Dynamics of cortical brain activity during movie viewing

Kaisu Lankinen
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Abstract

Movies can trigger perceptual, cognitive and emotional processes at multiple levels in the viewer's brain and thus provide useful tools to study human brain function. Furthermore, movies—as relatively natural stimuli—can help understand the brain activity supporting our everyday life.

Earlier, brain activity during movie viewing has been studied mostly with functional magnetic resonance imaging (fMRI). Although fMRI provides a spatial resolution of millimeters, the temporal resolution of fMRI is limited, as fMRI measures the relatively slow changes of blood flow in the brain. Magnetoencephalography (MEG) measures the electromagnetic activity of synchronized neuronal populations with a temporal resolution of a millisecond. This Thesis focuses on finding consistent MEG signals across different movie viewers. In naturalistic experimental settings, it is challenging to uncover the signals of interest from the measured brain activity due to the complexity of both the brain function and the measured signals. Movies are also typically shown to the subjects only once, so that signal averaging cannot be used to enhance the signal-to-noise ratio.

This Thesis aimed at developing MEG analysis tools that can capture complex brain responses to movies. Multiset canonical correlation analysis (MCCA) with spatial filtering, used to find consistent time-varying patterns of brain activity across viewers, played a major role in this Thesis.

The first study addressed the similarity of MEG signals of eight movie viewers. Because the single-trial MEG signals are noisy, the previously used intersubject correlation methods did not uncover consistent brain activity across the viewers. However, MCCA-based spatial filtering allowed extracting signals that were significantly correlated across the subjects in several frequency bands. These signals originated from brain areas relevant for movie viewing, mostly visual cortices.

The second study unraveled the dynamics of MEG signals originating in the somatosensory cortex during movie viewing. Tactile stimuli, presented once per second, probed the functional state of the somatosensory cortex during movie viewing. The evoked single-trial responses to these stimuli covaried with the appearance of haptic events in the movie. Thus, the movie contents continuously modulated the viewer's brain activity in a fine-grained manner.

The third study compared MEG and fMRI signals of the same subjects during movie viewing. The correlations both across and within the subjects were stronger for fMRI than MEG signals. General linear modeling between the MEG and fMRI data demonstrated similarity between the electromagnetic and hemodynamic brain activity in occipital, temporal and frontal cortices.

These studies demonstrate the feasibility of the developed and validated analysis approaches to uncover consistency in complex MEG signals measured during movie viewing. The results show that a part of the neuromagnetic brain activity is synchronized across viewers with high temporal accuracy in multiple brain regions.

Keywords brain, magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI), brain imaging, canonical correlation analysis, naturalistic stimulation, movie
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Tiivistelmä

Elokuvat synnyttävät katselijan aivoissa monitasoisia aistihavaintoihin, kognitioon ja tunteisiin liittyviä prosesseja ja tarjoavat siksi erinomaisen välineen elokututkimukseen. Elokuvien avulla päästään myös kohti aiempaa luonnollisempia koeasetelmia, mikä auttaa ymmärtämään aivojen toimintaa jokapäiväisessä toimintaympäristössämme.

Aiemmän elokuvan synnyttämää aivoitoimintaa on tutkittu lähinnä toiminnallisella magneettikuvauskella (functional magnetic resonance imaging; fMRI). Vaikka fMRI:n paikkatarkkuus on millimetrien laatu, fMRI:n aikatakatkuutta rajoittaa se, että menetelmä mittaa verenkiertoon liittyviä suhteellisiä hintaisa muutoksia. Magnetoenkefalografia (MEG) voidaan mitata hermosolopopulaatioiden magneettikenttä jopa millisekunnin tarkkuudella. Väitöskirjan tavoitteena oli löytää MEG-mittauksista luotettavasti toistuvaa aivoaktiviaatiota katsojien välillä. Kiinnostavien signaalien löytäminen on aivoitoiminnan joukosta on kuitenkin haastavaa luonnollisissa koeasetelmissa, joissa se aivoitoiminta että mitattu signaali ovat monimitkaisia ja ärsyke esitetään vain kerran.

Tässä väitöskirjassa tutkittiin uusia lähestymistapoja elokuvan katselun aikana mitattujen MEG-signaalien analyysiä. Keskeinen menetelmä oli kanonista korrelaatiota eri kohdekielitöiden mittasuaineiston välillä (MCCA; multi-set canonical correlation analysis) hyödyntävän spaatialinä suodatusmalli, jonka avulla löydettiin luotettavasti toistuvaa aivoaktiviaatiota kohdekielitöiden välillä.

Ensimmäisessä osatyössä tutkittiin MEG-signaalien samankaltaisuutta kohdekielitöiden välillä elokuvan katselun aikana. MEG-signaalien kohinaisuuden vuoksi luotettavia signaaleja eivät pystyty löytämään aiemmin käytetyillä menetelmillä. MCCA:n avulla löydettiin uusiitä eri taajauskaistoilta katsojien välillä korreloivia signaaleja lähinnä visuaaliseen prosessointiin liittyviltä aivomuidelta.


Kolmannessa osatyössä vertailtiin elokuvan katselun aikana mitattuja MEG- ja fMRI-signaaleja. Sekä kohdekielitöiden että katselukertojen väliset korrelatiot olivat suurempia fMRI -kui MEG-signaleille. Yhdistämällä MEG-ja fMRI-signaalit yleisen lineaarisen mallin (general linear model; GLM) avulla havaittiin samankaltaisuutta sähkömagneettiset ja hemodynaamisen aivotoiminnan välillä aivosia ja aivosia, ohimolohkolla sekä aivosia etuosissaka.

Tulokset osoittavat, että kehitettyjen menetelminen avulla voidaan löytää aivoaktiviaatiota elokuvan katselun aikana mitattujia MEG-signaalit ja että elokuvatoiminnasta on monimieltä. Katsojien kesken synkronoinnutta sähkömagneettista aivoaktiviaatiota useilla aivosalla.

Avainsanat
aivot, magnetoenkefalografia (MEG), toiminnallinen magneettikuvaus (fMRI), aivovuotaminen, kanoninen korrelaatioanalyysi, luonnolliset ärsykkkeet, elokuva

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Kaisu Lankinen
Acknowledgements................................................................................... 1
List of Abbreviations................................................................................ 5
List of Publications.................................................................................. 7
Author’s Contribution.............................................................................. 9
1. Introduction ........................................................................................ 11
2. Background ......................................................................................... 13
   2.1 Functional brain imaging ............................................................. 13
      2.1.1 Magnetoencephalography (MEG)......................................... 14
      2.1.2 Functional magnetic resonance imaging (fMRI) ................. 16
      2.1.3 The relationship between MEG and BOLD signals .......... 17
   2.2 Naturalistic stimuli in brain imaging ........................................... 18
      2.2.1 Hemodynamic brain activity during movie viewing ...... 19
      2.2.2 Electromagnetic brain activity during movie viewing ...... 20
   2.3 Social perception and cognition ................................................... 21
   2.4 MEG analysis approaches ........................................................... 22
      2.4.1 Intersubject correlation (ISC) ............................................. 23
      2.4.2 Canonical correlation analysis (CCA) ................................. 24
      2.4.3 General linear model (GLM) ............................................... 25
3. Aims of the Thesis .............................................................................. 27
4. Materials and methods ...................................................................... 29
   4.1 Participants ................................................................................. 29
   4.2 Stimuli ......................................................................................... 29
   4.3 Measurements ............................................................................. 30
      4.3.1 Magnetoencephalography ................................................... 30
      4.3.2 Structural and functional MRI ............................................ 30
      4.3.3 Behavioural ratings .............................................................. 31
   4.4 Data pre-processing ..................................................................... 31
      4.4.1 Preprocessing of MEG data .................................................. 31
      4.4.2 Pre-processing of fMRI data ............................................... 32
      4.4.3 MEG source-level analysis .................................................. 32
5. Summaries of the studies ................................................................... 33
   5.1 MCC uncovers synchronized MEG activity across subjects during
      movie viewing (Publication 1) ....................................................... 33
      5.1.1 Motivation ............................................................................ 33
      5.1.2 Methods ............................................................................... 33
      5.1.3 Results.................................................................................. 33
5.1.4 Discussion and conclusions.................................................. 35
5.2 Activity of the viewer’s somatosensory cortex covaries with the haptic contents of the movie (Publication 2) ........................................ 35
  5.2.1 Motivation ............................................................................ 35
  5.2.2 Methods ............................................................................ 35
  5.2.3 Results.................................................................................. 37
  5.2.4 Discussion and conclusions ................................................ 38
5.3 MEG and BOLD signals correlate during movie viewing (Publication 3) ............................................................................................................. 38
  5.3.1 Motivation ........................................................................... 38
  5.3.2 Methods ............................................................................... 39
  5.3.3 Results.................................................................................. 39
  5.3.4 Discussion and conclusions ................................................. 41
6. Discussion .......................................................................................... 43
  6.1 Methodological considerations .................................................... 43
    6.1.1 Spatial filtering with MCCA.............................................. 43
    6.1.2 Data-driven analysis of brain imaging data .........................44
    6.1.3 Experimental setup ............................................................ 45
  6.2 Brain activity during movie viewing............................................ 45
  6.3 Comparison of MEG and fMRI signals .......................................46
  6.4 Future perspectives ................................................................. 47
  6.5 Conclusion .................................................................................. 48
References ..............................................................................................49
Publications ...........................................................................................59
## List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>BEM</td>
<td>Boundary element method</td>
</tr>
<tr>
<td>BOLD</td>
<td>Blood-oxygen-level dependent</td>
</tr>
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<td>CCA</td>
<td>Canonical correlation analysis</td>
</tr>
<tr>
<td>EBA</td>
<td>Extrastriate body area</td>
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<tr>
<td>ECD</td>
<td>Equivalent current dipole</td>
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<tr>
<td>ECoG</td>
<td>Electrocorticography</td>
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<tr>
<td>EEG</td>
<td>Electroencephalography</td>
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<tr>
<td>FOV</td>
<td>Field of view</td>
</tr>
<tr>
<td>fMRI</td>
<td>Functional magnetic resonance imaging</td>
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<tr>
<td>HDR</td>
<td>Hemodynamic response</td>
</tr>
<tr>
<td>HRF</td>
<td>Hemodynamic response function</td>
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<tr>
<td>GLM</td>
<td>General linear model</td>
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<tr>
<td>ICA</td>
<td>Independent component analysis</td>
</tr>
<tr>
<td>ISC</td>
<td>Intersubject correlation</td>
</tr>
<tr>
<td>ISI</td>
<td>Inter-stimulus interval</td>
</tr>
<tr>
<td>LFP</td>
<td>Local-field potential</td>
</tr>
<tr>
<td>MCCA</td>
<td>Multi-set canonical correlation analysis</td>
</tr>
<tr>
<td>MCE</td>
<td>Minimum-current estimate</td>
</tr>
<tr>
<td>MEG</td>
<td>Magnetoencephalography</td>
</tr>
<tr>
<td>MNE</td>
<td>Minimum-norm estimate</td>
</tr>
<tr>
<td>MNI</td>
<td>Montreal Neurological Institute</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>NMR</td>
<td>Nuclear magnetic resonance</td>
</tr>
<tr>
<td>PCA</td>
<td>Principal component analysis</td>
</tr>
</tbody>
</table>
PET  Positron emission tomography
RF   Radio-frequency
SNR  Signal-to-noise ratio
SQUID Superconducting quantum interference device
SSS  Signal space separation
TE   Time to echo
TR   Repetition time
tSSS Temporal signal space separation
V5   Middle temporal visual area
This doctoral dissertation consists of a summary and the following three publications, which are referred to in the text by their numerals.


Author’s Contribution

**Publication 1:** Intersubject consistency of cortical MEG signals during movie viewing

I implemented and refined the data analysis together with M.K. I had the main responsibility for writing the manuscript with contribution from my co-authors.

**Publication 2:** Haptic contents of a movie dynamically engage the spectator’s sensorimotor cortex

I implemented and refined the data analysis together with M.K. I had the main responsibility for writing the manuscript with contribution from my co-authors.

**Publication 3:** Consistency and similarity of MEG- and fMRI-signal time courses during movie viewing

I contributed to the design of the data analysis, performed all the MEG analyses, and analyzed fMRI data with contribution from the second and the third author. I had the main responsibility for writing the manuscript with contribution from my co-authors.
1. Introduction

The central goal of human neuroscience is to understand how we with our brains make sense of the complex world around us, and how we perceive and interact with our environment and other people. Modern neuroimaging methods provide a useful way to explore these questions non-invasively with high temporal and spatial accuracy.

Because of the complexity of both the brain function and our environment, experimental settings in neuroscientific studies are typically simplified and well-controlled versions of the real-world events and tasks, e.g. viewing separate images or listening isolated words or sentences instead of, for example, following a continuous discussion. Although such simplified experiments have been useful for mapping the brain and pinpointing specific brain processes, it is evident that such stimuli are not representative of the real world we encounter in our everyday life.

Over the past 10 years, a growing trend in neuroscience has been to use naturalistic stimuli, such as movies and audio stories that mimic the real world. Spatially accurate functional magnetic resonance imaging (fMRI) that measures hemodynamic brain activity has been already used in such naturalistic experimental settings. However, fMRI suffers from the intrinsic sluggishness of the hemodynamic response, which limits fMRI's temporal accuracy. In contrast, electrophysiological methods, such as electroencephalography (EEG) and magnetoencephalography (MEG), measure directly the activity of neural cell populations with millisecond temporal accuracy, thus enabling studying dynamics of cortical brain activity in high temporal detail. However, MEG, which is the main method in this Thesis, has been used in naturalistic studies only rarely. One reason for this is the complex nature of MEG signals compared with fMRI and the difficulty of detecting the signals of interest amidst of other signals, which makes the data-analysis and interpretation challenging. Notably, typically used analysis methods for MEG, such as averaging evoked and event-related responses or studying induced rhythmic activity, are suboptimal in studying highly complex data arising in naturalistic experiments.

The aim of the studies in this Thesis was to find and develop new approaches to analyze MEG data recorded in naturalistic experimental settings, to increase the understanding of temporally varying brain processes in ecologically valid situations, and thus advance the future use of MEG in naturalistic experiments. In all the studies, a silent movie was used to mimic a naturalistic visual environment. Publication 1 introduced an analysis approach, based on spatial
filtering and multi-set canonical correlation analysis (MCCA), to find consistency in MEG signal time courses across the viewers of a 15-min movie. In Publication 2, the same approach was used to study moment-to-moment variation in single-trial somatosensory evoked responses during movie viewing to explore how the current movie content modulates these responses and thereby the function of a specified brain region. Finally, Publication 3 compared MEG and fMRI signals collected from the same viewers and demonstrated similarities between electromagnetic and hemodynamic brain dynamics during movie viewing.
2. Background

2.1 Functional brain imaging

Modern brain imaging methods provide useful tools to study the human brain non-invasively outside the skull. The widely used magnetic resonance imaging (MRI) can be used to image brain structure, while functional magnetic resonance imaging (fMRI) measures hemodynamic brain activity (for an overview, see e.g. Huettel et al., 2004). Metabolic processes of the brain can be studied using positron emission tomography (PET), which utilizes radioactive tracers injected to the circulation (Zimmer & Luxe, 2012). Magnetoencephalography (MEG) and electroencephalography (EEG) allow detection of electromagnetic fields and electric potentials evoked by neural cell populations (Hari & Puce, 2017).

Among these methods, structural MRI can have sub-millimeter spatial resolution, while the resolution of fMRI is typically a couple of millimeters depending on e.g. the magnetic field strength, imaging time, and other imaging parameters. The spatial resolution of PET depends on e.g. the detector element size and the used isotope, and it can also reach a couple of millimeters, whereas MEG and EEG often fall slightly behind fMRI and PET. However, depending on brain region and experimental design, it is possible to separate functional brain regions (e.g. representation areas of different fingers on primary sensory cortex) within millimeter range also with MEG. MEG and EEG have superior millisecond-range temporal resolution, while fMRI can detect brain activity with temporal accuracy down to half a second (with optimized design), and PET from seconds to minutes. Although MEG and EEG have similar temporal resolution, the slightly higher spatial resolution of MEG (reaching millimeter range under favorable circumstances) provides an advantage over EEG. MEG and EEG suit best for detecting cortical brain activity, whereas fMRI and PET, as well as EEG in some cases, can be used to study also subcortical structures.

All imaging methods have their own strengths and weaknesses, and the best approach depends on the research question. In the first two publications in this Thesis MEG was used, and in Publication 3 both MEG and fMRI were recorded.
2.1.1 Magnetoencephalography (MEG)

Magnetoencephalography picks up magnetic fields arising from synchronous activity of nerve-cell populations in the brain. MEG signals are recorded non-invasively outside the head with a sensor array placed close to the scalp. The following short overview of MEG is largely based on Hämäläinen et al. (1993), Baillet et al. (2001), Hansen et al. (2010), and Hari & Puce (2017).

The first MEG signals were recorded already 50 years ago (Cohen, 1968) using a single induction coil. Modern MEG devices have whole-scalp coverage (first by Ahonen et al., 1993) comprising even more than 300 sensors arranged usually in a helmet shape. High sensitivity for recording very small magnetic fields in the brain is achieved by using SQUID (superconducting quantum interference device) sensors (Zimmerman et al., 1970). The SQUIDs are connected to larger pick-up coils closer to the brain and a signal coil on top of the SQUID, to enhance the coupling of the brain’s magnetic fields to very small-diameter SQUIDs. The shape of the pick-up coil determines the spatial sensitivity pattern to the magnetic fields. A magnetometer consists of a simple loop that measures the magnetic field component along the direction perpendicular to the loop. Gradiometers measure the spatial derivative of the magnetic field. A planar gradiometer has two oppositely-wound loops in the same plane, and in an axial gradiometer the loops are on the same axis. Planar gradiometers are the most sensitive to sources directly beneath them, whereas the maximum signal from magnetometers and axial gradiometers originate from sources around the coils.

To obtain the superconductivity needed for operation of SQUIDs, the sensors are immersed in liquid helium inside an insulated dewar at the temperature of 4K (−269 °C). To reduce external interference, caused e.g. by traffic, power lines or electric devices, the MEG system needs to be located inside a magnetically shielded room, usually made from several layers of aluminum and mu-metal.

The MEG signals originate mostly from postsynaptic currents in the pyramidal neurons of the cerebral cortex. Synchronous activity of tens of thousands nearby neurons is needed to generate a large enough magnetic field to be detected with MEG. Parallel orientation of the apical dendrites of the pyramidal neurons in the cortex enables spatial summation of the electromagnetic fields arising from nearby neurons. In addition, temporal summation of the fields from nearby neurons is possible, because the characteristic time course of the postsynaptic currents is on the order of ten milliseconds. However, even after spatial and temporal summation, the magnetic fields remain on the order of tens or hundreds of femtoteslas (10⁻¹⁵ T), which is very weak compared e.g. with the magnetic field of the Earth that is on the order of tens or hundreds of mikroteslas (10⁻⁶ T).

The detection of electromagnetic fields outside of a volume conductor depends on the conductor shape. In a perfectly spherical conductor, magnetic fields arising from radially oriented source currents cannot be seen outside the sphere. Although the human head is not a perfect sphere, MEG’s sensitivity for detecting tangential currents is considerably better than for radial currents. In
cortical pyramidal neurons, the direction of net primary current flow is perpen-
dicular to the cortical surface, and thus activations in walls of sulci are picked
up better than those in the gyri. Moreover, in a spherical-like head shape, the
conductivity differences in tissues between the brain and the sensors do not sig-
nificantly distort the magnetic field. Thus, MEG has an advantage in spatial res-
olution over EEG, where the electric potentials on the scalp are dampened and
smeread by tissue conductivities that can vary approximately by a factor of 50
in the head. However, activity of deep sources can be typically detected better
with EEG than MEG, although e.g. brainstem responses can be picked up also
with MEG when an optimized experimental design is used (e.g. Parkkonen et
al., 2009).

The magnetic field outside the head, generated by a known primary cur-
rent distribution in the brain, can be calculated by solving a forward problem. If
the primary current distribution, head geometry and conductivities of different
layers in the volume are known, the magnetic fields can be calculated from Max-
well’s equations (Hämäläinen et al., 1993). Since the neural currents vary slowly
(at frequencies below 1kHz) in a small volume, the time-dependent terms in
Maxwell’s equations can be neglected and the quasistaic approximation can be
applied.

Estimation of brain activity from sensor signals is an ill-posed inverse
problem that does not have a unique solution, meaning that numerous different
current distributions in the brain could, in principle, produce similar magnetic
fields. However, with certain assumptions about the underlying sources, the so-
lution can be constrained (for reviews, see e.g. Hämäläinen et al., 1993; Baillet
et al., 2001).

In the simplest solution to the inverse problem, the primary source cur-
rent is modeled with a single point-like equivalent current dipole (ECD) (Hämä-
läinen et al., 1993). The ECD location, orientation and amplitude can be esti-
mated from the sensor-level field pattern by a non-linear least-squares search
(first applied by Tuomisto et al., 1983). ECD is usually a good approximation for
focal neural activity, such as, for example, sources of evoked fields in the pri-
mary sensory areas activated by simple stimuli. If a single current dipole model
is not adequate to explain the data, a step further is to use multidipole modeling,
where multiple ECDs can be fitted simultaneously or at different time points
(Hämäläinen & Hari, 2002).

Inverse solutions can also be obtained using methods, which make no as-
sumption of the number of active sources, only assuming that the sources are
distributed within a volume or a surface. Typically, the source space, usually the
cortical surface, is divided into a grid consisting of a large number of dipoles,
and their strengths are obtained by fitting to the measured data and applying
different constraints. Various estimation methods are available to find the most
plausible solution. In one of the most common approaches, minimum-norm es-
timation, the solution to the inverse problem is the source configuration ex-
plaining the data best while minimizing the L2 (minimum-norm estimate
(MNE); Hämäläinen & Ilmoniemi, 1994) or L1 (minimum-current estimate
(MCE); Matsuura & Okabe, 1995; Uutela et al., 1999) norm. MNE typically gives
blurred source estimates even when the source would be point-like, whereas MCEs are more focused (Hämäläinen & Hari, 2002).

Another common group of source localization methods is beamformers (Van Veen et al., 1997) that are based on spatial filtering either in time (Robinson & Vrba, 1999) or frequency domain (Gross et al., 2001; Kujala et al., 2008). The spatial filters are optimized to pass activity from a certain spatial location, while suppressing activity and noise originating from other locations, using a weighted sum of the sensor signals. Like distributed models (MNE and MCE), beamforming does not require \textit{a priori} assumptions about the number of active sources. A theoretical limitation of beamformers is that highly correlated sources cannot be identified, and beamformers also easily produce ghost sources (Van Veen et al., 1997).

In this Thesis, MNE was used to estimate the source-level activity, because the number of active sources was unknown and MNE is useful as a linear method. Moreover, MNE needs minimal prior information and assumptions of the sources, which was useful because the characteristics of MEG activity in response to a complex naturalistic stimulus were still unknown.

\subsection*{2.1.2 Functional magnetic resonance imaging (fMRI)}

Functional magnetic resonance imaging measures brain activity indirectly via hemodynamics. The following short overview is largely based on the textbook of Huettel et al. (2004).

Magnetic resonance imaging (MRI) is based on nuclear magnetic resonance (NMR). Typically, hydrogen nuclei, i.e. single protons, of the water molecules are the source of signal in MRI. A fundamental property of a proton is that it possesses a spin. Normally, the spins of the protons are oriented randomly, but when exposed to a strong uniform magnetic field in the MRI scanner, they align either parallel or antiparallel to the external magnetic field. Slightly more spins align parallel than antiparallel to the field, creating a net magnetization vector along the external magnetic field.

The spinning protons precess about the axis of the external magnetic field at a characteristic frequency, called Larmor frequency, which depends on the strength of the external field and the gyromagnetic ratio of the protons. To create the magnetic resonance signal, properly designed radio-frequency (RF) pulses are applied to the body at Larmor frequency (127.74 MHz at 3 T). These pulses flip the net magnetization vector to an angle with respect to the external field. After the RF pulse, the spins return to the original direction and simultaneously emit a signal that can be detected. Typically, two time-constants are used to describe this process. $T_1$ describes the recovery of the longitudinal net magnetization, whereas $T_2$ is related to the decay of the transverse net magnetization.

For spatial encoding of the signals in three orthogonal directions, additional gradient fields are applied so that the Larmor frequencies of protons vary in a systematic and well-known manner in different parts of the body. Separate slices can be selected by using an RF pulse with narrow bandwidth to selectively excite nuclei only in a certain part of the body.
Functional magnetic resonance imaging allows to study brain function instead of brain structure. Typically used technique in fMRI is the blood-oxygen-level-dependent (BOLD) contrast, discovered by Ogawa et al. (1990). BOLD fMRI is based on different magnetic properties of oxygenated and deoxygenated blood. More specifically, oxygenated hemoglobin is diamagnetic and deoxygenated blood is paramagnetic. During increased neuronal activity in a certain brain area, the consumption of oxygen increases, and more hemoglobin becomes deoxygenated. However, at the same time, oxygenated blood flow increases more than the consumption of oxygen, decreasing the relative concentration of deoxygenated hemoglobin. These changes can be seen as a stronger NMR signal and increased time constant $T_2^*$ describing the transverse relaxation time including the effects of inhomogeneities in the local magnetic field.

Thus, the BOLD signal reflects local changes in the concentration of deoxygenated hemoglobin and gives an indirect measure of brain activity. A typical hemodynamic response (HDR) to a short stimulus begins with a delay of a couple of seconds, peaks at 5–6 s and returns back to the baseline 15–20 s after the stimulus offset. In data analysis, the hemodynamic response is often modeled as a canonical hemodynamic response function (HRF). However, the actual shape of the HRF can vary in different brain areas and individuals (Aguirre et al., 1998; Handwerker et al., 2004). It can also change with age (D’Esposito et al., 1999; Richter & Richter, 2003), and it also depends on the stimulus type. However, for most studies of healthy subjects, the standard hemodynamic response function is sufficient.

2.1.3 The relationship between MEG and BOLD signals

Because the properties and origins of MEG and fMRI signal differ, a combined use of both methods could provide complementary views to brain function. However, the exact relationship between electromagnetic and hemodynamic brain activity is complicated, and thus combining these two imaging methods is not straightforward.

Previous animal and human studies have demonstrated that the BOLD signal correlates positively with the signal power of high-frequency (c.a. > 30 Hz) and negatively with that of the low-frequency (c.a. < 20 Hz) local field potentials (LFPs) measured invasively from visual (Logothetis et al., 2001) and auditory (Mukamel et al., 2005; Nir et al., 2007) cortices. The relationship between the BOLD signal and the non-invasively measured MEG and EEG signals has been studied extensively over the past 15 years (for MEG–fMRI studies, see for a review e.g. Hall et al., 2014). These studies have demonstrated correlation between the BOLD signal and task-induced changes in the oscillatory power of different MEG frequency bands, as well as between BOLD responses and MEG evoked responses. In general, MEG and BOLD signals seem to have a relatively good spatial agreement in sensory projection areas (e.g. Moradi et al., 2003; Brookes et al., 2005; Nangini et al., 2009; Stevenson et al., 2011) whereas MEG and fMRI spatial patterns often differ during more complex cognitive tasks (e.g. Furey et al., 2006; Liljeström et al., 2009; Vartiainen et al., 2011). Moreover, the temporal correlation between oscillatory MEG activity and BOLD signal can
depend on the brain region and frequency band (Kujala et al., 2014). Another factor contributing to the differences in spatial patterns of MEG and fMRI could be that fMRI likely receives the main contribution from neuronal ensembles connected via slow and thin fibres, whereas M/EEG weights the fast-conducting pathways (Hari & Parkkonen, 2015).

Recently, electrophysiological and hemodynamic activity has been compared also during more naturalistic experimental settings. Whittingstall et al. (2010) demonstrated that the mean source-level EEG activity (0.5–45 Hz) in primary visual area V1 was associated with BOLD signal with a ~5-s time difference between EEG and BOLD signals. They used 2-min movie clips as stimuli that were repeated 25 times. Moreover, the level of intersubject correlation of EEG signals during viewing of 30-s video clips has been found to covary with BOLD activity in higher-order brain areas, such as parietal, temporal and prefrontal brain regions (Dmochowski et al., 2014). Functional connectivity changes in MEG and fMRI were also compared during viewing of movies and rest (Betti et al., 2013). The topography of fMRI connectivity and changes induced by the movie was found to match well with MEG.

In this Thesis, Publication 3 presents a systematic comparison between MEG and fMRI responses to a 15-min movie.

2.2 Naturalistic stimuli in brain imaging

Functional brain imaging has contributed significantly to our understanding of the human brain function over the last decades. For example, we learn continuously more about how different brain areas are organized and functionally specialized, in which order they are activated, and how they interact and connect with each other. Brain imaging studies have relied for long on carefully controlled experimental designs and simplified stimuli in probing brain function. The advantage of using well-defined and simple stimuli, such as checkerboard images or beep sounds, is that the stimulus properties are well-known and can be varied in a controlled manner. These kinds of experiments have been important in studying specific brain areas or brain processes, especially in sensory systems. However, our everyday life is complex; the events and stimuli around us are continuous, overlap with each other and unfold with different time scales ranging from milliseconds for low-level perception to minutes, hours or years for social interaction (Hari et al., 2010). Moreover, our ongoing brain processes interact with the sensory input, as we are continuously in contact with our environment and other people. Thus, it is obvious that very simplified experimental settings cannot capture the complexity of our brain function, and it is unclear how the findings from well-controlled experiments generalize to the real world. For example, it has been shown that neural responses to complex stimuli, such as natural images, cannot be well predicted from the responses to artificial stimuli such as sinusoidal gratings (see e.g. Felsen et al., 2005), and that rich naturalistic stimuli engage brain areas more widely than simplistic stimuli (Bar-tels & Zeki, 2004a). There is also evidence that the human brain responds more
reliably to complex natural stimuli than to conventionally used simplified stimuli (e.g. Touryan et. al., 2005; Yao et al., 2007). Thus, naturalistic studies can reveal phenomena that the very simplified or controlled experiments cannot.

The use of naturalistic stimuli and experimental settings is slowly increasing in the human neuroimaging community (Spiers & Maguire, 2007; Hasson & Honey, 2012). The pioneering fMRI studies by Hasson et al. (2004) and Bartels & Zeki (2004a, 2004b) demonstrated that it is possible to associate brain activity reliably with complex naturalistic stimuli, i.e. movies, which was previously thought to be too difficult. In addition to experimental setups where the subjects are viewing movies, later studies have also let the subjects to listen audio narratives (e.g., Malinen et al., 2007; Wilson et al., 2007; Lerner et al., 2011; Brennan et al., 2012; Boldt et al., 2013; Nummenmaa et al., 2014b; Koskinen & Seppä, 2014), play video games (Kätsyri et al., 2013), listen to free-running verbal narratives (Stephens et al., 2010), or participating in a free conversation (Mandel et al., 2016) to mimic the real world in a brain imaging laboratory.

2.2.1 Hemodynamic brain activity during movie viewing

Using movies in neuroimaging experiments has provided new insights into human brain function. The work by Hasson et al. (2004) showed that hemodynamic activity, not only in primary and secondary visual and auditory areas but also in association cortices, is synchronized across subjects during viewing the same movie. Later studies have further demonstrated high synchronization of fMRI activity between the viewers in certain brain areas, and uncovered consistently behaving voxel groups across viewers (e.g. Bartels & Zeki, 2004a, 2004b, 2005; Golland et al., 2007; Malinen et al., 2007; Hasson et al., 2008a, 2008b, Jääskeläinen et al., 2008; Hanson et al., 2009; Hasson et al., 2010; Malinen & Hari, 2011; Lahnakoski et al., 2012a; Nummenmaa et al., 2012; Pamilo et al., 2012) during movie viewing. It has also been shown that emotion-containing video clips enhance intersubject synchronization (Nummenmaa et al., 2012). Moreover, it has been shown that a well-directed movie induced stronger intersubject synchrony than unstructured video clips from a street view (Hasson et al., 2008a) or home-made video clips of a speaking actor (Malinen & Hari, 2011), likely due to a better control over the viewer’s attention.

The recorded brain activity has also been linked to various movie features. Hasson et al. (2004) associated the peaks in hemodynamic activation in specific brain regions with certain events in the movie, e.g. the appearance of faces to activation of the fusiform gyrus and the appearance of buildings to activation of the collateral sulcus. The fMRI time courses in specific brain regions correlate statistically significantly to a variety of specific feature time courses in the movie, e.g. motion, contrast, color, language, or appearance of objects and body parts (Bartels & Zeki, 2004b; Bartels et al., 2008; Lahnakoski et al., 2012a; Lahnakoski et al., 2012b; Kautionen et al., 2014; Salmi et al., 2014). Furthermore, an attempt has been made to reconstruct the viewed videos from the recorded BOLD signals by learning an encoding model between the movie features and hemodynamic brain activity (Nishimoto et al., 2011).
In addition to increasing our understanding of perception of naturalistic visual scenes, movies have been used in studies of e.g. mental simulation of motor actions (Nummenmaa et al., 2014a), contagion of emotions (Nummenmaa et al., 2012), theory of mind (Wolf et al., 2010), perspective taking (Lahnakoski et al., 2014), memory encoding (Hasson et al, 2008c), and shared memories (Chen et al., 2017). Finally, movies have been shown to be useful in studying differences in the brain activity between healthy subjects and clinical populations, such as in autism (Hasson et al., 2010; Salmi et al., 2013; Glerean et al., 2016), in low-conscious state (Naci et al., 2012), in depression (Guo et al., 2015), and in psychosis (Rikandi et al., 2017).

2.2.2 Electromagnetic brain activity during movie viewing

Direct electromagnetic signals of neural cell populations can be measured invasively with electrocorticography (ECoG) and non-invasively with MEG and EEG.

ECoG recordings during movie viewing have demonstrated high within-subject correlation both in higher-order visual areas (Privman et al., 2007) as well as with wider coverage of the cortex (Meshulam et al., 2013). The brain responded highly selectively to specific features in the movie, such as faces, houses, actions and movements, at certain electrodes. Honey and colleagues (2012) showed also that fluctuations of gamma-band oscillations tracked lower-level properties of short or scrambled movie segments, whereas in higher-order regions the fluctuations were more reliable for long intact movie segments in primary sensory regions. Although ECoG provides high spatial and temporal resolution, the coverage of the electrodes in the cortex is limited and dictated by the individual clinical requirements, and the resulting different electrode placements in different patients make intersubject correlation analyses difficult. Typically, modulations in the signal power of high gamma-range activity (> 60 Hz) are studied with ECoG.

Some early MEG studies using naturalistic stimuli have attempted to classify short naturalistic stimuli on the basis of the recorded brain activity (Luo et al., 2007; Huttunen et al., 2012; Kauppi et al., 2013; Koskinen et al., 2013; Bridwell et al., 2015). Beyond the classification approach, between and within-subject correlations have been studied in a combined MEG and EEG work, where the subjects viewed a 17-min movie twice, and the signals were studied in 34 labeled brain regions (Chang et al., 2015). Source-level intersubject correlation during movie viewing has been studied also with MEG (Suppanen 2014) with the same data used in this Thesis. Relatively small, but still statistically significant, intersubject correlation coefficients were found in primary visual regions in four frequency band between 8 and 85 Hz. Significant intersubject EEG correlation during movie viewing has been demonstrated also in sensor space and these correlations depended on the arousing moments in the film (Dmochowski et al., 2012), ratings of audience’s interest for different scenes (Dmochowski et al., 2014), and the level of the viewers’ attention (Ki et al., 2016). Cohen et al. (2016) showed that intersubject correlations were stronger during viewing of audiovisual short videos than auditory stories alone.
In the above studies, the overall intersubject correlations were very low (typically less than 0.1) compared with intersubject correlation (ISC) values demonstrated for fMRI recordings (e.g. up to 0.78 in Kauppi et al., 2010). However, calculating ISC in short sliding time windows resulted in higher maximum correlation also for MEG and EEG signals (up to 0.5 in Chang et al. (2015) and 0.3 in Dmochowski et al. (2012)).

Correlations between low-level visual features (luminance changes) of the movie and EEG source-level signals in primary visual regions have been demonstrated by presenting a 2-min movie clip repeated 25 times (Whittingstall et al., 2010). Recently, Dmochowski and colleagues (2017) also modeled mapping between optical flow in the stimulus and sensor-level EEG responses with a hybrid encoding–decoding model, by using short 5-min movie clips. Their model used canonical correlation analysis (CCA) between the stimulus and spatially-filtered neural responses such that they are maximally correlated.

2.3 Social perception and cognition

Observing another person’s actions or sensations, in a movie as in real life, is reflected in the viewer’s brain activity in areas that are normally involved in processing the observer’s own actions and sensations. This phenomenon was first reported action observation in the monkey frontal lobe, in which the neurons fired both when the monkeys performed an action and when they saw another individual performing a similar action (Gallese et al., 1996; Rizzolatti et al., 1996). Vicarious activation may contribute to our understanding of the mental and bodily states of others and facilitate social interaction (for reviews, see e.g. Frith and Frith, 2007; Hari and Kujala, 2009).

In humans, a circuitry of the motor-function-related cortical regions is activated both during self-performed and observed actions (for a review, see e.g. Rizzolatti and Craighero, 2004). The somatosensory cortices also have a role in perception of social cues (for a review, see e.g. Keysers et al., 2010). For example, the somatosensory cortex is engaged while a person sees other people being touched (Keysers et al., 2004; Blakemore et al., 2005; Ebisch et al., 2008; Schaefer et al., 2009; Pihko et al., 2010; Meyer et al., 2011; Martinez-Jauand et al., 2012), during observation of actions (Avikainen et al., 2002; Oouchida et al., 2004; Rossi et al., 2002; Möttönen et al., 2005), and while the person observes pain of other people (e.g. Bufalari, 2007, Valeriani et al., 2008; Osborn et al., 2010). Finally, some brain areas involved in emotion processing are activated both when a person experiences emotions and witnesses emotions of others (for a review, see e.g. Bastiaansen, 2009).

Most of the previous studies demonstrating vicarious brain activity have been conducted in conventional experimental settings with simplified and repeated stimuli. Movies provide a useful tool to study the dynamics of vicarious brain activity in more naturalistic settings. For example, the viewer’s postcentral sulcus was activated with the appearance of acting hands in a movie (Hasson et al., 2004). Furthermore, mental simulation of actions and feelings of a
selected person in a boxing match was associated with activation of the ob-
server’s attentional and parieto-frontal action-observation network, as well as
somatosensory cortex (Nummenmaa et al. 2014a).

The movie used in all studies in this Thesis depicts a female character en-
gaged in a wide range of bodily activities in her environment, such as crawling,
climbing, or touching things, and it therefore provided a useful stimulus to study
the cortical dynamics of the related brain regions (Publication 2).

2.4 MEG analysis approaches

Complex naturalistic experiments bring new difficulties to data analysis, and
therefore new approaches and tools, such as computation of intersubject corre-
loration, have been introduced for the analysis of fMRI data. However, due to dif-
frent properties and behavior of the fMRI and MEG signals, it is not necessarily
straightforward to apply fMRI tools directly to MEG data.

Because the magnetic fields generated in the brain are very weak (on the
order of tens or hundreds femtoteslas), MEG signals are very sensitive to arti-
facts. For example, electromagnetic fields in the environment can be several or-
ders of magnitude higher than MEG signal, and cardiac activity, eye movements
or blinks, and muscular activity in the subject’s own body can be usually clearly
seen in the measured MEG signals. Furthermore, background brain activity that
is not related to the phenomenon of interest, “brain noise”, can be difficult to
separate from the signals of interest.

MEG experiments usually rely on repeating the stimulus and averaging
the brain responses. In addition to evoked or event-related responses, changes
in rhythmic brain activity can also be quantified over repeated events. The re-
corded time-varying signal \( x(t) \) can be considered to be \( x(t) = s(t) + n(t) \), where
\( s(t) \) is the deterministic signal, and \( n(t) \) represents uncorrelated random noise
(Hari et al., 1988). The utility of averaging is generally based on the assumption
that the brain responses are time-locked to the stimulus or other event, and the
noise is stationary and Gaussian. In addition, the responses and the state of the
subject are assumed to stay about the same from one stimulus to another, which
might not hold for very long measurement sessions. The number of repetitions
needed for a certain signal-to-noise ratio (SNR) depends on the stimulus, inter-
stimulus interval (ISI), latency of the response, and the studied modality and
phenomenon. Sometimes even thousands of stimulus repetitions are needed to
uncover a robust signal. With the assumptions above, averaging \( N \) responses
would improve the SNR by \( \sqrt{N} \) (Hari and Puce, 2017). Furthermore, the ampli-
tudes of some responses depend strongly on ISI. If this dependency is known,
the optimal ISIs can be determined to obtain the best SNR in a given time. Usu-
ally individual trials corrupted by artifacts are omitted from the averaging pro-
cess.

Repeated simple stimuli are feasible to study e.g. sensory processing.
However, for continuous movies or audio stories, tens of repetitions become impractical. Moreover, with a movie stimulus, the events in the movie are inter-
mingled and overlapping within each other, and it is difficult or even impossible
to determine the onsets and offsets of all the events. Moreover, segments contaminated by artifacts cannot be automatically discarded, because such a procedure would cause discontinuities to the otherwise continuous signal. Instead, the artifacts need to be suppressed during pre-processing.

Importantly, concentration on short epochs of the signal also loses information of longer-time-scale brain processes as well as information that variation of single responses over long time might carry. However, quantification of single-trial signals is compromised by the high noise level. *Publication 2* demonstrates an approach to first find consistent single-trial evoked responses, elicited by tactile probe stimulation once per second, and then follow their moment-to-moment changes during movie viewing.

Data-driven methods provide a useful way to analyze unaveraged data from naturalistic experiments and they are also suitable for analyzing long epochs of the signal time-series. Intersubject correlation, characterizing the amount of correlation between subjects in the signal time courses, has been used in naturalistic fMRI experiments with movies (e.g. Golland et al., 2007; Kauppi et al., 2010; Lahnakoski et al., 2012a; Nummenmaa et al., 2012; Pajula et al., 2012; Andric et al., 2016; Jääskeläinen et al., 2016; Lahnakoski et al., 2017). Independent component analysis (ICA; Hyvärinen et al., 2000) provides a data-driven method to find latent signal components that are assumed to be independent of each other. ICA has been also useful in finding physiologically meaningful components in fMRI signals (e.g. Bartels & Zeki, 2004b, 2005; Malinen et al., 2007; Jääskeläinen et al., 2008; Malinen & Hari, 2011; Lahnakoski et al., 2012b; Pamilo et al., 2012).

In this Thesis, multi-set canonical correlation analysis (see Section 2.4.2), a data-driven method that maximizes correlation between datasets, was used to uncover consistent signal components from MEG time courses. MCCA was used in all publications in this Thesis. *Publication 3* presents also comparison between the MCCA approach and ISC analysis (see Section 2.4.1).

### 2.4.1 Intersubject correlation (ISC)

One popular method in analyzing naturalistic neuroimaging data is intersubject correlation. ISC is especially suitable for naturalistic experiments, as it does not require a *priori* model of the stimulus, but quantifies the correlations between time-courses across subjects in a data-driven way.

In the ISC analysis, the data from different subjects are first registered to a common space, defined by a template brain or the average brain of the subjects. Next, Pearson’s correlation coefficients between the voxel time courses at the corresponding voxels are computed between all subject pairs. Typically, the summary statistics of the pair-wise coefficients across the subjects is reported for each voxel. Finally, a statistical threshold is determined for the correlation coefficients to indicate the voxels whose time courses vary in a similar manner across subjects.

In *Publication 3*, ISC analyses were performed for the same subjects’ fMRI and MEG data.
2.4.2 Canonical correlation analysis (CCA)

Canonical correlation analysis is a method for finding linear relationships between two multidimensional data sets, first introduced by Hotelling (1936). CCA finds canonical basis vectors for the datasets such that correlations between the projections of the data onto these basis vectors are maximized (Hardoon et al., 2004). For two zero-mean datasets \( \mathbf{X} \in \mathbb{R}^{N \times m} \) and \( \mathbf{Y} \in \mathbb{R}^{N \times n} \), where \( N \) is the number of samples and \( m, n \) dimensions of the datasets, these projections for feature vectors \( \mathbf{x} \in \mathbf{X} \) and \( \mathbf{y} \in \mathbf{Y} \) are obtained through a linear mapping

\[
\begin{align*}
\mathbf{u} &= \mathbf{Xw}_x \\
\mathbf{v} &= \mathbf{Yw}_y 
\end{align*}
\]

where \( \mathbf{w}_x \) and \( \mathbf{w}_y \) are the basis vectors with dimensions \( m \) and \( n \), respectively. The total number of projections, i.e. canonical variates, is \( d \leq \min(m, n) \). The function to be maximized is the correlation coefficient

\[
\rho = \max_{\mathbf{w}_x, \mathbf{w}_y} \text{corr}(\mathbf{u}, \mathbf{v}) \tag{2}
\]

where

\[
\text{corr}(\mathbf{u}, \mathbf{v}) = \frac{\mathbf{w}_x^T \mathbf{C}_{xy} \mathbf{w}_y}{\sqrt{\mathbf{w}_x^T \mathbf{C}_{xx} \mathbf{w}_x \mathbf{w}_y^T \mathbf{C}_{yy} \mathbf{w}_y}} \tag{3}
\]

where \( \mathbf{C}_{xy} \) is their respective cross-covariance matrix of \( \mathbf{x} \) and \( \mathbf{y} \), and \( \mathbf{C}_{xx} \) and \( \mathbf{C}_{yy} \) their autocovariance matrices. The problem can be formulated as a generalized eigenvalue problem, and the solution can be obtained by solving the equations

\[
\begin{align*}
\mathbf{C}_{xx}^{-1} \mathbf{C}_{xy} \mathbf{C}_{yy}^{-1} \mathbf{C}_{yx} \mathbf{w}_x &= \rho^2 \mathbf{w}_x \\
\mathbf{C}_{yy}^{-1} \mathbf{C}_{yx} \mathbf{C}_{xx}^{-1} \mathbf{C}_{xy} \mathbf{w}_y &= \rho^2 \mathbf{w}_y
\end{align*} \tag{4}
\]

where \( \mathbf{C}_{yx} \) is the cross-covariance matrix of \( \mathbf{x} \) and \( \mathbf{y} \), and \( \mathbf{w}_x^T \mathbf{C}_{xx} \mathbf{w}_x = 1 \) and \( \mathbf{w}_y^T \mathbf{C}_{yy} \mathbf{w}_y = 1 \). The eigenvalues \( \rho^2 \) are squared canonical correlations and the eigenvectors \( \mathbf{w}_x \) and \( \mathbf{w}_y \) are normalized canonical correlation basis vectors.

CCA can be extended to more than two datasets (multi-set canonical correlation analysis; MCCA; Kettenring, 1971). In this multi-set approach, basis vectors for each dataset are found such that the resulting canonical variates achieve maximum overall correlation between the sets. In practise, the MCCA algorithm takes multiple stages such that in each stage, the optimal basis vectors are found, with restriction that the resulting canonical variates are uncorrelated with the ones from previous stages. The formulation by Kettenring (1971) proposes five different objective functions with certain criteria to be optimized in finding the maximum overall correlation. The objective function used in the studies in this Thesis is MAXVAR, which is based on the eigenvalues of the correlation matrix.
where $i, j = 1, \ldots, K$, $K$ is the number of datasets, and $R_{ij}$ represents between-sets correlation blocks for pre-whitened data. In the first stage, eigenvectors corresponding to the largest eigenvalues in $R$ are found. The following stages go through a deflationary procedure, where the next basis vectors are found with the constraint that the resulting canonical variates are uncorrelated with the previous ones. Implementation by Li et al. (2009) was used in the studies in this Thesis.

CCA has been applied previously in neuroimaging (Hardoon et al., 2007; Correa et al., 2010a; Correa et al., 2010b; Varoquaux et al., 2010) in conventional experiments, but also in more realistic experimental settings with fMRI (Ylipaavalniemi et al., 2009; Karhunen et al., 2013; Bilenko et al., 2016), and recently also with MEG (Koskinen et al., 2012; Koskinen & Seppä 2014; Campi et al., 2013).

### 2.4.3 General linear model (GLM)

General linear modeling can be used to estimate how well the measured brain-imaging data are explained by a weighted sum of explanatory variables

$$U = \beta_0 + \beta_1 V_1 + \beta_2 V_2 + \cdots + \beta_s V_s + e_s,$$

where $U$ is the measured data (e.g. observed time course in a voxel), $\beta_s$ are the weights for explanatory variables $V_s$ ($\beta_0$ being the mean level of the signal), and $e_s$ are noise terms that are assumed to be independent and identically distributed normal variables with zero mean and variance $\sigma^2_e$. Typically, the variables $V_s$ describe stimulus time courses, e.g. boxcar functions where the stimulus is on or off at given intervals, and they are usually further convolved with a hemodynamic response function if the model is applied to fMRI data. Known sources of interference, such as linear drifts, body movements or respiration, can be also included into the model as nuisance factors. The explanatory variables are then fitted to the measurement data with least-squares estimation to find the optimal $\beta$-values. When equation (6) is formulated in a matrix form $U = VB + e$, estimates for $\beta$-values can be found by a least squares solution

$$b = (V^T V)^{-1} V^T U,$$

where $E(b_s) = \beta_s$ and $\text{Var}[b_j] = \sigma^2_e (V^T V)^{-1}$ (Friston et al., 1994).

GLM was used in Publication 3, where MEG and fMRI were combined to a common model.
3. Aims of the Thesis

The aim of this Thesis was to develop and validate methodology to analyze MEG data collected in naturalistic experiments, specifically during movie viewing, with the focus on temporal dynamics of brain activity. Thus, the work aimed at extending the application areas of MEG studies from conventional highly-controlled experiments to setups corresponding better to real-world situations. Moreover, the work was to shed light on neural correlates of social perception by investigating temporally accurate neuromagnetic brain activity recorded during movie viewing. The specific aims of the individual studies were

1. To develop an approach to uncover consistent MEG activity across movie viewers, and to investigate the spatiotemporal characteristics of these consistent signals (*Publication 1*)

2. To investigate how the movie content dynamically modulates the viewer’s brain activity, by following changes in single-trial tactile evoked responses in the somatosensory cortex (*Publication 2*)

3. To compare electromagnetic and hemodynamic brain signals (MEG and fMRI, respectively) during viewing of the same movie by applying both univariate and multivariate data-analysis approaches (*Publication 3*)
4. Materials and methods

4.1 Participants

Altogether 24 healthy adults volunteered as subjects in the experiments of this Thesis, and they gave their written informed consent before the experiments. MEG experiments had prior approval by the Ethics Committee of Helsinki and Uusimaa Hospital District, and fMRI recordings were approved by the ethics committee of Aalto University. All subjects had corrected or corrected-to-normal vision.

The data set used in Publication 1 and Publication 3 consisted of MEG recording of eight subjects (4 females, 4 males; mean age 29 years, range 23–51, all right-handed). The same subjects also participated in the fMRI study of Publication 3. Another sixteen subjects (8 females, 8 males; 2 left-handed; mean age 28 years, range 20–60 years) participated in the MEG experiment in Publication 2.

4.2 Stimuli

During all experiments, the subjects viewed a silent 15-min black-and-white movie “At Land” by Maya Deren (1944). This experimental movie depicts a female character wandering in her surroundings, involved in activities such as walking on a beach, climbing a tree, crawling on a table, walking down a forest path, picking up stones, and encountering other people.

In MEG recordings of Publications 1 and 3, the movie was delivered by using Experiment Builder software (SR Research, http://www.sr-research.com/eb.html) and projected to the screen located 130 cm in front of the subject (viewing angle 22° horizontal, 17° vertical). In MEG recordings of Publication 2, the film was presented using Presentation software (Neurobehavioral systems; http://www.neurobs.com/) and projected to the back-projection screen located 1.25 m in front of the subject (viewing angle 13° horizontal, 10° vertical; screen size 28 cm x 22.5 cm). In fMRI recordings of Publication 3, the
film was presented using Presentation software and delivered to a semi-transparent back-projection screen via a mirror (viewing angle 36° horizontal, 29° vertical) by projector Vista X3 REV Q (Christie Digital Systems, Canada, Inc.). In all experiments, the frame rate of the film was 24 frames/s.

In the experiment of Publication 2, the viewers received pneumatic tactile stimuli on the volar distal phalanges of their five left-hand fingers throughout the movie viewing and MEG-recording session. These stimuli were produced by expanding a thin plastic membrane with an air puff with a total stimulus duration of 178 ms (Mertens & Lütkenhöner, 2000). The fingers were stimulated in random order, one finger at a time, once every 1005 ms. Each subject received altogether 880 stimuli during the session.

The timings of the movie and tactile stimuli were aligned with MEG and fMRI data by trigger signals and were identical for all subjects.

4.3 Measurements

4.3.1 Magnetoencephalography

Magnetoencephalographic brain signals were recorded with a 306-channel whole-scalp neuromagnetometer (Elekta Neuromag™, Elekta Oy, Helsinki, Finland) in a magnetically shielded room (Imedco AG, Hägendorf, Switzerland) in the MEG Core of Aalto NeuroImaging, Aalto University.

The neuromagnetometer comprises 204 planar gradiometers and 102 magnetometers at 102 sensor units arranged in a helmet-shaped array. The head position of the subjects was determined by feeding currents to five head-position indicator coils attached to the scalp, and registering the resulting signals with the MEG sensor array. The locations of these coils with respect to three anatomical landmarks (nasion and two preauricular points) and additional points around the head were registered with 3D-digitizer (Fastrak®, Polhemus, Colchester, VT, USA). In the experiment of Publications 1 and 3, the head position was determined in the beginning of the movie, whereas in the experiment in Publication 2, continuous head-position monitoring was used.

The MEG signals were bandpass-filtered from 0.03 to 330 Hz and sampled at 1000 Hz. Both vertical and horizontal electro-oculograms (EOGs) were recorded in the all experiments. In addition, a 2-min measurement without a subject was conducted after each session for the estimation of the noise covariance for the minimum-norm estimation procedure.

4.3.2 Structural and functional MRI

All MRI data were acquired using a General Electric Signa 3-Tesla MRI scanner (General Electrics Healthcare, Milwaukee, WI, USA) with a 16-channel head coil at the Advanced Magnetic Imaging Centre of the Aalto NeuroImaging at Aalto University.

High-resolution T1-weighted structural MRI images (1.0 mm × 1.0 mm × 1.0 mm) were acquired using a spoiled-gradient-echo sequence to coregister and visualize MEG and fMRI data on the brain structure.
Functional MRIs were obtained using a gradient echo-planar-imaging with the following parameters: TR (repetition time) 2.015 s, TE (time to echo) 32 ms, flip angle 75°, 34 oblique axial slices with the slice thickness of 4 mm, image matrix of 64×64, voxel size 3.4 mm × 3.4 mm × 4.0 mm, and field of view (FOV) 22 cm.

4.3.3 Behavioural ratings

After the MEG recording in the experiment of Publication 2, the viewers watched the movie once again on a computer screen. They were asked to evaluate their level of engagement with the haptic contents of the movie by shifting continuously a cursor up and down on a scale presented on the screen. The scale was continuous from 0 to 1 (with 384 discrete values between 0 and 1) and the ratings were sampled at 5 Hz. The ratings of individual subjects were linearly normalized to range from 0 to 1 and averaged.

4.4 Data pre-processing

4.4.1 Preprocessing of MEG data

To suppress the external magnetic interference outside the brain, signal space separation (SSS; Taulu & Kajola, 2005) was applied in Publications 1 and 3, and temporal signal-space separation (tSSS; Taulu & Simola, 2006; Taulu & Hari, 2009) with head motion correction in Publication 2. The analyses were performed with Maxfilter software version 2.2 (Elekta Oy, Helsinki, Finland) with the default parameter settings. The data were also converted into the default head position with the same software.

Artifacts related to eye movements and blinks were suppressed from the MEG signals in Publication 1 and Publication 3 by multiple linear regression in consecutive 60-s time windows, using the recordings of both vertical and horizontal EOG channels. As movies can evoke coherent gaze patterns across the viewers (Dorr et al., 2010), statistical analysis was performed to ensure that there was no significant correlation between blinks and eye-movements and the canonical variates left after artifact removal.

The MEG signals were further filtered into frequency bands of interests. In Publication 1, the bands were 0.03–1, 1–5, 5–10, 10–15, 15–20, 20–25, 25–30, 30–40, 40–50, 50–60, 60–80, and 80–100 Hz. In Publication 2, only one band (1–40 Hz) was used, and in Publication 3 the bands were < 1, 1–4, 4–8, 8–11, 13–23, 25–45, and 55–100 Hz. In all studies, the 204 gradiometers were used in MCCCA analyses. MCCCA is able to estimate canonical variates up to the rank of the datasets. Thus, we applied principal component analysis (PCA) to reduce data dimensionality from the original 204 down to the degrees of freedom (rank) left after the SSS or tSSS artifact reduction. The ranks were 68 in Publications 1 and 3 and 67 in Publication 2 (minimum number of all subjects).
4.4.2 Pre-processing of fMRI data

Four dummy scans were removed from the beginning of the fMRI recordings. The pre-processing of fMRI data was performed with the SPM8 toolbox (http://www.fil.ion.ucl.ac.uk), and included standard pre-processing steps: motion-correction, slice-time correction, coregistration of functional images to anatomical MRI, normalization to MNI (Montreal Neurological Institute) standard space, and smoothing with an 8-mm full-width-at-half-maximum Gaussian kernel.

For voxel-wise comparison with MEG in Publication 3, the cortical fMRI voxel series were transformed to the same 'fsaverage' coordinate system as MEG. Those voxel time series that corresponded the locations of MEG sources (altogether 5124 locations per subject) were retained for further analysis.

4.4.3 MEG source-level analysis

For estimation of source-level MEG signals, we segmented and reconstructed the cortical surface from the T1-weighted magnetic resonance images of each subject using the FreeSurfer software (http://surfer.nmr.mgh.harvard.edu/) with the parameters described in FreeSurferWiki1.

To estimate the MEG sources in the cortex, we applied the minimum-norm estimation (MNE) method (Hämäläinen & Ilmoniemi, 1994) using MNE Suite software package (http://www.martinos.org/mne/). A single-compartment boundary element method (BEM) volume conductor model was constructed, and the estimates were calculated at discrete source locations separated by 7 mm on the cortical surface. MEG data from all 306 channels were used in the estimation.

In Publications 1 and 2, source-current estimates along three orthogonal axes (corresponding to two tangential and one normal orientation related to the cortical surface) were calculated with following parameters: ‘loose factor’ 0.4 to favor the dipole component normal to the surface, and ‘depth weighting’ to reduce the bias towards superficial currents. In Publication 3, only the source currents for dipole orientations normal to the cortical surface were estimated.

For group analyses and visualization, and for point-wise analyses in Publication 3, the source estimates of individual subjects were morphed into a common template brain (‘fsaverage’ provided by the Freesurfer software package).

1 http://surfer.nmr.mgh.harvard.edu/fswiki/RecommendedReconstruction
5. Summaries of the studies

5.1 MCCA uncovers synchronized MEG activity across subjects during movie viewing (*Publication 1*)

5.1.1 Motivation

This far, the majority of the studies using naturalistic stimuli have been conducted with fMRI, whereas electromagnetic signals, MEG or EEG, have been used only rarely in such experimental settings. However, MEG can provide more accurate information about the temporal dynamics of brain activity than fMRI, and gives a direct measure of electromagnetic brain activity arising from neural cell populations. In this study, the aim was first to develop a method to find consistent brain activity from unaveraged MEG signals measured during movie viewing, and then investigate the characteristics of the synchronized brain activity across viewers.

5.1.2 Methods

Eight subjects viewed the silent 15-min black-and-white “At Land” movie twice during MEG recordings. To find consistent brain signals across the viewers, we applied a data-driven spatial filtering approach based on MCCA to the MEG signals. The first 10 min of the recordings were used for training the model and the remaining 5 min for testing the statistical significance of the resulting canonical variates. The statistical significance of the deviance of the pair-wise correlations of the canonical variates between subjects from zero was evaluated with a two-tailed $t$-test. The significance level was $p < 0.05$ with Bonferroni correction. For topographic mapping of the contributing brain areas to these canonical variates, the canonical variates were correlated with the source currents estimated with the MNE method.

5.1.3 Results

Several statistically significant canonical variates were found in frequency bands 0.03–1 Hz and 1–5 Hz, with intersubject correlations up to 0.28 and 0.16, respectively. Additionally, statistically significant canonical variates were observed in narrow bands around 12, 24 and 36 Hz, corresponding to the frame rate ($\approx 24$ Hz) of the movie.
Figure 1 shows an example of the first canonical variates of all subjects in frequency bands 0.03–1, 1–5 and 5–10 Hz, demonstrating obvious similarity in the temporal behaviour of brain signals across subjects.

Figure 1. An example of the time-series of canonical variates for all subjects superimposed. The first canonical variates are shown for the test data in frequency bands 0.03–1, 1–5, and 5–10 Hz. The enlarged segments correspond to each other, and the amplitudes of the signals are scaled to have zero mean and standard deviation 1. Fig. 2 in Publication 1.

Figure 2. Topographical maps showing the correlation coefficients (colorbars) between the canonical variates and the source-current estimates in frequency bands 0.03–1 and 1–5 Hz. The maps represent averages across all 8 subjects morphed to an average brain surface. Fig. 4 in Publication 1.
The topographical maps, shown in Figure 2 for frequency bands 0.03–1 and 1–5 Hz, indicate that the highly correlated canonical variates originated mostly from occipital and posterior parietal cortices bilaterally, but also from superior temporal sulcus, inferior parietal cortex, and prefrontal areas, as well as close to functional V5/EBA (extrastriate body area) and motor/premotor areas.

5.1.4 Discussion and conclusions

This work succeeded in finding correlated MEG activity between subjects during movie viewing in physiologically meaningful brain regions. The data-driven spatial filtering with MCCA was able to extract consistent activity time series from noisy unaveraged MEG signals.

These results also demonstrate the feasibility of using MEG in studying brain activity in naturalistic experimental settings, and they extend the previous fMRI findings to recordings with high temporal accuracy.

5.2 Activity of the viewer’s somatosensory cortex covaries with the haptic contents of the movie (Publication 2)

5.2.1 Motivation

Previous brain imaging studies have shown that observing another person’s actions and feeling activates brain areas that support similar functions in the observer. Such vicarious brain activity has been demonstrated previously in premotor and somatosensory cortices using highly controlled and simplified experimental settings (for reviews, see e.g. Rizzolatti & Craighero, 2004; Keysers et al., 2010). In this study, the aim was to study how the activity in somatosensory cortex is dynamically modulated by the observed movie content.

In contrast to the typically used averaging of evoked responses, we aimed at following how the moment-to-moment state of the somatosensory cortex, probed by tactile stimuli presented to the fingers, changes during movie viewing. However, reliable detection of single-trial evoked responses poses a considerable challenge for data analysis. Thus, we also aimed at finding a feasible approach to analyze changes in unaveraged MEG responses to complex stimuli.

5.2.2 Methods

Experimental setup

The 15-min movie was shown once to 16 subjects during MEG recordings. To probe the moment-to-moment state of the somatosensory cortex, the viewers also received pneumatic tactile stimuli on their fingers, once every 1005 ms during the entire movie viewing. After the MEG recordings, the subjects evaluated
the level of their moment-to-moment subjective haptic engagement to movie events.

**MCCA-based spatial filtering**

In addition to the preprocessing described in Section 4.4.1, we filtered the MEG signals and selected 400-ms epochs time-locked to the onsets of the tactile stimuli.

Consistent responses across the subjects were uncovered by applying spatial filtering based on MCCA to the MEG signals over the whole duration of the movie. The first half of the movie (440 trials) was used for training the MCCA model, and the rest of the movie (last 440 trials) was used for the model validation. In statistical testing, correlations between these time-courses of eight randomly selected subject pairs (sampled without replacement from the pool of 16 subjects) were calculated for each component. A one-tailed t-test was used to find out whether the mean of these correlations deviated significantly from zero (significance level $p < 0.05$ with Bonferroni-correction).

The spatial filtering resulted in a set of uncorrelated canonical variates, each variate highlighting different aspects of the evoked responses. Most importantly, this procedure reduced noise in the individual responses, thus enabling single-trial analysis.

**Cortical sources of the signal components**

To validate that the MCCA canonical variates found in a data-driven method originated from feasible brain regions, activation maps (Haufe et al., 2015) were calculated from the spatial filter weights, and transformed from sensor-level to source-level by minimum-norm estimation.

**Temporal PCA**

The amplitude modulations of single-trial evoked responses throughout the movie were quantified, separately for each canonical variate, using temporal PCA. The first PCA score was selected, corresponding to projection of the data to the first PCA eigenvector. In practice, the PCA score reflects the match of single trials with the first PCA eigenvector, and thus quantifies the variation of the trials throughout the movie.

**Correlation between brain responses and behavioural ratings**

Finally, we computed the Pearson’s correlation between averaged PCA score and the time-series of behavioural ratings. The correlation was calculated with time lags between −20 and 20 s between the signals. 95% confidence intervals for the correlation coefficients were estimated by non-parametric stationary block bootstrapping, thus retaining temporal dependences in time-series as well as stationarity in the data. The bootstrapping was repeated 10,000 times.
5.2.3 Results

Spatial filtering with MCCA uncovered the most correlated signals, i.e. canonical variates, across the subjects in multi-channel MEG data. The first two canonical variates, MCCA1 and MCCA2, were statistically significant, with mean intersubject correlations of 0.17 and 0.1, respectively, for the test data. Notably, the signal waveforms of the canonical variates were more consistent across subjects than the original noisy raw signals (Figure 3). MCCA1 and MCCA2 showed different response characteristics, highlighting different parts of the response time series.

The correlation between PCA scores and the behavioural ratings was 0.38 for MCCA1 and 0.49 for MCCA2. Figure 4A shows the PCA score time-series of MCCA1 together with the behavioural ratings, illustrating the similarity of these signals. The maximum correlations were found with time lags of 7 s and 5 s for MCCA1 and MCCA2, respectively, the ratings lagging the PCA scores. Visual inspection revealed that the highest peaks in both PCA scores and behavioural ratings happened in the scenes where the main character of the movie was either moving or having haptic sensations.

The spatial locations of MCCA1 and MCCA2 revealed that the canonical variates originated from sensorimotor regions, contralateral to the delivery site of the tactile stimuli. Figure 4B shows the average activation map over 10 subjects.
5.2.4 Discussion and conclusions

Methodologically, this study introduced a novel approach to follow moment-to-moment modulation of MEG single-trial activity in a complex naturalistic experiment. Viewing the movie modulated responses to tactile stimuli in a fine-grained manner that was closely related to movie content. The results expand the current understanding of vicarious brain activation by demonstrating fluctuations in the functional state of the sensorimotor cortex during observation of a movie.

5.3 MEG and BOLD signals correlate during movie viewing (*Publication 3*)

5.3.1 Motivation

Previous fMRI studies and recently also MEG and EEG studies have demonstrated consistent temporal dynamics of brain activity across movie viewers. The relationship between electromagnetic and hemodynamic brain signals has been previously shown using simplified or repeated stimuli in experimental settings that lack ecological validity. Thus, little is known about the similarities and differences between MEG/EEG and fMRI dynamics during movie viewing.

This study presents a systematrical comparison between the electromagnetic and hemodynamic brain activity during movie viewing, by using MEG and fMRI data collected from the same subjects. Two methodological approaches were used to characterize similarities in MEG and fMRI time-courses. First, we
studied the feasibility of univariate voxel-wise correlations in revealing consistent brain responses between and within subjects in MEG and fMRI separately, as well as between MEG and fMRI signals. Second, we suggested an approach to first detect consistent MEG signals with spatial filtering, as in Publication 1, and then combine these with fMRI signals in a general linear model (GLM).

5.3.2 Methods

Eight subjects viewed the 15-min movie twice both during MEG and fMRI recordings.

In the first approach, voxel-wise Pearson’s correlations were calculated both within and across the subjects for the time series at corresponding anatomical locations, separately for MEG and fMRI. We also investigated whether this univariate voxel-wise correlation approach was able to find statistically significant correlations between MEG and fMRI signals.

The sensor-level MEG signals were filtered into 7 frequency bands, ranging from 0.03 to 100 Hz. MEG source currents were estimated by using minimum-norm estimation and they were morphed to a common template brain. The envelopes of MEG source currents were obtained by Hilbert transform, and the resulting signals were further low-pass filtered below 4 Hz. The cortical fMRI voxel time-series were transformed to the same coordinates with MEG signals. For MEG–fMRI comparison, MEG signal envelopes were convolved with the canonical hemodynamic response function before computing the correlation.

The statistical significance of all voxel-wise correlation coefficients was tested by non-parametric bootstrapping with circular-shifting performed 10,000 times. The $p$-values for the correlation coefficients were estimated from the resulting null distribution. For all voxel-wise calculations, the significance threshold was $p < 0.05$, with FDR correction for multiple comparisons.

In the second approach, the same MCCA spatial filtering method as in Publication 1 was first applied to find the most consistent canonical variates from noisy sensor-level MEG signals. The same MEG frequency bands were used as in the voxel-wise analysis. For training and testing the MCCA model, 10-fold cross-validation was used. We selected the first MCCA canonical variate in each frequency band, calculated its envelope by a Hilbert transform, low-pass filtered it below 4 Hz, and convolved it with the canonical HRF. Finally, the resulting MEG signal envelope was used as a regressor in a general linear model with fMRI voxel times to find the association between MEG signal envelopes and fMRI signals. The GLM was estimated separately for each frequency band.

5.3.3 Results

The voxel-wise analysis showed that the intra- and intersubject correlations were considerably stronger for fMRI data than for amplitude envelopes of MEG
(see Figure 5 for intersubject correlations). The voxel-wise MEG–fMRI comparison was insufficient to uncover reliable correlations between electromagnetic and hemodynamic signals at corresponding anatomical locations.

Applying MCCA-based spatial filtering captured the most consistent MEG activity across the subjects that originated mainly from occipital brain regions. Combining the envelopes of these canonical variates into the GLM model with cortical fMRI voxel time-series uncovered similarity between MEG and fMRI, shown in Figure 6. The association between MEG and fMRI was found mainly in occipital areas, but also in temporal, parietal and frontal regions.
5.3.4 Discussion and conclusions

The results show that inter- and intrasubject correlations in response to a movie were stronger for fMRI than MEG signals, and that the univariate correlation approach was suboptimal for describing similarities between MEG and fMRI. These findings highlight the difference in response characteristics of electromagnetic and hemodynamic signals and suggest the necessity of more advanced methods to compare MEG and fMRI signals.

The multivariate spatial filtering with MCCA, introduced in Publication 1, enhanced intersubject correlation compared with the univariate approach. Furthermore, combining the resulting consistent canonical variates into a GLM model of the fMRI data, uncovered positive correlation between MEG and fMRI in occipital areas, but also in temporal and frontal brain regions.

Thus, the results demonstrate that our approach was feasible in finding similarities between MEG and fMRI signals. They also show that electromagnetic and hemodynamic activities are correlated in functionally meaningful brain areas.
6. Discussion

The studies in this Thesis present feasible approaches to analyze complex MEG data recorded during movie viewing. The key methodology in all studies was based on spatial filtering with multiset canonical correlation that was used for finding consistent brain activity in unaveraged MEG data, both for 15-min-long continuous signals and short single-trial evoked responses. Comparison of electromagnetic and hemodynamic responses to the same movie aimed also at bridging the gap between MEG and fMRI studies using movies as stimuli.

The first study showed that MEG signals between the viewers were synchronized with high temporal accuracy (up to 10 Hz). The areas showing similar dynamics between the viewers were found in functionally meaningful brain regions, mostly in visual areas, but also in parietal and pre-motor regions. In the second study haptic movie content modulated viewers’ brain activity in sensorimotor brain areas dynamically during observation of the movie. The third study demonstrated similarity between the dynamics of electromagnetic and hemodynamic brain activity, mostly in occipital brain areas but also in temporal and frontal regions.

6.1 Methodological considerations

6.1.1 Spatial filtering with MCCA

Spatial filtering with multiset canonical correlation analysis allows data-driven exploration of the complex brain data recorded in naturalistic experimental settings. The method was efficient in finding consistent brain activity across movie viewers of a 15-min long film. In addition, Publication 2 demonstrated a novel approach for single-trial evoked-response analysis employing MCCA.

In these studies, the most important advantage of using MCCA was the extraction of signal components that were consistent across people. This approach is remarkably different from the traditional studies, in which the signal-to-noise ratio of the responses is enhanced by repetition of the stimulus that would be impractical with long stimuli, such as movies.

Comparison between the univariate voxel-wise correlation approach and multivariate modelling with MCCA in Publication 3 showed the latter to be superior in finding consistent signals between the subjects. Furthermore, unlike
voxel-wise modeling, MCCA approach does not assume anatomical correspondence between the subjects, but rather finds the optimum weights for the sensors in a data-driven way. Moreover, these weights provide information about the brain areas contributing to the signal components. A further advantage is that MCCA can also be applied conveniently at the sensor level, without having to deal with high-dimensional source-space signals.

The effectiveness of MCCA is based on using multiple datasets, here multiple subjects, and the performance of MCCA improves with the number of datasets as well as with the number of samples up to a certain limit (Correa et al., 2010). The major limitation of MCCA is that its effective use requires sufficient amount of data, i.e., several subjects and long recordings lasting at least several minutes. Furthermore, the method can find only those brain processes that are temporally coherent in the group. Thus, this approach is most effective in characterizing extrinsic brain activity that is time-locked to a common stimulus, and it cannot be used e.g., in resting-state studies.

In addition to ISC and MCCA, similarities in the data across subjects can be studied also by using group-ICA methods (for a review, see e.g., Calhoun et al., 2009), which have been applied previously in fMRI data analysis in studies using movie stimuli (Malinen et al., 2007; Wolf et al., 2010; Malinen et al., 2011; Pamilo et al., 2012; Naci et al., 2014; Kauttonen et al., 2015). Whereas the first MCCA component is always related to the highest correlation value, and the next components follow in descending order, independent components are not ordered, which requires an additional step in the analysis. In addition, no exact rules exist for estimating the correct number of independent components, and increasing the number of components to be estimated can result in different subdivisions of the networks revealed by ICA (Smith et al., 2009; Abou-Elseoud et al., 2010; Pamilo et al., 2012). In addition, while ISC or MCCA spatial maps usually cover relatively large areas, the spatial maps from ICA can be more sparse and thus more focused in some cases (e.g., Malinen et al., 2011). In a comparison between MCCA and group-ICA for fMRI data recorded during a visuomotor task, MCCA gave higher correlations across subjects than group ICA, but the spatial maps of group ICA were more focused than those of MCCA (Li et al., 2009).

6.1.2 Data-driven analysis of brain imaging data

Data-driven analysis of brain imaging data allows exploration of the data without using a pre-determined model between the stimulus and the brain signal. Thus, data-driven analysis seems suitable for naturalistic experiments, where the stimulus features and brain processes are difficult to model. However, the interpretation of the results can be difficult. What do the different signal components, activation maps or intersubject correlations tell about brain function? High intersubject correlations have been interpreted to reflect similarity of brain processes across individuals. However, also the variability of ISC values may reveal meaningful activation, especially in higher-order brain areas (Kauppi et al., 2017).
Even when the across-subjects synchrony is strong, it is not straightforward to tell which stimulus event caused the strongest synchrony. Inspecting the events in the movie that occurred around synchrony peaks or elevated activation (reverse correlation analysis) (Hasson et al., 2004; Dmochowski et al., 2012; Chang et al., 2015) can suggest relation between the stimulus and brain signals. However, it is not necessarily always clear how long a time window exactly should be inspected around the moment of high correlation, as latencies of the brain responses can vary with different types of features or events in the movie and between individuals. Moreover, movies contain many hierarchical levels of stimulus features (Kauttonen et al., 2015), and it is practically impossible to annotate them all and define their onset and offset times. Manual ratings, as we used in Publication 2, can help characterize some specific aspects of the movie contents. The same rating method has been used previously in correlating valence and arousal ratings with brain activity during movie viewing (Nummenmaa et al., 2012). In addition, annotations of visual and auditory stimulus features have been correlated with brain activity (Lahnakoski et al., 2012b; Kauttonen et al., 2014). However, the ratings can only capture a small set of dimensions from the highly complex stimulus, and there can be much variation in different annotators’ rating styles.

6.1.3 Experimental setup

The physical and technical challenges in bringing the real-world settings to a brain-imaging laboratory set limitations to the possible experiments. In addition, although a movie can mimic rather well the complexity of the visual world, it is unnatural in the sense that it is unidirectional, a stimulus which the subject has to passively view. Most of our everyday life is interactional; we actively interact with the world instead of being passive observers, and the presence of other people and the input from them affect continuously our own mental events and brain activity (Hari et al., 2015). Furthermore, typically only one person can be measured at the same time in MEG or fMRI scanner. However, recent technical development has introduced real-time interactive dual-MEG setups (Baess et al., 2012; Hirata et al., 2014) and fMRI setups (Montague et al., 2002), taking important steps towards more realistic experimental setups. In addition, EEG hyperscanning of multiple subjects can be carried out with less restrictions on instrumentation (for a review, see e.g. Babiloni & Astolfi, 2014).

6.2 Brain activity during movie viewing

In the studies in this Thesis, electromagnetic brain activity was characterized during movie viewing. In line with previous fMRI studies, the movie elicited significant synchronization across viewers in physiologically meaningful brain regions. Synchronization of the brain signals during a common experience has been suggested to tell how similarly the viewers see the world (Nummenmaa et al., 2012; Nummenmaa et al., 2014a). For example, in a study where the subjects were instructed to take a point of view of either an interior/exterior decorator or a detective while viewing a movie, their intersubject correlation in certain
brain regions increased when they took the similar perspective (Lahnakoski et al., 2014). Furthermore, the synchrony of brain activity between a speaker and a listener has been shown to be associated with enhanced communication between individuals (Stephens et al., 2010).

*Publication 1* showed that the intersubject synchronization occurred with high temporal accuracy up to 5 Hz, thus giving insights into brain processes occurring at temporal scales down to 200 ms. There is evidence of hierarchy of temporal windows, meaning that longer-latency responses typically occur in brain areas that are higher in the processing hierarchy and are anatomically more distant from primary sensory cortices (Hasson et al., 2008b). Although most of the correlations across viewers in *Publication 1* occurred in occipital areas, related to visual processing, intersubject synchronization in higher level association areas was observed as well. These findings suggest that the brain responses did not reflect only low-level visual processing. Furthermore, the synchronization at different frequency bands and different MCCA components occurred in slightly different cortical locations, likely related to functional segregation of neuronal processing. The brain areas with highest intersubject correlation largely overlapped with the “extrinsic network”, comprising large parts of the posterior cortex and reflecting processing of external sensory stimuli (Golland et al., 2007). In contrast, the “intrinsic” system comprises areas associated with internally oriented mental processes; it lacks significant intersubject correlation but forms a network whose voxel time courses correlate with each other within a subject. Thus, it is likely that the uncovered time-courses in *Publication 1* were stimulus-related. Further studies are needed to reveal non-stimulus-locked internally generated processes.

*Publication 2* demonstrated that functional state of the somatosensory cortex is dynamically modulated according to the observed movie content. This finding likely reflects slow modulation of activity in the somatosensory cortex by a visual input, which is reflected as changes in moment-to-moment evoked responses to movie-unrelated probe stimuli. The largest variation occurred in the long-latency (85–175 ms) parts of the evoked responses, suggesting that the later processing stages of the sensory input accounted for the variation. This study adds evidence to the literature of vicarious somatosensory perception with temporal dimension.

### 6.3 Comparison of MEG and fMRI signals

*Publication 3* presented a systematic comparison between MEG and fMRI signals during movie viewing. Comparing electromagnetic and hemodynamic signals is not straightforward, as MEG and fMRI signals have different neurophysiological origins and signal behaviour. Depending on the stimulus type, a single stimulus or event can elicit both transient changes (evoked or event-related responses) and suppression or increase in oscillatory activity in MEG signal, whereas BOLD signal behaviour is generally very smooth. Moreover, oscillations observed with MEG can occur across a wide range of frequencies up to 600
Discussion

47 Hz (for a review, see Hari & Puce, 2017), whereas the frequency range of fMRI is limited by the hemodynamic response, typically to less than 0.2 Hz.

Furthermore, combination of MEG data with structural or functional MRI involves several sources of spatial inaccuracies. Coregistration between the MEG coordinate system and structural MRI, using information from HPI coils and digitization, can cause spatial inaccuracies on the order of millimetres. Inaccuracies in estimating source activity from sensor-level data depends on the inverse estimation method and brain area, but usually should be within a centimeter. Finally, averaging and morphing the brain surface to a common template, both in MEG and fMRI, can decrease the spatial accuracy on the order of millimeters.

Several methodological approaches have been proposed to combine MEG or EEG and fMRI signals (e.g. He & Liu, 2008; Correa et al., 2010; Biessmann et al., 2011; Huster et al., 2012; Jorge et al., 2013; Dähne et al., 2015). In multivariate modeling, combining data from different modalities directly into a common model can be referred as early fusion scheme (Dähne et al., 2015). In comparison, the late fusion scheme is a two-step process, where the first step is to decompose the data into components separately for each imaging modality, and the second step is to combine the components into a common model. In the early fusion approach, challenges might occur if the data are not balanced, e.g. if they have very different signal-to-noise ratio. In combining MEG and fMRI in our data, we used the late fusion scheme by first finding signal components in MEG data by using MCCA, and then combine the data with fMRI by using GLM.

6.4 Future perspectives

The studies presented in this Thesis provide tools for MEG data analysis, especially in naturalistic experimental setups in which conventional analysis methods are suboptimal or insufficient. Besides movies, the methods developed and validated in this Thesis can be used also with other naturalistic stimuli, such as audionarratives (Koskinen & Seppä, 2014).

Importantly, the methods presented here for MEG can be applied in EEG analysis as well, which opens up new possibilities for future studies. Although MEG has some benefits over EEG, such as better spatial accuracy for locating the sources of cortical signals, the massive instrumentation of MEG sets certain limits for the experiments. Instead, easy mobility of EEG enables recording brain activity outside the laboratory, in true real-world settings, for example in a classroom (Poeppel et al., 2017). In addition, it is rather easy to record EEG from several subjects at the same time, rather than one or two at a time in MEG experiments, which provides new opportunities for studying intersubject synchrony. A promising new trend is also virtual reality, which allows building very realistic and naturalistic 3D-environments which can be combined with EEG recordings.

Finding a reliable method to relate the visual features or semantic contents of a movie to MEG signals remains future work. Occipital EEG has been
shown to correlate only with low-level visual features in a movie, such as contrast or optical flow between adjacent frames (Whittingstall et al., 2010; Dochnowski et al., 2017). Promising methods to link semantic movie contents with BOLD signal have been presented in fMRI literature, and validating their applicability to MEG or EEG signals would be an interesting subject for future work. For example, voxel-wise encoding modeling has turned out to be useful in relating both low-level features and semantic contents of movies to brain activity measured with fMRI (Nishimoto et al., 2011). Furthermore, it has been possible to decode information about the object and action categories in the movie from BOLD signal by employing hierarchical logistic regression modeling (Huth et al., 2016). Recently, also neural networks have been used to build encoding and decoding models between movie features and BOLD signals measured from subjects who were watching videos (Eickenberg et al., 2016; Güçlü & van Gerven, 2017; Shi et al., 2017; Wen et al., 2017). These studies have demonstrated that different hierarchical visual processing states can be described by different layers of the neural networks, such that early visual areas are related to low-level layers of the model and the later visual areas to higher-level net layers.

The methods presented in this Thesis provide useful approaches to take also MEG analysis to the next level. Importantly, extracting consistent signal features and meaningful information from complex and high-dimensional MEG data provides a good starting point for further analysis.

6.5 Conclusion

This Thesis demonstrated the feasibility of using MEG in naturalistic experimental settings. Unlike fMRI, MEG gives a direct measure of neural activity of neuronal populations. Its excellent temporal resolution enables tracking of the dynamics of brain activity and employing evoked responses to probe brain activity in high temporal detail. The studies of this Thesis demonstrated that it was possible to find across-subjects consistency in complex single-trial MEG activity recorded during movie viewing by applying spatial filtering based on MCCA. The findings give new insights into naturalistic visual processing by demonstrating synchronization of brain activity between the viewers of a movie and by showing that observation of haptic events in a movie modulates the viewer’s sensorimotor cortical activity in a fine-grained manner. The methods and approaches presented and validated in this Thesis provide new tools for using MEG in complex experimental settings and thus open new possibilities for understanding the dynamics of human brain activity in real-world contexts.
References


References


