5th International Summer School in Biomedical Engineering

Topic: Multimodal integration of functional brain measurements

Course Material

Detailed Scientific Programme:

Introduction, Keynote Speech

Wed	18/08	Afternoon	Arrival/ Registration	
Wed	18/08	13.30-14.30	Technical and Scientific Introduction	
Wed	18/08	14.30-15.00	break	
Wed	18/08	15.00-16.30	F.H. Lopes da Silva	Neural Mass Models: EEG/MEG and hemodynamic signals
Wed	18/08	Evening		Get-Together-Party

Symposium 1: Theory of data fusion

Organizers: Jan Schreiber

Thu	19/08	8:30-10:00	Bernd Fischer (Lübeck)	Medical Image Registration: A Challenge for Imaging and Numerical Analysis
Thu	19/08	10:00-10:30		break
Thu	19/08	10:30-11:30		self-study time and project work
Thu	19/08	13:00-13:50	Carsten Wolters (Münster)	Correction and registration methods in multimodal MRI applications
Thu	19/08	13:50-14:40	Christophe Grova (Montreal)	Integration of multimodal functional data using electrophysiology (EEG, MEG) and hemodynamic processes (fMRI, NIRS); Application in epilepsy
Thu	19/08	14:40-15:30	Matthew Casey (London)	How key structures in the brain combine sensory modalities
Thu	19/08	15:30-16:30		Break, self study time and project work
Thu	19/08	16:30-17:30		panel discussion

Symposium 2: Measurement modalities in human brain research

Organizers: David Moreno Dominguez

Fri	20/08	8.30-9.15	Jens Haueisen (Ilmenau)	Introduction to EEG/MEG
Fri	20/08	9.15-10.00	Robin Heidemann (Leipzig)	The basics of anatomical, functional and diffusion-weighted magnetic resonance imaging
Fri	20/08	10.00-10.30		break
Fri	20/08	10.30-11.15	Frederic Schoenahl	Introduction to PET/SPECT
Fri	20/08	11.15-12.00	Hellmuth Obrig	The blushing brain: Non-Invasive Optical Imaging, how it works and how to apply it
Fri	20/08	12.00-13.00		Lunch

Symposium 3: Simultaneous measurements

Organizers: Daniel Strohmeier, Theresa Götz

Fri	20/08	13.00-14.15	Matti Hämäläinen	Combination of EEG and MEG: Measurements, Sensor-Level Analysis and Source Modelling
Fri	20/08	14.15-14.30		break
Fri	20/08	14.30-15.45	Geertjan J.M. Huiskamp	Interictal epileptic spikes as measured in the brain, on the brain and outside the brain
Fri	20/08	15.45-16.00		break
Fri	20/08	16.00-17.30		Self study time and project work
Fri	20/08	18.15-20.15		Guided City Tour
Sat	21/08	8.30-9.45	Stefan Debener	Benefits and pitfalls of EEG-informed fMRI analysis
Sat	21/08	9.45-10.00		Break, self study time and project work
Sat	21/08	10.00-11.15	Frederic Schoenahl	PET,SPECT and hybrid techniques for functional explorations of the brain Concepts, instrumentation and applications
Sat	21/08	11.15-12.00		panel discussion
Sat	21/08	14.00-18.00		Canoing tour on Elbe

Social Programme

Sun	22/08	Whole day		All day excursion through Wörlitz Park

Symposium 4: Use of Priors

Organizers: Fahimeh Mamashli

Mon	23/08	08.30-10.00	Pedro Valdés-Sosa	EEG/MEG source modeling from a Bayesian perspective
Mon	23/08	10.00-10.30		break
Mon	23/08	10.30-11.30		Self-study time and project work
Mon	23/08	11.30-13.00		Lunch
Mon	23/08	13.00-14.15	Pedro Valdés-Sosa	Fitting Neural Field equations to EEG/MEG data
Mon	23/08	14.30-15.30	Gareth Barnes	Usage of a priori information in EEG/MEG source reconstruction
Mon	23/08	15.30-16.30		Self-study time and project work
Mon	23/08	16.30-17.30		Panel discussion

Symposium 5: Multimodal generative Models

Organizers: Manh Nguyen Trong

Tue	24/08	8.30-10.00	Ingo Bojak (Nijmegen)	Multimodal generative modeling: The road less traveled by
Tue	24/08	10.00-10.15		Break
Tue	24/08	10:15-11:00	Jean Daunizeau (London)	Symmetrical event-related EEG/fMRI information fusion in a variational Bayesian framework

Tue	24/08	11:00-12:00	Juha Voipio (Helsinki)	Infraslow EEG activity: Signal sources and recording techniques
Tue	24/08	12.00-13.00		Lunch
Tue	24/08	13:00-17.30		Project Work

Project work

Wed	25/08	8.30-11.30		Project work
Wed	25/08	11.30-13.00		Lunch
Wed	25/08	13.00-17.30		Project defences/ Adjournment
Wed	25/08	Evening		Barbecue

Departure (Thu, 26/08)

Abstracts and Papers:

Introduction and Keynote Speech

F.H. Lopes da Silva: Neural Mass Models are being applied to make a bridge between the activity of neuronal networks as reflected in EEG/MEG signals and hemodynamic signals as measured by way of functional MRI (BOLD), in order to gain insight in the working of neuronal networks underlying cognitive processes and pathological conditions. This constitutes a central feature of Dynamic Causal Modelling (DCM)1.
According to this approach the summed post-synaptic potentials generated by a neural mass model of neuronal networks are used in the forward mode to estimate the primary current density distribution of a brain area. This approach has been applied in a number of studies of brain rhythmic activities, both under normal and pathological conditions (epilepsy)2. Here we consider this approach in a wider context. The primary current density can be transformed into the signal recorded at EEG sensors, by applying a linear spatial convolution with the EEG lead field, i.e. the function which relates any source in the brain to the corresponding measurements at the EEG sensors. Simultaneously the summed post-synaptic potentials generated by the neural mass model can be transformed into a local vasomotor feed forward signal that is then further transformed by way of temporal convolution with the hemodynamic response function (HRF) into a simulated BOLD signal3. In this way the information obtained from the EEG signal and from the corresponding fMRI BOLD signal recorded from the same region of interest can be fused. This approach, however, is based on concepts that are still insufficiently established. Namely more research is needed to better understand how neural activities, generated by neural populations with complex geometrical configurations are transformed into cortical current distributions on the one hand, and how they are associated with BOLD signals on the other, as for example In the case of alpha rhythms4. Understanding these basic processes is important to be able to make insightful interpretations of multimodal imaging of brain processes.

1. *David O, Friston KJ.. 2003. A neural mass model for MEG/EEG: coupling and neuronal dynamics. Neuroimage. 2003 Nov;20(3):1743-55. Friston, K.J., Harrison, L., Penny, W. 2003. Dynamic causal modeling. NeuroImage 19: 1273 – 1302.*

2. *Lopes da Silva F, Blanes W, Kalitzin SN, Parra J, Suffczynski P, Velis DN.2003. Epilepsies as dynamical diseases of brain systems: basic models of the transition between normal and epileptic activity. Epilepsia:44 Suppl 12:72-83*

3. *Valdes-Sosa PA, Sanchez-Bornot JM, Sotero RC, Iturria-Medina Y, Aleman-Gomez Y, Bosch-Bayard J, Carbonell F, Ozaki T. 2008. Model driven EEG/fMRI fusion of brain oscillations. Hum Brain Mapp. 23;30(9):2701-2721de Munck JC, Gonçalves SI, Mammoliti R, Heethaar RM, Lopes da Silva FH. 2009.*

4. *Interactions between different EEG frequency bands and their effect on alpha-fMRI correlations. Neuroimage.;47(1):69-76.- de Munck JC, Gonçalves SI, Faes TJ, Kuijer JP, Pouwels PJ, Heethaar RM, Lopes da Silva FH. 2008. A study of the brain's resting state based on alpha band power, heart rate and fMRI. Neuroimage;42(1):112-21. - de Munck JC, Gonçalves SI, Huijboom L, Kuijer JP, Pouwels PJ, Heethaar RM, Lopes da Silva FH. 2007. The hemodynamic response of the alpha rhythm: an EEG/fMRI study. Neuroimage;35(3):1142-51.*

Symposium 1: Theory in data fusion

Bernd Fischer: Image registration is central to many of the challenges in medical imaging today. Examples include treatment verification by comparison of pre- and post-intervention images, creation of population averages, growth monitoring of tumours using time series, or rearrangement of histological sections, to name a few.
Image registration, has been subject to extensive studies in the past years. Its versatile and important applications have attracted researchers from various branches, including numerical analysts. In this talk we not only present an overview on state-of-the-art schemes and comment on fast implementations but also point out some of the mathematical challenges associated with these approaches. The talk is accompanied by a variety of real life examples.

5. *Bernd Fischer and Jan Modersitzki: Medical Image Registration: A Challenge for Imaging and Numerical Analysis, http://iopscience.iop.org/0266-5611/24/3/034008*

Carsten Wolters: A wide range of medical applications in clinic and research exploit images acquired by multimodal magnetic resonance imaging (MRI) sequences. First of all, MRI sequences can be severely distorted by means of field inhomogeneities and susceptibility artefacts and correction methods are needed before further analysis. Then, images resulting from different MR sequences have to be registered before further analysis is possible.
In my talk, registration and segmentation techniques are presented and discussed for MR image correction. Then, parametric and non-parametric registration methods will be presented for the registration of multimodal MR images. One focus will be on a new variational approach to correct EPI distortions. The approach is presented, evaluated and analyzed. EPI sequences are used in functional MRI (fMRI) and diffusion tensor MRI (DT-MRI) Following the reversed gradient method two EPI images with inverted phase encoding gradients are acquired in order to automatically estimate the field inhomogeneity. The idea is to develop an image registration scheme with a tailored transformation model applied reversely on both images. Mislocalizations due to inhomogeneities are restricted along one space direction and mirrored in both image volumes. The total amount of intensity has to remain unchanged during the correction. Due to this mass-preserving property, intensity distortions have to be corrected accordingly.
The accuracy of the new correction approach will be evaluated on a phantom scan first. Afterwards, successful applications to DT-MRI and fMRI datasets will be discussed, underscoring the applicability of the presented algorithm to real life applications.

6. *J. Olesch, L. Ruthotto, H. Kugel, S. Skare, B. Fischer and C. H. Wolters,A variational approach for the correction of field-inhomogeneities in EPI sequences, SPIE, Medical Imaging 2010: Image Processing, vol. 7623, nr.1, 76230K, 8 pages, 2010. http://link.aip.org/link/?PSI/7623/76230K/1, doi: 10.1117/12.844375*

7. *C.H. Wolters, A. Anwander, D.Weinstein, M.Koch, X.Tricoche and R.S.MacLeod, Influence of Tissue Conductivity Anisotropy on EEG/MEG Field and Return Current Computation in a Realistic Head Model: {A} Simulation and Visualization Study using High-Resolution Finite Element Modeling, NeuroImage, 30 (3), pp. 813-826, 2006. http://dx.doi.org/10.1016/j.neuroimage.2005.10.014*

8. *MastersThesis: Ruthotto, L.,Mass-preserving Registration of Medical Images, school = Institute for Computational and Applied Mathematics, University of Muenster, march 2010, German Diploma Thesis*

Matthew Casey: Our ability to rapidly process and act upon sensory information is an important animal attribute. While sensory processing is often considered to occur in isolation to other senses, this unisensory view of processing has changed over the last 30 years with a growing realisation that multisensory integration at all levels of the brain is important. Pivotal moments in this realisation include the discovery of the McGurk-MacDonald effect, which demonstrates how influential vision can be on speech processing; as well as oddities such as the rubber hand effect. Systematic studies of multisensory integration have provided insight into how brain structures develop and use multimodal stimuli. Such studies are exemplified by the superior colliculus (SC), which is the subcortical structure responsible for shifting our gaze to focus on prominent stimuli regardless of which sense the stimulus was detected in. In this hot topic presentation, I will provide a brief overview of some of the phenomena that demonstrate our multisensory capability. By way of example, I will then focus on how the brain integrates vision, audition and touch to shift our gaze in the SC, moderated by cortical feedback. To provide examples of how such integrated processing may help in combining non-invasive brain measurement modalities, to finish off I will explore how some of the principles of the SC relate to computational techniques.

9. *An essential introduction to the superior colliculus (SC) for all attendees is the "primer" article by King: A.J.King, "The Superior Colliculus," Current Biology, vol. 14:R335-R338, 2004. doi:10.1016/j.cub.2004.04.018; This explains the role of the SC, including how the senses are combined.*

10. *For attendees who wish to look closer at the detail of multisensory integration and the current forefront of our knowledge, then try the following (less accessible) article: L. Yu, B.A. Rowland, and B.E. Stein, "Initiating the Development of Multisensory Integration by Manipulating Sensory Experience," Journal of Neuroscience, vol. 30(14):4904-4913, 2010. doi:10.1523/JNEUROSCI.5575-09.2010*

Christopher Grova:
The purpose of this talk is to introduce main strategies used to combine functional neuroimaging data. Functional data explore different characteristics of brain activity, such as electrophysiology measuring directly neuronal activity using Magneto- or Electro-Encephalography (MEG /EEG) or indirectly through hemodynamic processes using functional Magnetic Resonance Imaging (fMRI) or Near Infra Red Spectroscopy (NIRS). By nature these exploration techniques are measuring activity of different origins covering different and complementary ranges of spatial and temporal resolution, suggesting the necessary need for multimodal integration. Several techniques of data fusion will be presented such as simultaneous acquisitions, comparative fusion, constrained fusion or symmetrical fusion of functional data. EEG, MEG and NIRS consisting in scalp measurements, estimation of brain activity requires the resolution of an ill-posed inverse problem. The integration of anatomical or functional prior in this context will be presented, as well as its relevance using a model comparison framework. The data fusion techniques will be illustrated in the field of the presurgical mapping of patient with epilepsy.

11. *Concordance between distributed EEG source localization and simultaneous EEG-fMRI studies of epileptic spikes. Grova C, Daunizeau J, Kobayashi E, Bagshaw AP, Lina JM, Dubeau F, Gotman J. Neuroimage. 2008 Jan 15;39(2):755-74. Epub 2007 Aug 25.*

Symposium 2: Measurement modalities in human brain research

Jens Haueisen: Electroencephalography (EEG) and Magnetoencephalography (MEG) are established methods for the non-invasive assessment of brain function. The methods comprise the measurement of the scalar electric potential and the vectorial magnetic fields produced by the electric activities in the brain. In this talk, the current state of the art in electric potential and magnetic field recording techniques will be outlined and some recent developments in recording techniques will be discussed. Commonalties and differences with other measurement modalities will be addressed. The most important advantage of both EEG and MEG, when compared to other modalities, is the high temporal resolution. Finally, differences in the sensitivities of EEG and MEG for various types of brain activities will be exemplified.

Robin Heidemann: Magnetic resonance imaging (MRI) has evolved into the most important tool for investigating the living human brain. MRI is a non invasive technique which offers a whole variety of different contrast mechanisms that are not available with other imaging modalities. In addition to anatomical imaging, based on specific tissue properties, it is also possible to acquire images which depend upon physiological function. One example is the change in blood flow and oxygen supply to brain areas, which is correlated with changes in the neural activity. This effect is used for functional MRI (fMRI). Another example of a different contrast mechanism is the diffusivity of water, which is the basis of diffusion-weighted MRI (DW MRI). The lecture will focus on the basic methodologies used in these MR applications (anatomical MRI, fMRI and DW MRI).

Hellmuth Obrig: Non-invasive Optical Imaging of human brain function relies on the principles of near infrared spectroscopy. Changes in haemoglobin oxygenation are determined based on diffuse optical spectroscopy yielding a rough topographic map when multiple probe pairs are used. The talk will explain some basic principles of the methodology, highlighting strengths and limitations of the method. Beyond the most commonly used continuous-wave approach, frequency- and time-domain extensions of the methodology will be discussed. The potential of the methodology especially in concert with other neurophysiologic functional techniques (EEG, fMRI) and examples of application in neurology and neuroscience will be given.

Symposium 3: Simultaneous Measurements

Stefan Debener: Electromagnetic fields as measured with electroencephalogram (EEG) are a direct consequence of neuronal activity and feature the same timescale as the underlying cognitive processes, while hemodynamic signals as measured with functional magnetic resonance imaging (fMRI) are related to the energy consumption of neuronal populations. It is obvious that a combination of both techniques is a very attractive aim in neuroscience, in order to achieve both high temporal and spatial resolution for thenon-invasive study of brain functions subserving cognition. During the last decade a number of research groups have taken up this challenge and developed different methods of EEG-fMRI integration. I will present one approach named EEG-informed fMRI analysis in detail. This requires the concurrent recording of both modalities and the subsequent linear decomposition of the EEG data with independent component analysis (ICA) before trial-by-trial fluctuations of the EEG can be used to predict the fMRI-BOLD response. Applications of this approach will be presented and more recent developments in the field will be discussed.

12. *EEG signatures of auditory activity correlate with simultaneously recorded fMRI responses in humans; Neuroimage 49; 2010 (849-864)*

13. *Trial-by-Trial Coupling of Concurrent Electroencephalogram and Functional Magnetic Resonance Imaging Identifies the Dynamics of Performance Monitoring; The Journal of Neuroscience, December 14, 2005, 25(50):11730-11737*

14. *Singel Trial EEG/fMRI reveals the dynamics of cognitive function, Debener, S. Ullsperger, M. Siegel, M., Engel, A., Trends in cognitive Science, Vol 10 No 12*

Matti Hämäläinen: Magnetoencephalography (MEG) and electroencephalography (EEG) are the only non-invasive methods to record brain activity with fine temporal resolution. With modern commercially available hardware, EEG and MEG signals can be simultaneously acquired at hundreds of locations.

However, estimation of the sources underlying the MEG/EEG signals is challenging because of the illposed electromagnetic inverse problem: there are current distributions invisible to either MEG or EEG or both and the estimates are sensitive to noise in the data. Therefore, early MEG and EEG studies were solely relying on analysis of the measured signals and their spatial distribution.

The introduction of the current dipole model was the first significant advance towards understanding the actual sources of both MEG and EEG. This parametric source model continues to be very useful especially in the analysis of evoked-response data. In the now standard time-varying dipole model, the locations and orientations of the sources are assumed to be constant over the whole epoch of interest while their amplitudes are allowed to vary to reflect changes in the strength of regional activity captured by the dipoles.

When anatomical MRI data became routinely available during the 1980s, it became possible to visualize the source locations in the anatomical context. The use of boundary-element and finite-element approaches in forward modeling also became feasible with MRI segmentation algorithms capable of delineating the boundaries of different tissue compartments.

Since the principal sources of MEG and EEG signals are on the cortex and oriented perpendicular to the cortical mantle, a reconstruction of the individual cortical geometry from MRI can be used as an anatomical constraint in distributed source estimates. The standard l2-norm regularizer results in a widespread current estimate but has the benefit of a closed-form solution. It is well known that an l1-norm regularizer favors sparsity but the source waveforms at a given location usually exhibit unrealistic jerky behavior. We have recently proposed to mitigate this problem by employing an l1 norm over space and an l2 norm among suitable temporal basis functions.

This lecture will discuss the relationship of MEG and EEG, benefits from combining these two closely related methods, and basic principles of MEG/EEG source modeling. The concepts introduced in the theoretical section will be illustrated by selected examples from our recent MEG/EEG studies.

15. *Magnetoencephalography, D Cohen, Massachusetts General Hospital, Charlestown, MA, USA; and Massachusetts Institute of Technology, Cambridge, MA, USA, E Halgren, University of California at San Diego, La Jolla, CA, USA,2009*

16. *Magnetencephalographic characterization of Dynamic Brain Activation: Basic principles and Methods of Data collection and source analysis, Matti Hähäläinen and Ritta Hari*

17. *Cancellation of EEG and MEG Signals Generated by Extended and Distributed Sources Seppo P. Ahlfors, Jooman Han, Fa-Hsuan Lin, Thomas Witzel,,John W. Belliveau, Matti S. Hämäläinen, and Eric Halgren; Human Brain Mapping 000:000–000 (2009)*

18. *The advantage of combining MEG and EEG: Comparison to fMRI in focally stimulated visual cortex ,Dahlia Sharon, Matti S. Hämäläinen, Roger B.H. Tootell Eric Halgren and John W. Belliveau, NeuroImage 36 (2007) 1225-1235*

19. *Quantification of the benefit from integrating MEG and EEG data in minimum ℓ2-norm estimation A. Molins, S.M. Stufflebeam, E.N. Brown, M.S. Hämäläinen, NeuroImage 42 (2008) 1069-1077*

Frederic Schoenahl: PET, SPECT and their main derivations PETCT and SPECTCT are nowadays major tools for oncology diagnostic, and can resolve functional problems at the scale of a molecular probe – with more than 5000 nuclear imaging machines scattered worldwide, the use of these cameras slowly meet the standards of routine clinical modalities. The history of emission techniques SPECT and PET reminds us however, that the first outstanding achievements of these modalities were dedicated to physiological functions research, and in particular to the brain. In that field nuclear imaging became pioneering and mandatory components for any investigation of the brain functions. During this lecture, both modalities are presented from the technology and imaging point of view and the technological challenges encountered for hybrid cameras, in particular PETCT and PETMR. Base concepts and methodology for brain research (activation, mapping, compartmental modelling) will be discussed too.

20. *http://www.mit.edu/~glb/node1.html*

21. *http://www.brain-spect.com/index.htm*

22. *Attenuation compensation in cerebral 3D PET:effect of the attenuation map on absolute and relative quantitation; Habib Zaidi, Marie-Louise Montandon, Daniel O. Slosman; Division of Nuclear Medicine, Geneva University Hospital, Geneva 4, Switzerland Received: 21 May 2003 / Accepted: 4 August 2003 / Published online: 22 October 2003; © Springer-Verlag 2003*

23. *The potential of PET/MR for brain imaging; Wolf-Dieter Heiss; Eur J Nucl Med Mol Imaging (2009) 36 (Suppl 1):S105–S112, DOI 10.1007/s00259-008-0962-3*

24. *POSITRON EMISSION TOMOGRAPHY; John M. Ollinger and Jeffrey A. Fessler; IEEE Signal Processing Magazine,14(1):43-55, January 1997*

25. *A Combined PET/CT Scanner for Clinical Oncology; Thomas Beyer, David W. Townsend, Tony Brun, Paul E. Kinahan, Martin Charron, Raymond Roddy, Jeff Jerin, John Young, Larry Byars, and Ronald Nutt; J NucÃMed 2000; 41.-1369-1379*

26. *The Clinical Role of Fusion Imaging Using PET, CT, and MR Imaging Habib Zaidi, PhD, PD,*,Marie-LouiseMontandon, PhD, Abass Alavi, MD, PhD (Hon), DS (Hon); PET Clin 3 (2009) 275–291 doi:10.1016/j.cpet.2009.03.002 1556-8598/09/*

27. *Categorical and correlational analyses of baseline fluorodeoxyglucose positron emission tomography images from the Alzheimer's Disease Neuroimaging Initiative (ADNI) Jessica B.S. Langbaum, Kewei Chen, Wendy Lee, Cole Reschke, Dan Bandy, Adam S. Fleisher, Gene E. Alexander, Norman L. Foster, Michael W. Weiner, Robert A. Koeppe,, William J. Jagust, Eric M. Reiman, and the Alzheimer's Disease Neuroimaging Initiative 1; NeuroImage 45 (2009) 1107–1116*

Geertjan Huiskamp: Interictal spikes as measured in a regular EEG or in an MEG are hallmarks of epilepsy and as such are important in the diagnosis of this

disorder. Their spatial distribution over the scalp often shows a dipolar pattern which suggest that the sources generating the spikes are focal and can be localized using advanced source imaging techniques.
Since the cortical location of the focus of such spikes has a strong relation with the area in which epileptic seizures are generated, source localization based on interictal spikes can be used in the evaluation of candidates for surgical treatment of epilepsy. In the surgical treatment of epilepsy it is of great importance that the focus of the seizure is removed, but that other cortical areas containing critical function remain untouched. Therefore, in difficult cases in a monitoring session prior to surgery grids of electrodes are placed directly on the surface of the brain (Electro-Cortico-Graphy or ECoG) in order to record seizures and to probe critical motor-, language- and other functions.
Data recorded during such a session, that can typically last a week, can be regarded as the gold standard for validating similar data recorded noninvasively. This talk will focus on the relation between interictal spikes as measured intra-cranially to those measured outside the skull with MEG prior to the implantation of electrode grids. Interictal spikes measured intra-cranially often show a complex spatio-temporal character for which it is obvious that it cannot be described by an equivalent single dipole source, whereas for the same spikes as measured with MEG the dipole model seems adequate.
MEG may reflect only part of the spikes - and only a part of a spike - that can observed intra-cranially. This issue will be discussed both from a clinical and from a modelling point of view.

28. *Huiskamp G, Agirre-Arrizubieta Z, Leijten F. Regional differences in the sensitivity of MEG for interictal spikes in epilepsy. Brain Topogr. 2010 Jun;23(2):159-64.*

29. *Agirre-Arrizubieta Z,, Huiskamp GJ, Ferrier CH, van Huffelen AC, Leijten FS. Interictal magnetoencephalography and the irritative zone in the electrocorticogram. Brain. 2009 Nov;132(Pt 11):3060-71.*

30. *Huiskamp G, Agirre-Arrizubieta Z. Interictal ECoG spikes as reflected in MEG. Conf Proc IEEE Eng Med Biol Soc. 2009;2009:1930-3.*

Symposium 4: Use of priors

Pedro Valdes Sosa (1): Estimation of the sources of the EEG/MEG is an ill posed problem requiring additional prior knowledge best formulated in a Bayesian framework. Such prior knowledge takes the form of constraints about the mathematical properties of the sources, their anatomical location, temporal evolution, as well as possible relation with other imaging modalities. In this tutorial we shall describe the successive steps of Bayesian modeling of the EEG/MEG:
a)Model specification --from simple minimum norm models to spatio-temporal formulations with non overlapping sources. The commonalities and differences of many different techniques will be discussed.
b) Estimation via Maximization of the posterior (MAP), MCMC, and variational techniques, with emphasis on methods for penalized regression from the Statistical Learning field which promise to solve problems with Ultra-High Dimensionality.
c) Model evaluation, comparison and averaging of models.
The tutorial will end with an outline of the outstanding problems in Bayesian EEG/MEG modeling: multimodal data fusion, estimation of state space models, and incorporation of neural mass and neural field model assumptions.

31. *P.A. Valdés-Sosa, M. Vega-Hernández, J.M. Sánchez-Bornot, E. Martínez-Montes, and M.A. Bobes, "EEG source imaging with spatio-temporal tomographic nonnegative*

independent component analysis.," Human brain mapping , vol. 30, 2009, pp. 1898-910.

32. *M. Vega-Hernández, E. Martínez-Montes, J.M. Sánchez-Bornot, A. Lage-Castellanos, and P.A. Valdés-Sosa, "Penalized least squares methods for solving the EEG inverse problem," Stat. Sinica , vol. 18, 2008, pp. 1535-1551.*

33. *A. Galka, O. Yamashita, T. Ozaki, R. Biscay, and P. Valdés-Sosa, "A solution to the dynamical inverse problem of EEG generation using spatiotemporal Kalman filtering," Neuroimage , vol. 23, 2004, pp. 435-453.*

34. *N.J. Trujillo-Barreto, E. Aubert-Vázquez, and P.a. Valdés-Sosa, "Bayesian model averaging in EEG/MEG imaging.," NeuroImage , vol. 21, 2004, pp. 1300-19.*

35. *N.J. Trujillo-Barreto, E. Aubert-Vázquez, and W.D. Penny, "Bayesian M/EEG source reconstruction with spatio-temporal priors.," NeuroImage , vol. 39, 2008, pp. 318-35.*

36. *T. Hastie, R. Tibshirani, and J. Friedman, The Elements of Statistical Learning: Data Mining, Inference, and Prediction , Springer, 2009.*

37. *A. Tarantola, Inverse Problem Theory , SIAM, 2005.*

Pedro Valdes Sosa (2): It is surprising that EEG source imaging has, to date, developed with relative independence from mesoscopic modeling of neural ensembles. In spite of this, the initial results in the statistical state space identification of neural mass model parameters from the EEG/MEG [1] , has been followed by very effective proposals for neural model constrained inverse solutions. Linearized versions of these models have been developed in the frequency domain [2] and the full nonlinear models have addressed in the time domain [3,4,5] . However instead of modeling the brain as a set of separate neural masses best modeled by stochastic differential equations (SDE), attention has shifted to differential-integral neural field equations [6] from which wave-like activity may be obtained. Thus the inverse problem requires as a prior Stochastic Partial or Integral equations. The forward problem for this type of model has been addressed by [7] [8] [9] , but relatively little work [10] [11] has been carried out for the solution of the related inverse problem, a basic limitation being computational tractability. We outline possible solutions and give examples of testing the pioneer neural field model of Nunez [12] against data.

38. *P.a. Valdes, J.C. Jimenez, J. Riera, R. Biscay, and T. Ozaki, "Nonlinear EEG analysis based on a neural mass model.," Biological cybernetics , vol. 81, 1999, pp. 415-24.*

39. *R.J. Moran, K.E. Stephan, S.J. Kiebel, N. Rombach, W.T. Connor, K.J. Murphy, R.B. Reilly, and K.J. Friston, "Bayesian estimation of synaptic physiology from the spectral responses of neural masses," NeuroImage , vol. 42, 2008, pp. 272 - 284.*

40. *[J.J. Riera, X. Wan, J.C. Jimenez, and R. Kawashima, "Nonlinear Local Electrovascular Coupling . I : A Theoretical Model," vol. 914, 2006, pp. 896 -914.*

41. *J.J. Riera, J.C. Jimenez, X. Wan, R. Kawashima, and T. Ozaki, "Nonlinear Local Electrovascular Coupling . II : From Data to Neuronal Masses," vol. 354, 2007, pp. 335-354.*

42. *J. Daunizeau and K.J. Friston, "A mesostate-space model for EEG and MEG," NeuroImage , 2007.*

43. *[G. Deco, V.K. Jirsa, P.A. Robinson, M. Breakspear, and K. Friston, "The Dynamic Brain : From Spiking Neurons to Neural Masses and Cortical Fields," PLoS Computational Biology , vol. 4, 2008.*

44. *V.K. Jirsa, K.J. Jantzen, A. Fuchs, and J.A. Kelso, "Spatiotemporal Forward Solution of the EEG and MEG Using Network Modeling," IEEE Transactions on Medical Imaging , vol. 21, 2002, pp. 493-504.*

45. *I. Bojak, T.F. Oostendorp, A.T. Reid, and R. Ko, "Connecting Mean Field Models of Neural Activity to EEG and fMRI Data," Brain Topography , vol. 23, 2010, pp. 139-149.*

46. *P.A. Valdes-Sosa, J.M. Sanchez-Bornot, R.C. Sotero, Y. Iturria-Medina, Y. Aleman-Gomez, J. Bosch-Bayard, F. Carbonell, and T. Ozaki, "Model driven EEG/fMRI fusion of brain oscillations.," Human brain mapping , vol. 30, 2009, pp. 2701-21.*

47. *A. Galka, T. Ozaki, U. Stephani, and M. Siniatchkin, "A data-driven model of the generation of human EEG based on a spatially distributed stochastic wave equation," Cogntive Neurodynamics , vol. 2, 2008, pp. 101-113.*

48. *J. Daunizeau, S.J. Kiebel, and K.J. Friston, "Dynamic causal modelling of distributed electromagnetic responses," NeuroImage , vol. 47, 2009, pp. 590-601.*

49. *P. Nunez, "Generation of human EEG by a combination of long and short range neocortical interactions," Brain Topography , vol. 1, 1989, p. 199–215.*

Gareth Barnes: We have to supply some prior information to solve the ill-posed MEG/EEG inverse problem. These priors could be predominantly functional (for example source covariance structure), anatomical (for example grey matter structure) or a mixture of both [1]. I will describe how different priors are implicit in different commonly used inversion algorithms [2]. I will go on to talk about methods one could use to judge the utility of these different prior assumptions for MEG/EEG imaging [3,4].

50. *[1] Multiple sparse priors for the M/EEG inverse problem. Friston K, Harrison L, Daunizeau J, Kiebel S, Phillips C, Trujillo-Barreto N, Henson R, Flandin G, Mattout J. Neuroimage. 2008 Feb 1;39(3):1104-20. Epub 2007 Oct 10.*

51. *[2] A new approach to neuroimaging with magnetoencephalography. Hillebrand A, Singh KD, Holliday IE, Furlong PL, Barnes GR.*

52. *[3] A verifiable solution to the MEG inverse problem. Barnes GR, Furlong PL, Singh KD, Hillebrand A. Neuroimage. 2006 Jun;31(2):623-6. Epub 2006 Feb 9.*

53. *[4] Selecting forward models for MEG source-reconstruction using model-evidence. Henson RN, Mattout J, Phillips C, Friston KJ.Neuroimage. 2009 May 15;46(1):168-76. Epub 2009 Feb 11.*

Symposium 5: Multimodal generative models

Ingo Bojak : The simple idea of combining the highly complementary information from different non-invasive neuroimaging modalities turns out to be technically

complicated on two related levels: how to implement this integration and how to interpret its results. We argue here that data-driven statistics and generative modeling represent two different strategies: The former is easier to implement but more difficult to interpret, the latter more difficult to implement but easier to interpret.
We next consider what computational units are appropriate to the generative modeling approach. Due to the high density of neurons in cerebral cortex, every pixel of a neuroimage represents the activity of at least 105 neurons. Furthermore, coherent neuronal activity dominates the signal. This implies that effectively one always deals with "neural masses" when analyzing neuroimaging data. Mean field models (MFMs) in particular describe such neural mass action by averaging over neural variability while explicitly retaining salient underlying features, like neurotransmitter kinetics.
The question then arises how such neural masses should be connected to form dynamical networks that can be compared with the distributed activity we observe in the densely connected brain. In this context we will survey the range of existing generative modeling approaches - continuum MFMs, dynamic causal modeling (DCM), and mesh models - and discuss some of their applications. We finish with some speculations about the future of this field, in particular about fusing DCM and MFMs.

54. *Neural masses: Deco G, Jirsa VK, Robinson PA, Breakspear M, Friston K (2008) The dynamic brain: From spiking neurons to neural masses and cortical fields. PLoS Comput Biol: e1000092.*

55. *Continuum MFMs: Bojak I, Liley DTJ (2010) Axonal velocity distributions in neural field equations. PLoS Comput Biol 6: e1000653.*

56. *DCM :Friston KJ, Harrison L, Penny W (2003) Dynamic causal modelling. NeuroImage 19:1273–1302.*

57. *Mesh models: Bojak I, Oostendorp TF, Reid AT, Kötter R (2010) Connecting mean field models of neural activity to EEG and fMRI data. Brain Topogr 23:139-149.*

58. ** MFM/DCM fusion: Daunizeau J, Kiebel SJ, Friston KJ (2009) Dynamic causal modelling of distributed electromagnetic responses. NeuroImage 47: 590–601.*

Juha Voipio: Electroencephalography (EEG) is usually recorded with a limited signal bandwidth such as 0.5 to 70 Hz. High-pass filtering (recording in AC-coupled mode) was originally introduced in order to eliminate electrode offset potentials and drift, which had orders of magnitude higher amplitude than the signals of interest. However, it has become evident that in many cases signals below 0.5 Hz carry essential information, and the current practice of high-pass filtering can cause significant distortion of EEG data. Interpretation of infraslow EEG signals is challenging, since both neuronal and non-neuronal mechanisms can contribute to signal generation. Recording of a genuine EEG signal sets new requirements to the amplifier, electrodes and the electrode-skin interface. However, technical problems have been solved, and nowadays DC-coupled EEG can be used as a routine bedside method in the clinic. The presentation will provide an overview of infraslow EEG activity, and of neuronal and non-neuronal mechanisms that are likely to be involved in signal generation. In addition, adequate recording techniques for infraslow EEG and sources of artefacts will be discussed.

59. *Infraslow EEG Activity: Sampsa Vanhatalo, Juha Voipio and Kai Kaila, Chapter 25 from Electroencephalography: Basic Principles, Clinical Applications and Related Fields, 5th Edition, Lippincott Williams & Wilkins, Baltimore 2005*

60. *Evaluation of commercially available electrodes and gels for recording of slow EEG potentials; P. Tallgren, S. Vanhatalo, K. Kaila, J. Voipio; Clinical Neurophysiology 116 (2005) 799–806*

Jean Daunizeau: In this work, we propose a symmetrical multimodal EEG/fMRI information fusion approach dedicated to the identification of eventrelated bioelectric and hemodynamic responses. Unlike existing, asymmetrical EEG/fMRI data fusion algorithms, we build a joint EEG/fMRI generative model that explicitly accounts for local coupling/uncoupling of bioelectric and hemodynamic activities, which are supposed to share a common substrate. Under a dedicated assumption of spatio-temporal separability, the spatial profile of the common EEG/fMRI sources is introduced as an unknown hierarchical prior on both markers of cerebral activity. Thereby, a devoted Variational Bayesian (VB) learning scheme is derived to infer common EEG/fMRI sources from a joint EEG/fMRI dataset. This yields an estimate of the common spatial profile, which is built as a trade-off between information extracted from EEG and fMRI datasets. Furthermore, the spatial structure of the EEG/fMRI coupling/uncoupling is learned exclusively from the data. The proposed data generative model and devoted VBEM learning scheme thus provide an un-supervised well-balanced approach for the fusion of EEG/fMRI information. We first demonstrate our approach on synthetic data. Results show that, in contrast to classical EEG/fMRI fusion approach, the method proved efficient and robust regardless of the EEG/fMRI discordance level. We apply the method on EEG/fMRI recordings from a patient with epilepsy, in order to identify brain areas involved during the generation of epileptic spikes. The results are validated using intracranial EEG measurements.

61. *“Symmetrical event-related EEG/fMRI information fusion in a variational Bayesian framework” http://www.fil.ion.ucl.ac.uk/~jdaunize/publications.htm*

62. *a review of EEG/fMRI fusion 'EEG-fMRI information fusion: biophysics and data analysis', http://www.fil.ion.ucl.ac.uk/~jdaunize/publications.htm*