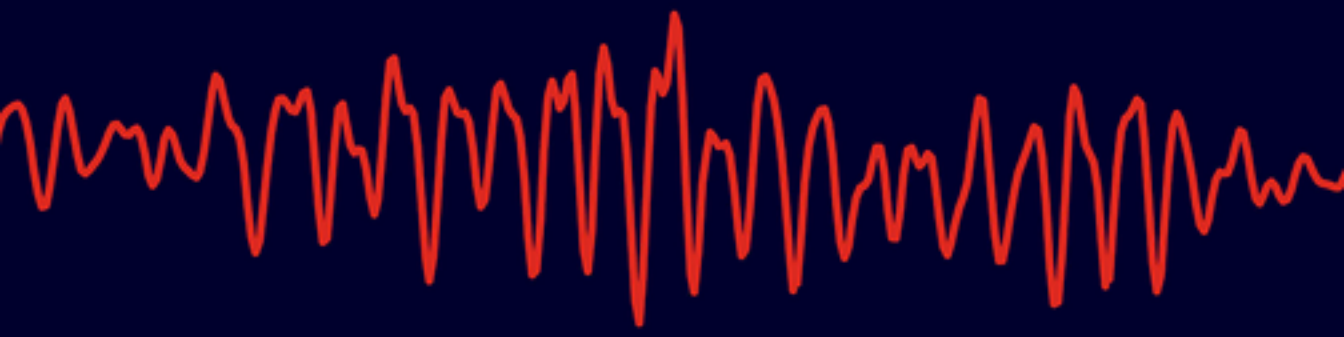

MEG–EEG PRIMER

RIITTA HARI
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MEG–EEG PRIMER

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Published in the United States of America by Oxford University Press
198 Madison Avenue, New York, NY 10016, United States of America.

Library of Congress Cataloging-in-Publication Data
Names: Hari, Riitta, author. | Puce, Aina, author.
Title: MEG–EEG primer/by Riitta Hari and Aina Puce.
Description: New York, NY: Oxford University Press, [2017] | Includes bibliographical references and index.
Identifiers: LCCN 2016039489 | ISBN 9780190497774 (alk. paper)
Subjects: | MESH: Magnetoencephalography—methods | Electroencephalography—methods | Brain—physiology | Brain Mapping | Brain Diseases—diagnosis
Classification: LCC RC386.6.M36 | NLM WL 141.5.M24 | DDC 616.8/047548—dc23
LC record available at https://lccn.loc.gov/2016039489

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Printed by Marquis, Canada

CONTENTS

PREFACE

The aim of this primer is to provide an introduction to the basic principles of magnetoencephalography (MEG) and electroencephalography (EEG). MEG and EEG are time-sensitive methods that allow the noninvasive study of human brain activity. We target our message to beginning and intermediate users of MEG/EEG, assuming that most readers will be graduate students or postdoctoral fellows in systems, cognitive, affective, social, or clinical neuroscience, or perhaps faculty looking to move into these areas. We also hope that scientists interested in interdisciplinary research linked to these research fields may find this primer useful.

Even the best tools cannot yield sound results if the principles underlying the recording techniques, the generation of the signals, as well as the fundamentals of the analysis methods are not well understood. In this primer we thus focus on the basic physical and physiological background of MEG and EEG signals and principles of appropriate experimentation, data analysis, and interpretation. Our goal is to provide the reader with useful information on the practical aspects and typical technical problems faced in MEG or EEG recordings. We thus discuss at some length possible sources of artifacts, the procedures to judge the quality of the recording, and the care required in physiological interpretation.

Consequently, we do not exhaustively review the existing MEG and EEG literature but rather give examples of typical signals and refer to previous review papers and textbooks. Whenever possible, we try to point out connections to interesting brain functions and brain-imaging methods to emphasize that the MEG and EEG technologies are not independent of other approaches in neuroscience.

MEG and EEG have often been discussed separately, which has led many researchers to neglect their close relationship. The current neuroscience literature frequently examines results of one or two functional neuroimaging methods in a fairly unbalanced manner. For example, both MEG and EEG papers often cite functional magnetic resonance imaging (fMRI) literature, MEG papers more often cite EEG literature than vice versa, and fMRI papers either largely ignore electrophysiology or may cite scalp or invasive electric potential measurements (electrocorticography or depth electrode measurements) but rarely MEG. To remediate this problem, we try to discuss MEG and EEG in parallel, hoping that the very direct connections between these two methods thereby become clear. At the same time, it is important to develop a common language to facilitate successful interdisciplinary science.

We are indebted to our research teams and colleagues for feedback on the contents of this book, and especially the following individuals who have commented on drafts:

Elizabeth Bendycki, Sara Driskell, Tommi Himberg, Aapo Hyvärinen, Matti Hämäläinen, Veikko Jousmäki, Miika Koskinen, Kaisu Lankinen, Nancy Lundin, Ben Motz, Timo Nurmi, Ben Ramsden, Elina Pihko, Eero Smeds, and Noah Zarr. We thank Satu Ilta for drawing and redrawing the illustrations, and Lotta Hirvenkari for additional assistance in image preparation. We thank Elizabeth da Silva, Mia Illman, Isaiah Innis, Veikko Jousmäki, Anne Mandel, Timo Nurmi, and Lauri Parkkonen for help in the collection of some new MEG/EEG data for illustrations in this primer and Nancy Lundin and John Purcell for modeling the EEG caps and nets in Chapter 6. We acknowledge Matti Hämäläinen and Ben Ramsden for in-depth discussions on the contents of this primer. Finally, we thank the Staff at the Indiana University Libraries, Bloomington, for their determination in sourcing the more difficult-to-access publications.

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PREAMBLE

In the early 1990s, a 38-year-old man entered the magnetoencephalography (MEG) laboratory of the Brain Research Unit of the Helsinki University of Technology. He had suffered from epileptic seizures since the age of 14. His seizures typically started by convulsions of the side of his face, which then progressed to a full-blown generalized seizure with loss of consciousness. Now his generalized seizures were well controlled with modern antiepileptic drugs, but he was left with a type of "focal epilepsy," consisting of frequent convulsions of his left face but without associated loss of consciousness (see Chapter 19). These convulsions could occur spontaneously or could be triggered by touching the left side of his mouth or gum: he had a rare type of reflex epilepsy that was touch-triggered.

Because of the resistance of the facial convulsions to medication, surgery was planned to remove the brain area, or "epileptic focus," that was generating the convulsions. Typical for patients with focal seizure disorders, he had already gone through an exhaustive set of examinations to identify the epileptic focus; the examinations included multiple scalp electroencephalography (EEG) and videotelemetric recordings, as well as positron emission tomography (PET). Despite this extensive work-up, the brain regions responsible for the epileptic seizures had not been identified. The hope was now to put MEG to the task as it is not affected by the skull, which dampens and smears EEG signals. The first whole scalp-covering MEG device had just been developed in Finland to simultaneously pick up signals from both hemispheres.

During the MEG recording, the patient triggered a seizure by touching his left gum with his tongue. Figure P.1 shows MEG signals recorded over a 20-s interval where, soon after the touch, epileptic spikes, sharp transients, and complex spikes started to appear in the right hemisphere (red trace in panel a), contralateral to the touched gum. The abnormal discharges soon became continuous and spread to the left hemisphere as well (both traces in b), and simultaneously convulsions were observed to start in the patient's left cheek. The whole seizure, as determined from the MEG signals, lasted for 14 seconds and then ended abruptly (in both traces in c).

The source analysis of the MEG signals—aiming to attribute the measured signals to particular brain regions—indicated that the epileptic discharges started from the face representation area of the right primary motor cortex and then spread, within 22 ms, to the left hemisphere (see the insert of Figure P.1). This time lag was determined by careful analysis of the time courses of the sources of right- and left-hemisphere spikes, and it agreed with interhemispheric conduction via myelinated fibers of about 1 μm in diameter (Aboitiz

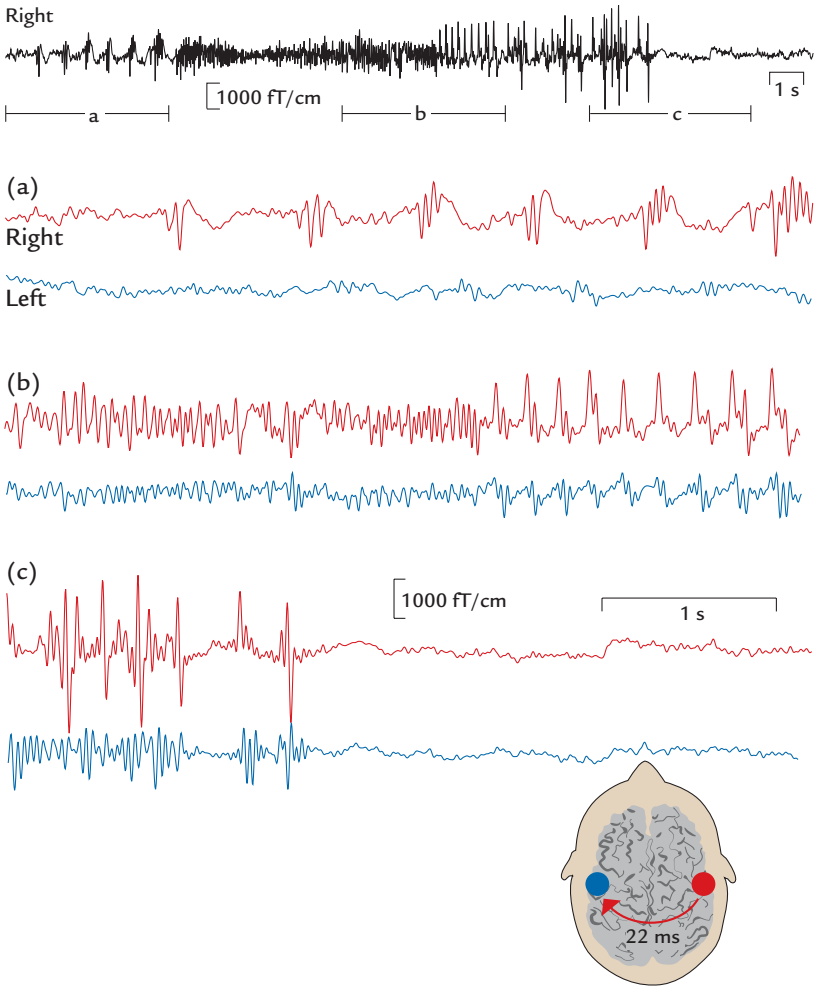

FIGURE P.1. **MEG signals in a patient with touch-triggered focal epilepsy.** A 20-s trace from one (planar) MEG sensor over the right sensorimotor region is shown at the top of the figure, with calibration bars for signal amplitude and time. The segments **a, b,** and **c** indicate times of interest that are magnified in the subsequent traces from homologous right- (red) and left-hemisphere (blue) MEG sensors. **(a)** Immediately after touch, epileptic spikes appear in the right hemisphere. **(b)** Abnormal discharges are seen in both hemispheres but are significantly larger on the right. **(c)** The epileptic discharge ends abruptly in both hemispheres. The schematic axial section of the brain depicts the transfer of the spikes in 22 ms from the right to the left hemisphere. Adapted and reprinted from Forss N, Mäkelä JP, Keränen T, Hari R: Trigeminally triggered epileptic hemifacial convulsions. *Neuroreport* 1995, 6: 918–920. With permission from Wolters Kluwer Health, Inc.

et al., 1992). Thus the primary epileptic focus had been identified in the right hemisphere with a "mirror" focus in the left hemisphere (Forss et al., 1995).

The quite rare types of epileptic discharges seen in this patient raise several questions: How do MEG and EEG differ from each other? What essential steps do we need to take to record MEG and EEG signals, and how can we be sure that the measured signals

arise from the brain and not from some external source or from another part of the body? How do we preprocess, analyze, and model the signals, and how do these results relate to findings obtained by other neuroimaging methods? How do we interpret the results from the neuroscience and clinical points of view? How can we expect these methods to improve in the future? In this primer, we try to address most of these questions.

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SECTION 1

CHAPTER 1

INTRODUCTION

When all you have is a hammer, everything looks like a nail.

Abraham Maslow

Neuronal communication in the brain is associated with minute electrical currents that give rise to both electrical potentials on the scalp (measurable by means of electroencephalography [EEG]) and magnetic fields outside the head (measurable by means of magnetoencephalography [MEG]). Both MEG and EEG are noninvasive neurophysiological methods used to study brain dynamics, temporal changes in the activation patterns, and sequences. Their differences mainly reflect differences in the spread of electric and magnetic fields generated by the same electric currents in the human brain. In this chapter, we give an overall description of the main principles of MEG and EEG, going deeper into details in the following chapters.

MEG AND EEG SET-UPS

Figure 1.1 illustrates MEG and EEG measuring set-ups. During the MEG recording (top panel), the subject is sitting with her head inside a helmet-shaped "dewar" vacuum flask that in this specific device houses an array of 306 extremely sensitive magnetic-field detectors (middle panel, left); the name of this vacuum-insulated flask honors its inventor, James Dewar (1842–1923). To eliminate or dampen external ambient magnetic disturbances, the measurements are performed within a magnetically shielded room. To unravel which part of the brain the MEG signals are coming from, the position of the head with respect to the sensor array must be determined before each session, and it is often continuously monitored during the recording. Eye movements and blinks that cause prominent artifacts in the recording are best monitored by means of an electro-oculogram or with an infrared camera (as shown in Figure 1.1, top panel), although they can be detected also from the frontal MEG channels. During the recording, the subject must keep her head as still as possible in the relatively tight helmet-shaped dewar housing the sensor array. She can speak and moderately move her hands and eyes, although in that case some artifact-suppression methods may be needed. Her facial and bodily actions can be recorded with a video and monitored with response pads, accelerometers, and surface electromyogram (electrical activity from muscles).

During the EEG recording (Figure 1.1, bottom panel), the subject is free to move, although head and body movements may cause artifacts and, as with MEG, are in most

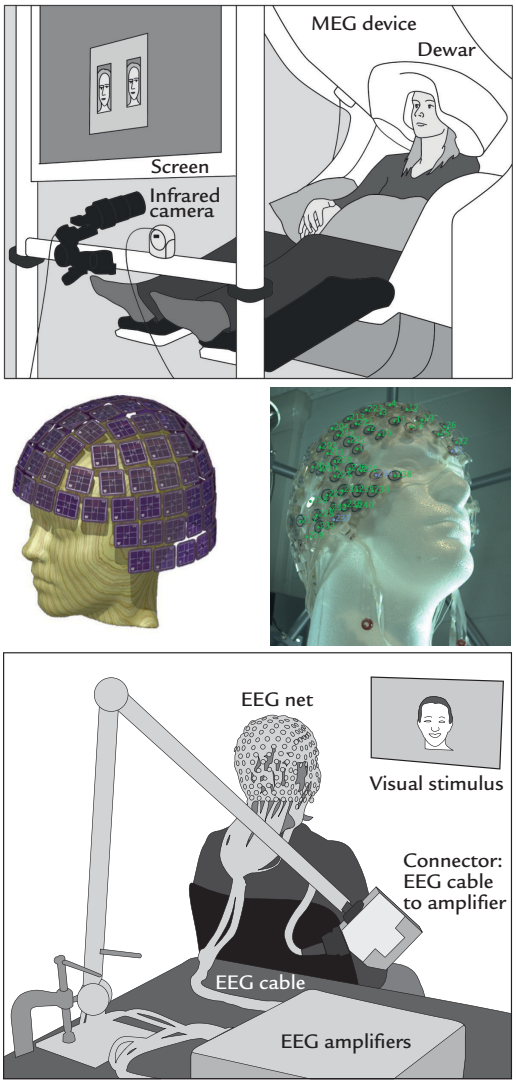

FIGURE 1.1. **MEG and EEG recording setups.** Schematic MEG layout (top panel) displays subject sitting comfortably with her head placed in a "dewar." In front of her are a back-projection screen for visual stimulus presentation and an infrared camera for monitoring eye movements. EEG setup (bottom panel) shows a subject, with attached EEG sensors, sitting in front of a computer monitor for visual stimulation. EEG amplifiers appear in the foreground. Middle panels show MEG (left) and EEG (right) sensor arrays, respectively.

cases discouraged. The subject wears an EEG cap or elasticized "net," in this case with 256 electrodes, attached to the scalp (middle panel, right). A response pad is in the subject's lap (not seen in the figure), and a monitor to present visual stimuli is situated in front of the subject. To avoid external electrical interference, EEG is preferably measured inside a Faraday cage that dampens power-line artifacts and other electrical noise, although recordings of sufficient quality can also be performed in regular rooms, operating theaters, and even in real-life settings using mobile EEG devices.

EEG can be recorded simultaneously with MEG provided that the EEG electrodes and wires are nonmagnetic and do not take up too much space so that the subject's head can fit into the MEG helmet.

EEG and MEG signals are closely related. Figure 1.2 shows that a neuronal current (depicted with an arrow) in a local brain area, here representing activation of the auditory cortex in response to an abrupt sound, generates both MEG (magnetic field, left) and EEG (electric potential, middle) signal distributions. The pattern of the magnetic field follows the right-hand rule (right panel): when the right thumb points the direction of the current, the fingers show the direction of the magnetic field lines (that of course surround the current in three dimensions, although only the upper part is shown in the figure). The MEG and EEG patterns are at right angles with respect to each other (Figure 1.2). The electric potential distribution on the scalp is more widespread than the corresponding pattern of the radial component of the magnetic field, here also computed on the scalp, although in practice the MEG signals are recorded about 20 mm above the scalp. This difference between the MEG and EEG patterns arises because the layered structure of the head with different electrical conductivities for the cerebrospinal fluid, skull, and scalp tissues leads to lateral spread, or "smearing" of the electric potentials, while the magnetic field is unaffected and its spread is only due to the distance between the brain sources and the sites where the MEG is recorded.

If we have measured the magnetic field at multiple locations outside the head and/or the potential distribution on the scalp, we can estimate the locations and strengths of the "source currents" giving rise to the measured signals. In other words, the field and potential distributions can be used to compute the site of the original current. This inference of the sources of the measured signals is the so-called *inverse problem*, which is discussed further in Chapters 3 and 9.

In MEG, tiny magnetic fields, in the order of femto- and picotesla (1 fT = 10^{-15} tesla and 1 pT = 10^{-12} tesla), are detected with an array of sensors that are located around the head.

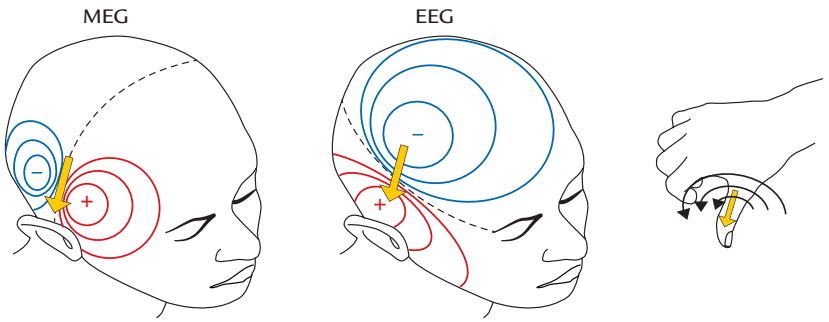

FIGURE 1.2. **Relationship between the site and direction of intracellular current and MEG and EEG signal distributions on the head.** The schematic example depicts isofield lines for MEG (left) and isopotential lines for EEG (center) about 100 ms after a sound that activates the auditory cortex; the elicited net current (dipole) is displayed by the yellow arrow. The MEG and EEG patterns are rotated by 90 degrees with respect to one another. For MEG, positive and negative signs signify magnetic flux leaving and entering the head, respectively. For EEG, positive and negative signs indicate the polarities of the scalp potentials. The broken lines on each field pattern show the respective isofield and isopotential lines where the signal is zero. The MEG pattern can be understood on the basis of the "right-hand rule" that is illustrated in the panel on the right: when the current flows to exit the right thumb, the magnetic field lines curl in the direction of the fingers of the right hand.

TABLE 1.1 Approximate sizes of different magnetic fields of the environment and the body (in units of femtotesla or 10^{-15} tesla = 10^{-15} T)

Magnetic resonance imaging	3,000,000,000,000,000 (= 3 T)
Steady magnetic field of the earth	50,000,000,000
Magnetocardiogram	100,000
Brain's alpha rhythm	1,000
Brain's evoked responses	100
Sensitivity of a magnetometer	3
Noise within a shielded room	1

As the typical MEG signal is of the order of 100 fT and thus a mere 10^{-8} times the strength of the earth's steady magnetic field, the best-quality MEG recordings are carried out inside special magnetically shielded rooms (see Chapter 5). However, even there, only the most sensitive sensors can pick up the brain's tiny magnetic fields. For approximate sizes of different magnetic fields in the environment and body, see Table 1.1.

The most commonly used sensors are SQUIDs (superconducting quantum interference devices), which do not make direct contact with the head as they are immersed within the large, vacuum-insulated liquid-helium-containing dewar. The magnetic fields emanating from the head induce current flow in the SQUIDs. The circuit associated with the SQUID functions as a flux–voltage amplifier, transforming the magnetic flux sensed by the SQUID to a voltage readable by the computer.

In EEG, electrodes are fixed to the scalp and potentials (i.e., voltage differences) are measured between two electrodes at a time. Scalp EEG signals typically are about 50 to 100 μV (1 μV = 10^{-6} volt) in amplitude, whereas intracranial EEG signals can be an order of magnitude larger. The smaller amplitude of the scalp EEG is the result of the increased distance between the sources in the brain and the electrodes and signal attenuation by the scalp, the skull, and the cerebrospinal fluid. (One very important additional factor is the size of the active area, as the potential decreases considerably slower as a function of distance for larger areas of active tissue.) Compare these EEG potentials with the up to 1 million times higher voltages (of 110–240 V) used to power home appliances.

Because of their small size, both MEG and EEG signals must be amplified. They need to be filtered before they are digitized (sampled to discrete values) and subjected to further analysis; we discuss these preprocessing steps in Chapter 7.

■ COMPARISON OF MEG AND EEG

When examining the properties of MEG and EEG signals, it is convenient to assume, as the first approximation, that the head is a sphere where we have only local activations that we model as "current dipoles." In a sphere, the relationships between (neural) currents and the associated magnetic fields and electric potentials are relatively simple, and they serve as good first approximations for the interpretation of real MEG and EEG signals as well.

To avoid confusion, it is necessary to first make a distinction between different dipoles: a current dipole, an electric dipole, and a magnetic dipole, all shown schematically in Figure 1.3. The *current dipole* (Figure 1.3, top), indicated here as a yellow arrow, is an approximation to describe locally moving charges (i.e., a current concentrated to a point). As we

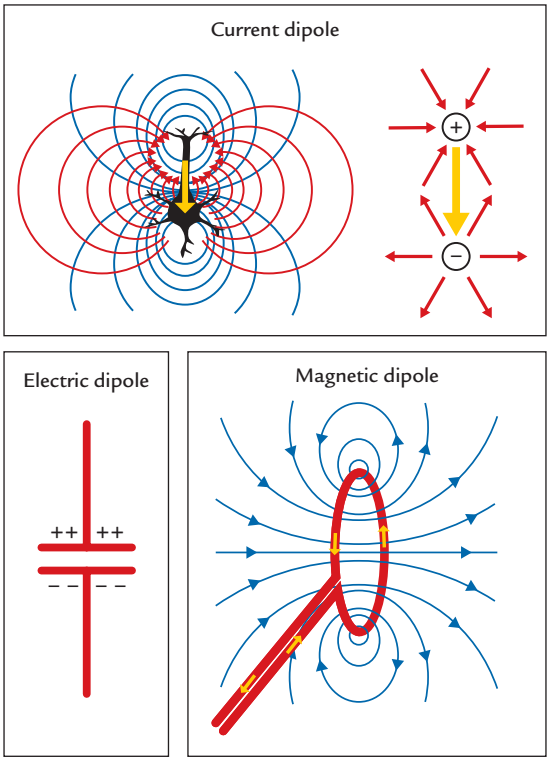

FIGURE 1.3. **Three types of dipole. Top.** A current dipole (yellow arrow) depicted in two different ways. At left, the blue lines show the isopotential lines and the red lines show the paths of the volume (return) currents in a schematic neuron. At right, the volume currents have been replaced by two radially symmetric current distributions: currents (red arrows) entering the positive end of the dipole and currents leaving the negative pole of the dipole. **Bottom left.** An electric dipole (a charged capacitor) with no current flow. **Bottom right.** Magnetic dipole (a current loop) with the associated magnetic field lines (shown in blue).

explain in Chapter 3, the current dipole represents the intracellular "primary current" due to net flow of ions within soma and dendrites of the activated neurons.

Because the current dipole is situated in a conducting medium (a volume conductor), the primary current is always associated with return currents (or volume currents) that close the loop. The obvious reason is that the currents cannot accumulate in any part of the brain because of small capacitances of the tissues.

In Figure 1.3 (top panel), the volume currents associated with the current dipole are presented as current paths that connect the two ends of the neuron; the left schematic shows these paths as red lines and the right schematic shows an equivalent distribution of two radially symmetric current distributions, one at each end of the activated neuron (red arrows). For the neuron on the left, the blue isopotential lines indicate where in the extracellular space the potential is the same. Current dipoles like these are commonly used as source models for MEG and EEG signals.

Positive and negative static charges, such as, for example, in a charged capacitor, form an *electric dipole* (Figure 1.3, bottom left), which does not generate electric current or a magnetic field. The *magnetic dipole* (Figure 1.3, bottom right) is a current loop that, in the ideal

case, does not produce any electric potential, but a very focal magnetic field goes through the loop and returns via the environment, as is shown by the blue field lines.

To understand how MEG and EEG signals are generated, it is useful to examine three types of current dipoles situated in a sphere (Figure 1.4): a radial dipole, a tangential dipole, and a deep source in the middle of the sphere. It is through a combination of these types of currents that we can represent currents of *any* orientation in the sphere, because we can divide any current into tangential and radial components with respect to the sphere's surface. Radial currents are oriented along the radius of the sphere, and tangential currents are orthogonal (at 90°) to them (see the dashed lines depicting two radii in Figure 1.4a). A local current in the middle of the sphere is always radial.

Figure 1.4 additionally illustrates some interesting properties of magnetic fields generated by currents in a spherical volume conductor. Note that all current dipoles (arrows) shown in the figure represent the primary (intracellular) currents.

First, the radial currents (both the intracellular current represented by the arrow and the associated return currents that are not illustrated in this image) are symmetric with respect to the direction of the current dipole, and due to this symmetry the radial currents do not produce any magnetic field outside the sphere. This rather surprising result can be demonstrated formally (see, e.g., Hämäläinen et al., 1993). In contrast to radial dipoles, tangential current dipoles are associated with volume currents that are *not* symmetric with respect to the primary current (and thereby also not with respect to the sphere) and *do* produce a net magnetic field outside the sphere. Note, however, that even in that case the magnetic field outside the sphere can be computed directly from the size of the primary current, without taking into account the volume currents.

Thus the magnetic field (MEG signal) produced by the three dipoles in Figure 1.4a is exactly the same as without the radial dipole (Figure 1.4b). Because all dipoles in the center of the sphere are radial, the external field is still the same even without the middle (deep) dipole (Figure 1.4c). In other words, all magnetic fields outside the ideal sphere arise from tangential currents only or from the tangential components of tilted (i.e., not perfectly tangential or radial) currents.

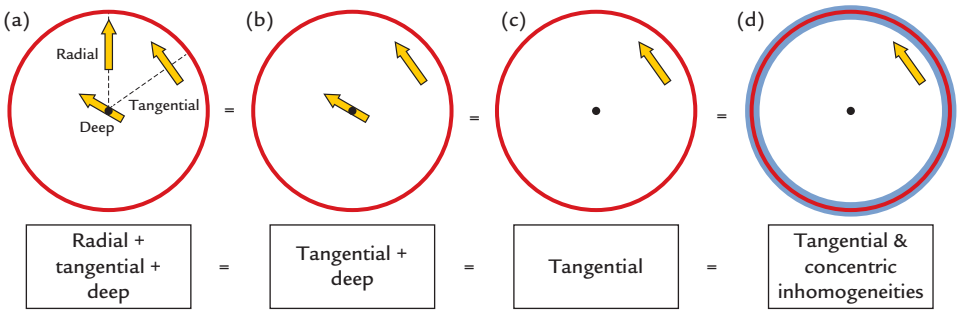

FIGURE 1.4. **MEG in a nutshell.** Panel (**a**) shows a radial, a tangential, and a deep dipole in a spherical volume conductor. The produced external magnetic field pattern will be identical for this panel and for panels (**b**)–(**d**), and even for panel **d**, where concentric inhomogeneities have been added to the sphere. See text for further explanation. Adapted and reprinted from Hari R, Levänen S, Raij T: Timing of human cortical functions during cognition: role of MEG. *Trends Cogn Sci* 2000, 4: 455–462. With permission from Elsevier.

Keep in mind that we are speaking here about a fundamental property of the generation of magnetic fields within a sphere, meaning that it is the current orientation with respect to the sphere that matters, and it is not possible to see magnetic fields produced by the radial currents by any manipulations, such as tilting the orientation of the MEG sensors (outside the head) with respect to the dipole orientation.

Another important point is that the external magnetic field remains the same even if the sphere is comprised of concentric shells of different electrical conductivities (Figure 1.4d). Concentric inhomogeneities mean that the conductivity $\boldsymbol{\sigma}$ (see Chapter 3) is a function of the radius $\boldsymbol{r}$ only: $\boldsymbol{\sigma}(\boldsymbol{x}) = \boldsymbol{\sigma}(\boldsymbol{r})$, where x is a point in the medium. Here the brain, the cerebrospinal fluid, the skull, and the scalp can be considered to form concentric inhomogeneities.

We can thus say that MEG sees directly into the brain, without distortion by the intervening tissues, and we are left with the notion that—in a sphere that contains only concentric shells of electric inhomogeneities—solely tangential currents (or the tangential components of tilted currents) will contribute to MEG signals measured outside the sphere. Although the real head is not an ideal sphere, these main principles are most useful in understanding the neuronal contributions to the MEG signals.

Figure 1.5 continues these MEG-in-a-nutshell considerations. Panel (a) shows that the magnetic field for two currents of opposite directions at the same place is equal in size but opposite in polarity. Panel (b) demonstrates the linear additivity of the magnetic fields. Panel (c) repeats the message from Figure 1.4 in that radial currents do not produce any magnetic field outside the sphere. As a consequence, one can add to the sphere any number

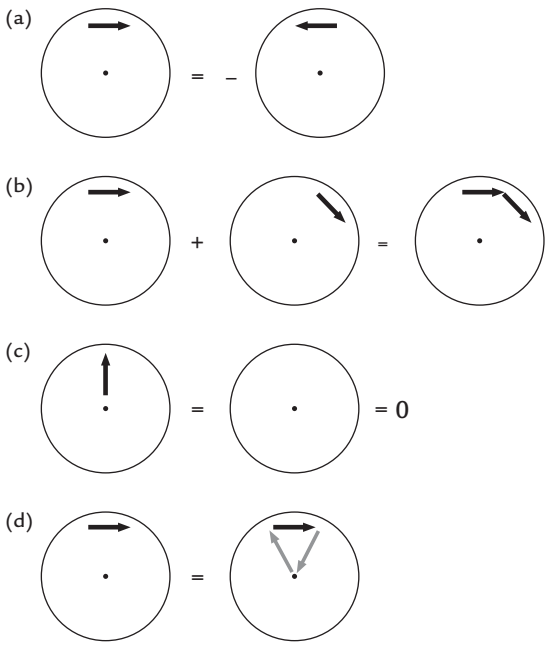

FIGURE 1.5. Schematic presentation of magnetic fields associated with different current dipole configurations. (a) If the current flow reverses, the polarity of the magnetic field will reverse as well. (b) Superposition principle of magnetic fields. (c) Radial currents do not produce any external magnetic field. (d) Since radial currents do not produce any magnetic field, one can add those to any existing current distributions. Here the gray arrows (that pass the origin of the sphere) have replaced volume currents. See text for further explanation.

of radial currents as was done in panel (d), where a tangential current was replaced by a current loop running via the origin of the sphere. The formed current loop will produce a magnetic field that is equal to that produced by the tangential current dipole (Hari & Ilmoniemi, 1986). This equivalence has been used to build "dry phantoms" to test the accuracy of MEG localization: a tangential current dipole in a sphere can be replaced with a triangular current loop that passes through the origin of the sphere.

For EEG, the situation is different because all of the currents, of different orientations and different depths, contribute to the EEG potentials on the surface of the sphere. Moreover, the electric inhomogeneities (such as the skull and scalp) dampen and smear the potential distribution, resulting in the more widespread pattern for EEG than MEG as was shown in Figure 1.2. For radial currents, the maximum scalp potentials are just above the current location, whereas tangential currents produce potential maxima of different polarities at the two ends of the current dipole. For both MEG and EEG, the distance between the two extrema depends on the depth of the tangential current.

An interesting point to add is that, compared with the identical dipole in an infinitely large homogeneous conductor, the interface between the head and air (or brain and skull) in fact magnifies the potential at the surface by a factor of three (Hari & Katila, 1982). We will fine-tune these general principles about MEG/EEG generation in the following chapters when the anatomy and physiology of the human brain are taken into account.

The main source currents of both MEG and EEG arise in the cortical pyramidal neurons. A pyramidal neuron (see Figures 1.6 and 2.1) consists of a cell body (soma), dendrites that receive input from other cells, and an axon that carries the neuron's impulse to other neurons. Because of their shape (elongated apical dendrites) and alignment perpendicular to the cortical surface, the pyramidal neurons effectively generate intracellular currents perpendicular to the cortical surface. This critical spatial alignment sets the scene for microscopic currents associated with each apical dendrite to collectively sum to (detectable) macroscopic net currents at the cortical surface, so that each pyramidal neuron can be considered to be a tiny current dipole, as shown in Figure 1.6.

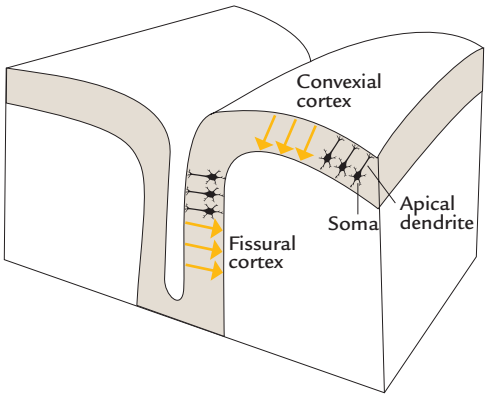

FIGURE 1.6. **Convexial and fissural currents.** Schematic representation of neurons (black) with the main axis oriented perpendicular to the cortical surface. The somas of the neurons are in the deeper layers of cortex, and the current flow following excitation of the apical dendrites can be modeled as intracellular current dipoles (yellow arrows). Note that the current flow may be of the opposite direction, depending on the type of postsynaptic current (excitatory/inhibitory) and the locations of synapses (see Figure 2.1).

Nonpyramidal neurons lack these essential geometric hallmarks and therefore contribute very little to measurable MEG/EEG signals. These geometric proclivities of pyramidal neurons thus yield mainly radial current sources in the convexial cortex (the upper surfaces of the gyri) and tangential currents in the walls of cortical fissures (or sulci); see Figure 1.6.

EEG measures voltage differences between different parts of the scalp and is most sensitive to currents in convexial cortex just under the electrode, but in addition to these superficial radial currents, it can also sense tangential currents and (strong) deep currents. For example, auditory-evoked brainstem responses can be picked up far more easily with EEG than with MEG. However, the broad spatial sensitivity of EEG also means that it may be difficult to discern multiple active sources from the recorded signals.

The high sensitivity (and, in the case of a sphere, even selectivity) of MEG to tangential currents means that MEG mainly measures activity occurring in the walls of cortical fissures. This is an advantage, as about two-thirds of the cerebral cortex is located within fissures (including all primary sensory cortices) that are difficult places to reach even with intracranial recordings. Because of MEG's insensitivity to electric inhomogeneities, the inverse solution (computing the most likely generator currents, or the "sources") on the basis of the measured signal patterns is more straightforward for MEG than for EEG. For EEG, additional assumptions are required about the conductivities of different head-tissue layers.

An additional important difference between MEG and EEG is that EEG recordings measure voltage differences (potentials) *between* two recording sites (i.e., between "active" and "reference" electrodes; see Chapter 5), whereas MEG recordings provide information on the magnetic flux or its gradient exactly at the measurement site.

A major advantage of EEG is that it is relatively inexpensive and portable, relative to MEG, and it can be more easily incorporated for simultaneous use with functional magnetic resonance imaging (fMRI), transcranial magnetic stimulation, and transcranial direct current stimulation.

All methods have their own characteristics that make them appropriate tools for some purposes but not for others. For cutting, for example, scissors are the tool of choice for making tiny paper decorations, whereas a sharp knife would be preferred for slicing an apple into many pieces. Similarly, all functional neuroimaging methods have their own niches. MEG and EEG are optimal and complementary methods to reveal the brain's neurodynamics, the temporal variations of brain activity at a (sub)millisecond time scale. In principle, simultaneous recordings of MEG and EEG provide the most complete direct picture of the ongoing neuronal mass activity in the human brain.

STRUCTURE OF THIS PRIMER

After this brief introduction to MEG and EEG, we begin our tour with a concise survey of brain structure and function, which is necessary to place MEG and EEG results into the proper perspective, and we discuss the neural currents underlying MEG and EEG (Chapter 2). We then proceed to the basic physics of electricity, currents, volume conduction, magnetic fields, and superconductivity (Chapter 3). We next review briefly the history of EEG and MEG recordings and give an overview of the most common spontaneous and evoked EEG and MEG signals (Chapter 4), which completes Section 1 of the book.

Section 2 deals with the practicalities of acquiring and analyzing data. In Chapters 5 and 6, we discuss instrumentation, including shielding and stimulators, as well as practical aspects of sound MEG/EEG experimentation. We next, in Chapters 7 and 8, describe data acquisition and preprocessing of signals and discuss common artifacts and their prevention

and elimination. In Chapter 9, we proceed to common methods of data analysis, including signal averaging, some single-trial analysis methods, and source analysis.

In Section 3, in Chapters 10 through 18, we provide examples of various MEG and EEG signals, including spontaneous and stimulus-, task-, and event-related activity, always attempting to discuss MEG and EEG findings side by side. We also describe simultaneous recordings from two or more individuals ("hyperscanning"). We briefly examine the use of MEG/EEG in various brain disorders in Chapter 19. We discuss considerations for using MEG/EEG to study brain function in Chapter 20 and briefly discuss some pitfalls of data interpretation, some of which can result from improper filtering, interference between several neural sources, and the spread of the same activity to far-away sensors. Finally, we look to the future and special state-of-the-art techniques (Chapter 21). The most recent advances in MEG and EEG research include applications of machine learning, and the use of peripheral measures (e.g., heart-rate variability, hand acceleration, muscular activity, etc.) as correlates of brain signals. We also look to future improvements in data acquisition and analysis.

We hope that after reading this primer you, our reader, independent of your education and training, will be on equal footing with the members of your multidisciplinary MEG/EEG research team as far as the basics of these methods are concerned. Your metaphorical toolbox will then contain—in addition to a hammer for nails—a screwdriver for screws, a wrench for nuts, and whatever other gadgets and gizmos that might be needed.

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CHAPTER 2

INSIGHTS INTO THE HUMAN BRAIN

Anatomy is usually right but boring,
physiology is usually wrong but exciting.

Semir Zeki

We know almost everything about the brain,
except how it works.

Rodolfo Llinas

The aim of MEG and EEG recordings is to obtain new information about human brain function, especially with respect to the millisecond-range neurodynamics in both the healthy and diseased brain. Here we review some basic principles of human brain structure and function that may be relevant for the design and interpretation of MEG and EEG recordings.

OVERVIEW OF THE HUMAN BRAIN

Our brains are the product of evolution, individual development (ontogenesis), and culture. Stated briefly, the brain is an organ that predicts the future on the basis of the past, thereby helping the individual survive and perpetuate the species. Genetic information settles the main framework for brain development, but it is the individual–environment interaction that shapes the human brain and mind throughout life. The healthy human brain remains plastic during the entire lifespan, allowing the individual to keep gathering and remembering information and to learn new skills.

Different brain regions are connected to other parts of the brain as well as to the sensory and motor periphery by fibers (axons) that form the brain's white matter. The white color refers to the visual appearance of myelin sheaths that surround a large number of these fibers and allow them to conduct impulses faster than without myelin sheaths.

In newborns and infants, maturation of cortical areas can be judged on the basis of myelination (Dehaene-Lambertz & Spelke, 2015). The earliest brain areas to mature, already before birth, are the primary sensory projection cortices and the visual-motion-sensitive cortical area MT/V5. The maturation of the corpus callosum, the superhighway of information transfer between the hemispheres, continues up to early adulthood (Tanaka-Arakawa et al., 2015). Follow-up studies with different structural magnetic resonance imaging (MRI) methods indicate that brain development beyond infancy progresses by thinning of the different areas of cortex in a specific order (Gogtay et al., 2004).

Whereas myelinization was originally quantified by staining of postmortem histological samples, special MRI sequences can now estimate myelin content noninvasively (Glasser & Van Essen, 2011).

HOW TO OBTAIN INFORMATION ABOUT BRAIN FUNCTION

Historically, brain injuries and the accompanying sensorimotor and cognitive deficits have been informative regarding the putative functional roles of specific brain regions, and quintessential information relating to brain–behavior relationships has been obtained from animal neurophysiology. Most recently, the emergence of various neuroimaging methods has allowed noninvasive studies of the structure and function of the human brain in living individuals to be performed, in contrast to the previous focus on postmortem studies of brain structure.

We can now use fMRI, positron emission tomography, scalp EEG, intracranial EEG, MEG, and near infrared spectroscopy for recordings of brain activity. The information obtained by these methods can be converged with results of transcranial magnetic stimulation (TMS), transcranial direct current stimulation, or intracranial electric brain stimulation that may perturb or stimulate certain brain functions.

Many neuroimaging manuscripts depict beautifully colored "blobs" of brain activity related to various stimuli and tasks. However, we must remember that only lesions can be localized, not functions. Similarly, as the lack of electricity after a broken fuse does not mean that the fuse generates the electricity, a behavioral symptom after a brain lesion (or transient suppression of activity by direct electrical stimulation of the cortex or by TMS may not have anything to do with the real function of that brain area. Local lesions may also have severed the connections between brain regions so that the behavioral manifestations may arise from other parts of the brain. Consider, for example, the famous case of Phineas Gage, in whom a rather restricted brain lesion in the prefrontal cortex resulted in dramatic deficits in affect and cognition, likely because the lesion also affected the brain's widespread interareal connections, thus causing symptoms that cannot be explained by the lesion site only (Van Horn et al., 2012).

Information about cognitive functions can be obtained at various temporal and spatial scales. In addition to brain measurements, it is always important to carefully describe the behavioral phenomena of interest and their changes under controlled modifications of the tasks. Without sufficient characterization of behavioral phenomena, especially motor behavior and its context, appropriate interpretation of neural activity may be compromised. In certain experiments, it may be useful to also record other signals of interest (e.g., heart rate, pupil dilation, etc.) to follow changes in the subject's physiological state.

TIMING IN HUMAN BEHAVIOR

Accurate timing is important for many brain processes devoted to perception, action, and cognition. The relevant time scales vary from tens of microseconds (e.g., in directional hearing) to tens and hundreds of milliseconds (e.g., in cortical processing of sensory information) to seconds and minutes. Table 2.1 gives some examples of temporal scales of human behavior and some neuronal events.

Although millisecond timing is needed, for example, for dancing to a fast salsa rhythm, multisensory asynchrony—such as the time lag between voice and visual mouth movements in a movie—can be tolerated for surprisingly long time spans of up to 100 to 250 ms (see Chapter 15).

TABLE 2.1 Comparison of different temporal scales of human behavior and neural activity

• Auditory localization	50 μs
• Auditory click separation	1 ms
• Action potential	1–3 ms
• One cycle of gamma oscillation	25 ms
• One cycle of beta oscillation	50 ms
• One cycle of alpha oscillation	100 ms
• Reaction time	150–300 ms
• Multisensory asynchrony	100–250 ms
• Attentional blink	500 ms
• Preparation for motor action	500–2000 ms

Note: ms = milliseconds; μs = microseconds.

The relevant time windows of brain information processing seem to be hierarchically organized and supported by spatially different networks, so that the shortest time windows (associated with the most rapid processing) occur in brain areas closest to sensory projection cortices and the longest time windows in nonsensory brain regions. This organizational principle has been demonstrated from seconds to tens of seconds using fMRI (Hasson et al., 2008) and from milliseconds to hundreds of milliseconds with MEG; the MEG data further indicate that multiple time windows can exist within the same brain area (Hari et al., 2010).

In general, slower brain rhythms can modulate faster ones, as "nested oscillations" (Hyafil et al., 2015). For example, during speech perception, specific integration windows exist for consonants (20–50 ms) and syllables (200–300 ms) (Boemio et al., 2005), as well as for phrases (up to 2 s) (Bourguignon et al., 2013). In several brain disorders, such as Parkinson's disease, temporal sequencing of action may slow down (Avanzino et al., 2013). MEG/EEG have just the right temporal sensitivity for monitoring these rapid changes.

FUNCTIONAL STRUCTURE OF THE HUMAN CEREBRAL CORTEX

The human cerebral cortex, a 3- to 4-mm thick layer on the brain surface and the main target of MEG and EEG studies, is only about 1.5% of body weight but consumes about 15% of total blood flow (the whole brain uses about 20%). Lamination of pyramidal neurons differs between neocortex (that has six layers and comprises 90% of total cortical area) and allocortex (including the hippocampus and the olfactory cortex located in the mesial temporal lobes), which has only three or four layers.

In trying to understand how the brain works, keep in mind both the functional generality of the cerebral cortex as a whole and its variability from area to another. The functional generality suggests the existence of some kind of fundamental operations that are connected to the vertical (from depth to surface along the main orientation of the cortical pyramidal cells) organization of the cortex, whereas the diversity of "cytoarchitectonic" areas (that differ, e.g., in cell size and organization) may be the result of different afferent projection systems and efferent target structures, that is, the connections between the brain and the world.