W1-1: Neuronal Current Imaging with MRI: Current status and future prospects

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Functional MRI as a field has seen profound growth. This growth is due to several factors. First, activation induced hemodynamic changes are robust and repeatable. Functional contrast to noise is typically about 5/1, allowing high quality functional images to be created less than an hour. Second, fMRI is non-invasive. Third, fMRI scanners are ubiquitous - as most hospitals have fMRI-capable scanners. Fourth, the hemodynamic response is rapid enough and resolution high enough (\(< 1\) sec & \(< 2\) mm\(^3\)) to fill a relatively unique temporal and spatial niche in the exploration of human brain function. Over the years, fMRI has advanced not only in the number of users, range of applications, and sophistication of questions asked, but also with regard to technical advances and the types of functional contrast available. Currently, investigators have claimed to see fMRI-based activation-induced changes in blood oxygenation (most popular and most robust), blood volume, perfusion, diffusion, CMRO\(_2\), temperature, and highly localized magnetic fields. In this lecture, I will discuss these contrasts with a focus on what is known as "neuronal current" MRI. This term encompasses an array of methods that promise to detect neuronal activity directly by sensitization to highly transient and extremely small changes in magnetic field, induced by electrical current that propagates through, presumably, dendritic clusters. Lastly, I will discuss what the most promising directions in neuronal current MRI are, and will describe what I think will be required for this technique to be a successful and highly utilized method in neuroimaging.

W1-2: Magnetic Resonance Imaging in Microtesla Fields

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We use a Superconducting QUantum Interference Device (SQUID) coupled to an untuned, second-derivative gradiometer, to detect nuclear magnetic resonance (NMR) and magnetic resonance imaging (MRI) in microtesla magnetic fields. The protons are prepolarized in a magnetic field of typically 40-150 mT, and the oscillating signal produced by the precessing spins is detected after the polarizing field is removed. Our MRI system operates at 0.132 mT, that is, an NMR frequency of 5.6 kHz. The magnetic field noise, referred to the lowest loop of the second-derivative gradiometer, is 0.8 fTHz\(^{-1/2}\). We have imaged phantoms containing water with an in-plane resolution of better than 1 mm, and acquired three-dimensional \textit{in vivo} images of a human forearm with an in-plane resolution of 2 mm. The low magnetic field implies that magnetic susceptibility variations within the sample induce much less distortion compared with conventional high-field MRI, enabling us to obtain distortion-free images in the presence of metals. We have measured the longitudinal relaxation time \(T_1\) of different concentrations of agarose gel in water, and find much greater \(T_1\)-contrast in low fields (below 1 mT) than in high fields. In preliminary experiments, we have measured \(T_1\) in specimens of normal and cancerous prostate tissue removed surgically. The values of \(T_1\) in normal tissue are typically 60% higher than in tumors; by comparison, there is no significant difference in high-field MRI. We have imaged larger specimens to obtain \(T_1\)-maps, thereby enabling us to determine the spatial variation of \(T_1\). Furthermore, we have obtained \textit{in vivo} \(T_1\)-maps of the human forearm. These results suggest that it should be possible to obtain \textit{in vivo} \(T_1\)-weighted contrast images of prostate tumors. This work was supported by the U.S. Department of Energy and the National Institutes of Health.
Abstract/Workshop 1

S6-3: Ultra-low field MRI: a new method for human brain mapping

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A variety of techniques have been developed to noninvasively image human brain function that are central to research and clinical applications endeavoring to understand how the brain works and to detect pathology (e.g. epilepsy, schizophrenia, etc.). Current methods can be broadly divided into those that rely on hemodynamic responses as indicators of neural activity (e.g. fMRI, PET) and methods that measure neural activity directly (e.g. MEG and EEG). The approaches all suffer from either poor temporal resolution, poor spatial localization, or indirectly measuring neural activity. A recently proposed imaging method - ultra-low field MRI - has inherent properties which can be advantageously exploited to enhance human brain mapping techniques. The ULF MRI method relies on the pre-polarization of a sample at relatively high (~100 millitesla) field prior to each imaging step performed at a low (10..100 microtesla) measurement field. The utilization of a low field defines the two most unique features of the technique. First, ULF-MRI can be naturally combined with MEG in the same system to directly provide structural maps for MEG-localized sources. It enables easy and accurate integration of MEG and MRI/fMRI, because microtesla MR images can be precisely matched to structural images provided by high-field MRI and other techniques. And, second, the Larmor frequency at this regime (400..4000 Hz) overlaps with "slow" molecular dynamic processes such as diffusion, intra-molecular motion, chemical reactions, and biological processes such as protein folding, catalysis and ligand binding thus enabling new contrast mechanisms. Yet more compelling is the fact the Larmor frequency at ULF can be tuned to overlap with a band of the neural activity spectrum enabling imaging the direct consequences of neural activity. Here we report our results in advancing the ULF-MRI technique.

W1-4: A 304-channel SQUID system for MEG and low field MRI

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SQUID-based systems have potential for simultaneous recordings of functional brain information by magnetoencephalography (MEG) and anatomical information by low field magnetic resonance imaging (LF MRI). This is a very interesting issue for the growing number of users of MEG SQUID systems installed in clinical environments. We modified our 304-channel SQUID system, originally developed and optimized for biomagnetic applications, with the aim to employ it also for observing the precession of nuclear magnetism in low fields of a microtesla or less. The 304-channel SQUID system operates in a highly magnetically shielded environment provided by a 7-layer mu-metal walk-in room BMSR-2 (Berlin Magnetically Shielded Room - 2). The setup enables MEG recordings in a frequency bandwidth from DC up to 8 kHz.

To record magnetic resonance precession, coil systems for the polarization and for the observation of the nuclear magnetization were adapted to the SQUID set-up. In practice, the SQUID readout electronics has to be fast enough to switch off the SQUIDs during polarization (heavy for the SQUIDs) and for short dead times after switching off the polarizing field. In the case of the 304-channel SQUID system, a dead time of less than 300 microseconds can be realized (see poster of Hartwig).

The vector design of the 304-channel SQUID system allows the recording of the spatial structure of the MR precession in the polarized voxels. From the spatially resolved data and by using the known voxel positions, the magnetic moments of the voxels can be estimated. This means that LF MRI is already possible, to some extend, by using a multi-channel SQUID system without any frequency or phase encoding. This feature of the multi-channel SQUID system can be further improved by polarization encoding (see poster of Nieminen).

W1-5: Feasibility of neuronal current MRI at low fields

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The possible use of the resonant mechanism between some spectral components of the neuronal activity and the spin dynamics in ultra-low field MRI experiments - for the implementation of the nc-MRI techniques and proposed by Kraus et al, 2008 (Neuroimage) - is validated theoretically by means of "realistic" simulations of the neuronal activity.
of a modelled neuronal network. Simulations use characterized realistic neurons to reproduce neuronal currents and neuronal networks based on biophysical details: the distribution of the local magnetic field inside a MRI cubic voxel (having dimension 1.2 mm) is hence evaluated. The dynamics of water 1H spins as a consequence of the neuronal field and applied fields is extrapolated integrating the Bloch equations. The characteristics of the expected MR signals are discussed in relation to: a) the specifics of the NMR sequence used; b) the properties of the neuronal activity; c) the requirements of the MRI instruments and the experimental parameter (field homogeneity, concomitant gradients, etc.). Benefits and experimental difficulties of the technique are illustrated, also in relation with high-field MRI approaches and still existing and future emerging technologies.

**Workshop 2: Does occipital gamma reflect more than stimulus representations?**

**W2-1: Spontaneous oscillations in primary visual cortex contain stimulus specific information**

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Recent MEG studies in our laboratory show that non-invasively measured gamma activity localized to visual cortex in human participants concurs both phenomenologically (in terms of its time frequency characteristics and its timing with respect to the stimulus) and functionally (in terms of its dependence on stimulus parameters) with invasive measurements of the local field potential in primate visual cortex. Here we present some evidence that information about cardinal stimulus properties such as spatial frequency and orientation, typically attributed to receptive field properties of single neurons in primary visual cortex, is also contained in the temporal pattern of gamma activity measured noninvasively in man. Neurophysiological literature suggests that gamma activity reflects local integration processes in the underlying microscopic network. Hence the stimulus specific responses observed in our experiments are likely to represent macroscopic fingerprints of differential collective network states that emerge from the neuronal level. We further review some recent data, which show that this stimulus specificity is sustained for as long as the stimulus is static. Therefore, sustained gamma states may represent a record of the static visual world, which may in turn facilitate rapid and salient responses to changes. To further pursue this question, we experimentally induce static stimulus-specific gamma states in primary visual cortex and examine whether subsequent behavioural and evoked responses to stimulus changes depend on the preceding stimulus-specific gamma state.

**W2-2: Visual gamma oscillations in normal and pathological brain functioning**

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There is evidence that patients with schizophrenia are impaired in early visual processing, going along with abnormal neural synchronisation in the gamma frequency range in the EEG. However, it is not known whether those deficits underlie well known difficulties of schizophrenic patients in object recognition. Here, we recorded cortical magnetic fields from chronic schizophrenia patients, first-episode, never-medicated patients, and two groups of matched healthy controls during the Mooney Face task. Mooney Faces are two-tone pictures of human faces that require the integration of individual features into a coherent percept. We also recorded data in a larger group of healthy controls to localize face specific oscillations. MEG signals were analysed for spectral changes in oscillatory activity in the frequency range of 30-130 Hz via wavelet transformation. Source reconstruction was performed using LCMV beamforming. In healthy controls face specific activity was found in the high gamma frequency range (60-90Hz), localized in the fusiform face area (FFA). Compared to healthy controls, schizophrenia patients showed a decrease in high-frequency gamma activity on parieto-occipital sensors, associated with reduced face detection rates. Comparison of source power for visual processing between chronic schizophrenics and matched controls revealed a trend for higher power in the high gamma range in healthy controls bilaterally in the lateral occipital complex (LOC), but not in FFA. The analysis of neural oscillatory activity in first-episode patients revealed a reduction in the high-frequency range compared to controls, albeit less profound than in chronic schizophrenia patients. This suggests that a progressive impairment in local synchronisation processes may take place in schizophrenia, eventually leading to perceptual dysfunctions.