Society B 68: 411-436 Sorrentino et al. (2014) Inverse Problems 30: 045010

High-resolution diffusion MRI by msPOAS
Karsten Tabelow (Weierstrass Institute)

In this talk we present a new method msPOAS for adaptive smoothing diffusion magnetic resonance imaging data. The procedure is based on the propagation-separation approach and uses the geometry of the measurement space of (voxel) positions and (gradient) orientations to reduce noise in the measured image volumes. We will elaborate on the principles of the algorithm and show applications to high resolution diffusion MRI data.

Nonlinear approaches to neural system identification
Lucas Theis (MPI Tuebingen)

Due to their conceptual and computational simplicity, generalized linear models (GLMs) represent a popular choice for the probabilistic characterization of neural spike responses. However, their limited flexibility necessitates choosing an appropriate feature space to model nonlinear behavior which can be difficult in practice. I will present nonlinear extensions to generalized linear models which are able to extract nonlinear features from data automatically. Despite losing global convergence guarantees, these models are able to learn complex stimulus-response relationships with simple off-the-shelf optimization routines and can outperform typical GLMs by large margins. I will further show how they can be used to improve spike extraction from two-photon calcium images and discuss the quantification of the quality of spike train predictions.

Opportunities and Challenges in EEG-based Assessment of Cognitive Status in Severe Brain Injury
Jonathan D. Victor (Cornell) Nicolas D. Schiff

Severe brain injury presents an immense burden to affected individuals, their families, and society. While many individuals eventually recover some level of function, they typically have overwhelming motor disability. This confounds the determination of cognitive capacities via standard behavioral means, and motivates the development of assessment strategies that bypass the motor system, such as functional brain imaging and electroencephalography (EEG). EEG is an especially attractive approach because it can capture events at behaviorally relevant timescales of less than one second, it is widely available, and measurements can be made over a prolonged period of time. The latter consideration is especially important for assessing patients with severe chronic brain injury because their level of arousal can fluctuate substantially and unpredictably. Nevertheless, developing EEG-based paradigms to assess cognitive function presents challenges. Some of these are generic: electrical signals recorded on the scalp constitute a spatially-averaged mixture the activity of large and heterogeneous populations of neurons, and inferring the sources of these signals is an ill-posed problem. Scalp-recorded signals invariably contain artifacts, due both to other bioelectric sources (such as muscle activity) and environmental sources; this problem is exacerbated in this subject population as they are unable to cooperate, and may be in an electrically noisy environment. Moreover, artifacts may have complex dynamics and covariation across time, as they may be coupled to level of arousal or environmental events. Finally, the EEG is intrinsically multivariate it is a broadband signal recorded at dozens of scalp locations. Since the particular dynamical features of interest may not be known in advance or even predictable from normal subjects, there is the potential for a massive multiple-comparisons problem. While practical strategies exist for meeting each of these challenges, there is much room for improvement and improvements will directly translate into more precise and reliable evaluation tools.

Statistical Pitfalls in Cognitive Neuroscience
Eric-Jan Wagenmakers (University of Amsterdam)

In this presentation I discuss three statistical pitfalls that are particularly relevant for cognitive neuroscience. The first pitfall concerns the fact that the difference between significant and not significant is itself not necessarily significant (i.e., the imager's fallacy). The second pitfall concerns the misinterpretation of the p-value as evidence against the null hypothesis; specifically, I will show that when p is about .05, the evidence against the null is anecdotal at best. The third pitfall is perhaps most serious,

and it concerns the presentation of exploratory analyses as confirmatory. All three pitfalls can be avoided, but it requires that cognitive neuroscientists change the way they design their experiments and analyze their data.

ABC and the statistical challenges of big simulation
Richard Wilkinson (University of Nottingham)

'Big data' has been the focus of much recent research and looks at how to learn when datasets are so large that traditional methods of analysis break down. In this talk, I will talk about the complimentary challenge presented by 'big simulation', namely, how can we analyse simulators that are so complex that traditional statistical methodology cannot be used. I will describe and review a class of algorithms that are known as approximate Bayesian computation (ABC) methods, which have been developed to fit complex simulators to data (calibration). ABC methods have rapidly become popular in the biological sciences over the past decade. The simplest form of the algorithm is very easy to implement, and can nearly always be applied, allowing us (in theory) to fit any simulator to data. or complex simulators, in practice we have to use more efficient (and more complex) versions of ABC in order to do the analysis. I will review the main approaches taken to implementing ABC for expensive simulators, and outline some recent work that uses Gaussian process emulators of the simulator in order to enable inference for genuinely expensive stochastic simulators.

Localisation microscopy with quantum dots using non-negative matrix factorisation
Chris Williams (University of Edinburgh)

We propose non-negative matrix factorisation (NMF) to model a noisy dataset of highly overlapping fluorophores with intermittent intensities. We can recover images of individual sources from the optimised model, despite their high mutual overlap in the original data. This allows us to consider blinking quantum dots as bright and stable fluorophores for localisation microscopy. We compare the NMF results to CSSTORM, 3B and bSOFI techniques. Joint work with Ondrej Mandula, Ivana Sumanovac Sestak and Rainer Heintzmann.

Poster Abstracts

Just How Complex Are Purkinje Cell Complex Spikes?
Amelia Burroughs (University of Bristol)

Despite comprising only 10% of brain volume, the cerebellum contains approximately 80% of all neurons. Cerebellar activity is critical for motor control and coordination and is necessary for learning movements. The Purkinje cell is the only neuronal type to project out from the cerebellar cortex and influence downstream motor processing. Purkinje cell spike trains must therefore represent all computations performed within the cerebellar cortex. Purkinje cells fire two distinct types of action potential: simple spikes (SS) and complex spikes (CS). These are thought to mediate different aspects of cerebellar operation. SSs are stereotypical, sodium-mediated action potentials that are elicited intrinsically (30Hz). CSs are infrequent (1Hz) and are composed of an initial sodium-mediated action potential that is then followed by a number of high-frequency (500Hz) secondary components (spikelets). The quantitative analysis of CS components remains a novel area of study, but it is likely that changes in CS waveform are functionally significant. I aim to use a combination of mathematical techniques to quantitatively describe the CS waveform. By implementing an annealing algorithm I show that CSs are not unitary events but form a number of distinct clusters based on waveform dynamics. Discrete CS waveforms may differentially modulate SS firing within the same cell and also differentially affect downstream target nuclei activity. In this way, specific CS waveforms may underlie different aspects of cerebellar operation and ultimately motor behaviours.

APACE: Accelerated Permutation Inference for the ACE Model
Xu Chen (University of Warwick)

Heritability studies of imaging phenotypes are becoming more commonplace. Heritability, the proportion of phenotypic variance attributable to genetic sources, is typically estimated with variance components (e.g. in SOLAR) or structural equation models (e.g. in OpenMx), but these approaches are computationally expensive and cannot exploit the sensitivity of spatial statistics, like cluster-wise tests. Thus, we developed a non-iterative estimation method for the ACE model; this method is accurate and is so fast that it allows the use of permutation, which provides sensitive family-wise error corrected voxel- and cluster-wise inferences. Specifically, we fit the ACE model to twin data at each voxel and make inference on summary and aggregate measures of heritability. We call our Matlab-based tool using these inference approaches "Accelerated Permutation Inference for the ACE Model (APACE)", and are distributing it freely at http://warwick.ac.uk/tenichols/apace.

A Method for Fast Whole-brain Aggregate Heritability Estimation
Xu Chen (University of Warwick)

Heritability, the proportion of variability attributable to genetic sources, is a vital quantitative genetic measure and, in particular, non-zero heritability is needed to certify a trait as a "phenotype". However heritability can also be used as a general measure of biological validity, e.g. ranking different pre-processing techniques by heritability of the resulting phenotype. While such comparisons can be done element-wise over the phenotype (e.g. by voxels or surface elements), a whole-brain summary of heritability can simplify the comparisons. In this work we propose a simple measure of aggregate heritability that is easy to compute and involves no ACE model fitting. We derive analytical results that show this aggregate measure is closely related to the average of element-wise heritability. Using real data we found that this extremely fast

aggregate heritability is highly similar to that from the traditional (more computationally intensive) mean heritability summaries obtained by fitting ACE model.

Robust and explorative analysis of EEG data
Benedikt Ehinger (University of Osnabrueck)

Explorative data-driven analysis of EEG is burdened with problems related to the multiple comparison problem. In a standard EEG experiment testing a large number of electrodes and time points for potential effects is associated with a highly elevated familywise error rate. Furthermore correction procedures that do not take in account the highly correlated structure of the data result in increased type II errors. In addition, high inter-subject variability leads to outliers that possibly skew the data and result in unreliable effects. In order to overcome these problems, we fitted mass-univariate GLMs on single subject trials and in a second step estimated effects based on beta-weights over subjects for all time points and electrodes (Pernet, 2011). In our experiment, we study the role of prediction of visual information during eye-movement behavior. We displayed peripheral stimuli and, after a delay, instructed the subjects to perform saccades onto the stimulus. During the saccade, we exchanged the stimulus with a modified version in some of the trials. We analyzed pre- and post -saccadic ERPs in a 4x2 unbalanced factorial design. The EEG data (64 Channels, 500Hz) were corrected for multiple comparisons by the threshold free cluster enhancement method. This method corrects individual each sample statistic instead of an extended cluster-based statistic. To account for outliers, we used Yuens t-test and bootstrap-percentile methods of trimmed means as robust statistical methods for group level comparisons. We found a significant main effect of changing the stimuli that closely resembles a P300 and, importantly, highly significant interactions modulating this main effect. These approaches allow analyses that show considerably improved sensitivity and robustness. Especially interactions can be analyzed readily using the GLM framework in a flexible and explorative way.

The Fast and Powerful Method for Multiple Testing Inference in Family-Based Heritability Studies with Imaging Data
Habib Ganjgahi (University of Warwick)

Estimation of heritability for neuroimaging phenotypes like cortical thickness, fractional anisotropy and BOLD activations, is essential in imaging genetic studies. Voxel-wise heritability measurements were made possible by genetic analysis tools optimized for imaging research, such as the SOLAR/SOLAReclipse. The mass-univariate nature of voxel-wise analyses present a challenge to account for elevation in false positive findings because of multiple testing. Many standard correction methods for multiple testing, including cluster-wise inference cannot be readily used in imaging genetic studies because of the strict assumption for non-independence of the sample. Here, we are presenting a fast and powerful permutation test for general pedigree studies that provide traditional, spatial inferences for images. Heritability estimation is performed using variance component models. In this approach, the phenotype covariance matrix is decomposed into two components, one for the additive genetic effect and one for the combination of individual-specific environmental effects and measurement error ($\Sigma = 2\sigma_A^2\Phi + \sigma_E^2 I$). These parameters are estimated by maximizing the likelihood function under a multivariate normal assumption. An orthogonal transformation (based on the eigenvectors of the kinship matrix) is used to accelerate computation. two permutation tests are proposed to correct the multiple testing errors in imaging heritability studies. The first method is based on the permuting the kinship covariance matrix and

fitting the model repeatedly and applying the likelihood ratio test as a test statistic to derive the uncorrected p-value. In this method, the nonlinear maximum likelihood function is optimized by the numerical method in each permutation, which is computationally intensive.

The second method is based on constructing an auxiliary regression model on squared residuals and the kinship covariance matrix eigenvalues. After orthogonal transformation of the data, the second moment of residuals has a linear relationship with the additive genetic effect and the kinship matrix eigenvalues $E(\epsilon_i^2) = h^2(\lambda_g i - 1) + 1$ (without loss of generality we assume that the data is scaled to unit variance) where ϵ and λ_g are transformed residuals and the kinship matrix eigenvalues respectively. We propose to use half of the explained sum of squares as a test statistic. In this case, permuting the eigenvalues and calculating the test statistic in each permutation calculate the uncorrected p-values.

Finally, in each permutation, maximum statistic and maximum cluster size is captured to derive the empirical distribution of these statistics and their critical values. Computer simulation was used to validate the permutation tests and random field cluster size inference for multiple testing error correction in imaging heritability studies. We simulated smooth images of size 64 by 64 containing a circular region of true heritability for a family of 52 and 138 subjects; heritability was varied, h2 = 0.2, 0.4, 0.6, 0.6. 500 permutations were used, and the entire simulation was repeated with 100 realized datasets. Voxel-wise, we found permutations and parametric-likelihood-based inferences gave nearly identical control of false positives and comparable power. Cluster wise inference revealed that random field findings are generally conservative and does not work for low cluster forming thresholds (fig1, right panel). Cluster wise inference based on the LRT statistic image showed that this method works better than RFT however we found that permuting the eigenvalues and using LRT as a test statistic affected by effect size (fig2.). Finally the permutation method based on the auxiliary regression was faster and controlled the false positive rates at the desired level (fig1, left panel) and had the greatest power.

Is Z enough? Impact of Meta-Analysis using only Z/T images in lieu of estimates and standard errors

Camille Maumet (University of Warwick)

Introduction

While most neuroimaging meta-analyses are based on peak coordinate data, the best practice method is an Intensity-Based Meta-Analysis (IBMA) that combines the effect estimates and their standard errors (E+SE's) [5]. There are various efforts underway to facilitate sharing of neuroimaging data to make such IBMA's possible (see, e.g. [2]), but the emphasis is usually on sharing T-statistics. However, guidelines for (non-imaging) meta-analysis are clear that T-statistic- based meta-analysis is suboptimal and is to be discouraged [1]. But even if E+SE's are shared, the units must be equivalent, and different software, models or contrasts can lead to incompatible units. Using 21 studies of pain in control subjects, we compare the use of IMBA using only T-statistics to use of E+SE's.

Methods

Our reference approach is an IBMA based on a 3-level hierarchical model: level 1, subject FFX; level 2, study MFX; level 3: meta- analysis MFX (FLAME MFX) or FFX (FLAME FFX), using FSL's FLAME method [6]. In the absence of E+SE's, there are a number of methods to combine Z-scores [3]. We focused on three of them: Stouffer's method [7], Weighted-Z [8,4], Z MFX [5] and Z Permutation. We also investigated two alternative approaches using only the E¡92¿s: Random-Effects GLM (RFX GLM) and

Contrast Permutation.

Conclusions

We have compared seven meta-analytic approaches in the context of one- sample test. When only contrast estimates are available, RFX GLM was valid, closest to FLAME MFX reference. When only standardised estimates (i.e. Z/T's) are available, permutation is the preferred op6on as the one providing the most faithful results. Further investigations are needed in order to assess the behaviour of these estimators in other configurations, including meta-analyses focusing on between-study differences.

Global tractography within a Bayesian framework

Lisa Mott (University of Nottingham)

Diffusion-weighted magnetic resonance imaging quantifies the diffusion of water in the brain to understand the underlying tissue and enables the reconstruction of white matter tracts in the brain non-invasively and in-vivo by tractography, which is essential to understanding the brain's structure and functions.

Currently, the two commonly used tractography methods do not allow for statistically testing for the existence of a connection between two brain regions of interest (ROIs). However, global tractography (Jbabdi et al. 2007) parametrises these connections between two brain regions at a global level and hence, known connections can be acknowledged in the algorithm. Within such a framework the intensity within each voxel is modelled using a partial volume model (Behrens et al. 2003), while we can do model selection to choose between the model where a connection exists between 2 ROIs and the model where there is no such connection.

In this talk we first discuss how one can efficiently estimate the parameters of the partial volume model when fitted to data for a single voxel. The partial volume models allows a number of fibre orientations to be modelled within one voxel. Although regularisation methods have been used in this setting, we introduce thermodynamic integration methods instead which enable for formal model comparison leading to accurate estimation of Bayes Factors. Furthermore, we introduce a new method for tractography, termed as fully probabilistic tractography, that allows model uncertainty (i.e. the number of different fibre orientations) to be taken into account. Finally, we discuss how these methods that applied for a single voxel can be used to construct an MCMC algorithm for doing efficient inference for global tractography.

References

[1] Behrens,T.E.J.,Woolrich,M.W.,Jenkinson,M.,Johansen-Berg,H.,Nunes,R.G.,Clare,S.,Matthews,P.M.,Brady,J.M. and Smith,S.M. 2003. Characterization and Propagation of Uncertainty in Diffusion-Weighted MR Imaging. *Mag.Res.inMed*50,pp.1077-1088.

[2] Jbabdi,S.,Woolrich,M.W.,Andersson,J.L.R. and Behrens,T.E.J. 2007. A Bayesian framework for global tractography. *NeuroImage*37,pp.116-129.

Estimating non-stationary brain connectivity networks

Ricardo Pio Monti (Imperial College)

Understanding of the functional architecture of the human brain is at the forefront of neuroimaging. In many applications functional networks are assumed to stationary

resulting in a single network estimated for the entire time course. However recent results suggest that the connectivity between brain regions is highly non-stationary even at rest.

As a result, new methodologies are needed to comprehensively account for the dynamic nature of functional networks. Such approaches must be capable of accurately estimating networks but also highly adaptive to rapid changes that may occur.

In this poster we describe the Smooth Incremental Graphical Lasso Estimation (SINGLE) algorithm which can be used to estimate dynamic brain networks from fMRI data. The proposed method builds on the strength of penalised regression methods and strongly related to network previous work such as the Graphical and Fused Lasso. Consequently, the resulting objective function is convex and can be solved efficiently via an Alternating Directions Method of Multipliers algorithm. This allows for the proposed algorithm to solve large scale problems ¡96¿ we further discuss approximations which can be used to improve running times for practical applications.

We provide a simulation study to demonstrate the capabilities of the proposed method and apply it to task-based fMRI data. The results demonstrate the capabilities of the proposed method and highlight the Right Inferior Frontal Gyrus and the Right Inferior Parietal lobe as dynamically changing with the task.

Finding the right spot - Background correction in ratiometric calcium imaging using independent background measurements

Marlene Pacharra (TU Dortmund) Vanessa Hausherr, Ramona Lehmann, Julia Sisnaiske, and Christoph van Thriel

In neuroscience, imaging of transient calcium responses to a range of stimuli (e.g. neurotransmitters, chemicals) in neuronal cells is an important tool to assess cell functionality. After loading fluorescent Ca2+ indicators into living cells ratiometric measurements are used to quantitatively determine the intracellular calcium concentration during stimulation. Without a valid estimation of background fluorescence, the amplitudes of these measured calcium transients cannot be compared across experiments. In order to control for such sample-based differences, a standard approach is the use of an independent background measurement of a cell-free region that is subsequently subtracted from the fluorescence intensity in all the Regions of Interest (ROIs, cells).

We investigated across three different cell types from mice (neuronal progenitor cells, primary cortical neurons, trigeminal ganglion neurons) and three biological replicates, ($< 1\mu$m vs. $> 10\mu$m from a cell) and size of the cell-free control area ($46\mu\text{m}^2$ vs. $200\mu\text{m}^2$), in which the background measurement is made, affects background-corrected calcium amplitudes. We hypothesized that if (a) the background measurement area is close to a cell and (b) the background measurement area is large, the background-corrected amplitudes should be larger since the noisy background can be better eliminated.

Depending on location, cell type and replicate, size of background measurement area influenced background-corrected amplitudes differently sometimes resulting in substantially smaller or larger background-corrected amplitudes. Across all cell types, background-corrected amplitudes were larger, if the background measurement was made close to a cell as opposed to further away from a cell.

Background correction based on a single independent background measurement is implemented in many software applications for calcium imaging. Results obtained using this approach should be treated carefully. If amplitudes are to be compared across experiments our results suggest that experimenters should control size and location of the background measurement area.

Bayesian model selection and estimation: Simultaneous mixed effects for models and parameters

Daniel J. Schad (Charite Hospital Berlin)

Bayesian model selection and estimation (BMSE) are powerful methods for determining the most likely among a set of competing hypotheses about the mechanisms and parameters that generated observed data. In group-studies, full inference is provided by mixed-effects or empirical/hierarchical Bayes' models, which capture individual differences (random effects) as well as mechanisms/parameters common to all individuals (fixed effects). Previous models have assumed mixed-effects either for model-parameters (e.g., Pinheiro & Bates, 2000) or for the model-identity (Stephan et al., 2009). Here, we present a novel Variational Bayes' (VB) model which considers mixed-effects for models and parameters simultaneously. As a first step, we evaluate a method estimating mixed effects for parameters via expectation maximization (EM), while treating models as a fixed-effect (cf. Huys et al., 2011). Based on Monte Carlo simulations of (generalized non-linear) reinforcement learning models of decision-making we show that the EM method efficiently recovers true effects from the data, and that it can be used to estimate GLMs at the level of individual-specific parameters. We derive model-evidences and error bars for fixed effects via importance sampling and demonstrate via simulations that this can be used to test hypotheses on the data. Second, we evaluate our new VB method to simultaneously consider mixed effects for models and parameters, and compare it to a sufficient statistics approach, where mixed effects for parameters (Huys et al., 2011) and models (Stephan et al., 2009) are computed separately and combined for inference. Monte Carlo simulations show that both approaches provide successful estimation of model probabilities when uncertainty is low, but - as theoretically expected - reveal a higher correct probability mass of the new VB method under conditions of uncertainty. Compared to previous approaches (Huys et al., 2011; Stephan et al., 2009), the new VB method thus provides more precise inference in Bayesian model selection under uncertainty, and allows reducing biases in parameter estimation. Our new method suggests that we can and should understand the heterogeneity and homogeneity observed in group studies by investigating contributions of both, the underlying mechanisms and their parameters. We expect that this new mixed-effects method will prove useful for a wide range of group studies in computational modeling in neuroscience.

Pain-free Bayesian inference for psychometric functions

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To estimate psychophysical performance, psychometric functions are usually modeled as sigmoidal functions, whose parameters are estimated by likelihood maximization. While this approach gives a point estimate, it ignores its reliability (its variance). This is in contrast to Bayesian methods, which in principle can determine the posterior of the parameters and thus the reliability of the estimates. However, using Bayesian methods in practice usually requires extensive expert knowledge, user interaction and computation time. Also many methods—including Bayesian ones—are vulnerable to non-stationary observers (whose performance is not constant).

Our work provides an efficient Bayesian analysis, which runs within seconds on a common office computer, requires little user-interaction and improves robustness against non-stationarity. A Matlab implementation of our method, called PSIGNFIT 4, is freely available online. We additionally provide methods to combine posteriors to test the difference between psychometric functions (such as between conditions), obtain posterior distributions for the average of a group, and other comparisons of practical interest.

Our method uses numerical integration, allowing robust estimation of a beta-binomial model that is stable against non-stationarities. Comprehensive simulations to test the numerical and statistical correctness and robustness of our method are in progress, and initial results look very promising.

Spatial Modelling of Multiple Sclerosis for Disease Subtype Prediction
Bernd Taschler (University of Warwick)

Magnetic resonance imaging (MRI) has become an essential tool in the diagnosis and managing of Multiple Sclerosis (MS). Currently, the assessment of MS is based on a combination of clinical scores and subjective rating of lesion images by clinicians. We present an objective 5-way classification of MS disease subtype as well as a comparison between three different approaches. First we propose two spatially informed models, a Bayesian Spatial Generalized Linear Mixed Model (BSGLMM) and a Log Gaussian Cox Process (LGCP). The BSGLMM relies on a regularised probit regression model and accounts for the binary nature of lesion maps and the spatial dependence between neighbouring voxels. On the other hand, the LGCP accounts for the random spatial variation in lesion location where the centre-of-mass of each lesion is considered as a realisation of a Poisson process that is driven by an underlying, non-negative intensity function. Both models improve upon mass univariate analyses that ignore spatial dependence and rely on some level of arbitrarily defined smoothing of the data. As a comparison, we consider a machine learning approach based on multi-class support vector machine (SVM). For the SVM classification scheme we use a large number of quantitative features derived from three MRI sequences in addition to traditional demographic and clinical measures. We show that the spatial models outperform standard approaches with average prediction accuracies of up to 85%.

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