12.1 Introduction

The treatment of certain complex neurological diseases, such as pharmacologically intractable epilepsy, brain tumors, and arteriovenous malformations, often includes surgical intervention. In all cases, accurate localization of the lesion to be resected is of paramount importance, and the margin between therapeutic treatment and debilitating side effects due to surgery is very narrow. Several additional factors contribute to the success of surgery, chief among which is the accurate identification of the cortical areas that are responsible for certain brain functions, such as sensation, movement, and speech. This latter procedure, known as functional brain mapping, is critical, because resection of such vital brain areas can have devastating results.
A number of noninvasive functional imaging modalities, including functional magnetic resonance imaging (fMRI) (Binder et al., 1997; Cuenod et al., 1995), positron emission tomography (PET) (O’Leary et al., 1996; Peterson et al., 1988), regional cerebral blood flow (rCBF) (Friberg, 1993), and single photon emission computed tomography (SPECT) (Gomez-Tortosa et al., 1994), can map brain functions with varying degrees of success. However, the most reliable approach to map the human brain still relies on direct electrical stimulation of the exposed cortex (Ojemann et al., 1989), a procedure that is highly invasive and unpleasant, and it is performed mostly intraoperatively on an awake patient.

Recently, however, completely noninvasive procedures have been successfully used for brain mapping (Breier et al., 2000; Ebersole and Wade, 1990; Gallen et al., 1994; Hamalainen et al., 1993; Papanicolaou et al., 1999; Zouridakis et al., 1998b). These procedures rely on the fact that performance of certain brain functions activates only a small population of cortical neurons whose activation gives rise to electromagnetic signals that can be recorded externally. The electrical aspects of brain activation are recorded in an electroencephalogram (EEG) by placing a set of electrodes on the scalp, while the corresponding magnetic aspects can be captured in a magnetoencephalogram (MEG) by placing an array of coils close to the head.

Electrical or magnetic source imaging (SI) refers to the localization of the intracranial sources that give rise to externally recorded electrical or magnetic signals, respectively. This procedure is a form of functional imaging and combines the neurophysiological EEG or MEG data with structural MRI scans. That is, while MRI alone provides information on the brain’s anatomy, SI provides information about its function. Moreover, SI provides very high temporal and spatial resolution, which makes it far superior than any other functional imaging modality in that respect.

In this chapter we introduce the basic principles that make EEG- and MEG-based SI procedures possible, and the equipment used to accomplish it. Additionally, we provide a few concrete examples that demonstrate the usefulness of SI as a valuable clinical tool for functional brain mapping.

12.2 Neurophysiological Signals

12.2.1 Origin of Activity

When considering surface neurophysiological activity, two major aspects must be distinguished. The first one is the characterization of the sources underlying the observed signals. The human brain is composed of vast numbers of electrically active neurons and other supporting cells (e.g., glial cells) that are assembled in functional groups. In particular, the outer surface of the brain, the cerebral cortex, consists of a thin and highly compact intricate network of cells arranged in layers (Kandel et al., 1991). The average thickness of the cortex is 2.5 mm, and its density reaches an impressive 10^5 cells per millimeter which form approximately 10^15 synapses. Conceptually, the building block of the cerebral cortex is a column, a structure of neurons arranged radially to the head surface, with a diameter of about 0.5 to 3 mm (Kelly, 1991). A specific type of neurons in a column, called pyramidal cells, have a linear structure with dendrites that are arranged parallel to each other. In the resting state, each of these neurons is negatively polarized relative to the surrounding electrolyte solution, because of the activity of the cell membrane. When a cell is in the active state, large quantities of positive and negative ions — namely, sodium (Na^+), potassium (K^+), and chloride (Cl^-) — cross the cell membrane, moving from the intracellular to the extracellular fluid, and vice versa. For all practical purposes, this ion movement is equivalent to a current flow, and it is responsible for all electrophysiological signals recorded externally. In particular, the electrical potentials and the magnetic fields recorded on the scalp as the EEG and MEG, respectively, result mainly from the temporal and spatial summation of postsynaptic activity generated along the apical dendrites of the pyramidal neurons. These fields represent the synchronous activation of a large number of neurons, estimated to be between 10^4 and 10^5 cells (Okada et al., 1992; Williamson and Kaufman, 1987).

The second aspect of surface neurophysiological activity is the influence of the tissues surrounding the active neurons, the so-called volume conductor effects. A detailed analysis of the relationship between the intracranial sources and the extracranially recorded signals is beyond the scope of this chapter, but
excellent reviews can be found elsewhere (Hamalainen et al., 1993; Williamson and Kaufman, 1987). Briefly, neural activity can be represented mathematically as a current density in a closed volume of finite conductivity. Outside this volume, the conductivity and current density are zero. The intracellular currents give rise to an electric field outside the cells which, in turn, results in currents that flow passively through the rest of the conducting medium. Thus, the total current density can be divided into two components, primary (intracellular) and secondary (extracellular). The primary currents are more interesting in neurophysiology, because they are associated directly with cell activation. Under specific conditions (Lewine, 1990), that are fairly well approximated in many practical applications, it can be assumed that the electromagnetic fields recorded on the scalp as the familiar EEG and MEG are associated mainly with the primary (intracellular) currents, and thus they represent cell activation.

The relationship between the intracranial sources and the extracranially recorded biological signals can be computed as a function of the distance between the observation point and the source location. Both the magnetic field and the potential are inversely proportional to the square of this distance.

12.2.2 Localization of the Sources

Determining the extracranial potentials and magnetic fields that result from the intracranial current sources is known as the forward problem. Conversely, the inverse problem requires localization of the intracranial current sources that give rise to the externally recorded electrical potentials (EEG) and magnetic fields (MEG). Unfortunately, the inverse problem has no unique solution, as the corresponding mathematical equations can be satisfied by an infinite number of possible source configurations. To overcome this limitation, it is necessary to solve a “constrained inverse problem” and make assumptions for both the sources and the surrounding head tissues (Morse and Feshbach, 1963). These assumptions must be neurophysiologically based, otherwise the results computed and their interpretation may be completely erroneous (Jayakar et al., 1991; Nunez et al., 1991). A typical approach involves the so-called “quasi-static” approximation (Plonsey and Heppner, 1967) under which all potentials and currents at any given instant in time are determined by the properties of the sources at that time only. Moreover, the various brain tissues are assumed to be linear and completely characterized by their electrical conductivity, which is frequency independent. The medium can be inhomogeneous, if its conductivity is different for different compartments, and anisotropic, if the conductivity of the tissues is different along different directions in the three-dimensional space.

12.3 Mathematical Modeling

12.3.1 Source Models

Over the past several years, many different approaches have been developed to identify the sources that explain the fields recorded on the head surface. The most common approach has been to describe the activation of a well-localized (Nunez et al., 1991) small population of neurons at a particular point in time as a single equivalent current dipole. Indeed, when a neuron is activated, ion currents flow through it and this “electrical generator” can be modeled as a small current dipole, with a moment of about $10^{-13}$ A m. A schematic diagram of such an arrangement is shown in Figure 12.1.

However, to identify the sources that account for a complex field distribution over a time interval, a series of single dipoles is required (Supek and Aine, 1993). These dipoles can move in position and orientation over time, and when displayed on a single image, they appear as a moving dipole. Another approach is to consider current distributions in the brain (Ioannides et al., 1990; Morse and Feshbach, 1963; Okada et al., 1992; Wang et al., 1992), and estimate several fixed dipoles at discrete points within a region of interest. Spatiotemporal source modeling (Baumgartner et al., 1991; Scherg, 1992; Scherg and von Cramon, 1985) is yet another approach that takes into consideration overlapping activity of multiple generators. In this case, dipoles are fixed in location and orientation, but they can vary over time in strength and polarity to explain the temporal evolution of the recorded fields.
In general, solutions for multiple-dipole sources are much less reliable than those for a single dipole (Cuffin, 1998), because in the former case the solutions provided are very sensitive to noise. Thus, most clinical applications still use single-dipole approaches.

12.3.2 Volume Conductor Models

Volume conductor models have evolved from extremely simple (Rush and Driscoll, 1978) to very realistic and computationally intensive ones (Fender, 1991). The first and simplest model was that of an infinite, homogeneous, isotropic medium. The next sophistication level considered a homogeneous but bounded medium (specifically, a sphere) as a head model (Wilson and Bayley, 1950). Later on, to account for the various tissue layers within the head, several concentric-sphere models were developed (Ruth and Driscoll, 1968; Schneider, 1972; Witmer et al., 1972) that included three concentric spheres to account for the scalp, skull, and the brain. More recently, however, additional approaches, such as the eccentric-sphere model (Mejis and Peters, 1987) and the four-shell model, have been proposed. The latter uses a cerebrospinal fluid layer underneath the skull, and it is especially useful for hydrocephalic patients (Nishijo et al., 1996).

However, more realistic head models can be obtained if, instead of using arbitrary spheres, MRIs are employed to determine the curvature of a particular subject’s head and fit the spheres of the multicompart ment model (Lopes da Silva et al., 1991). More realistic models computed entirely from MRIs (Mejis and Peters, 1987) are implemented using numerical techniques, such as the boundary element method (BEM) (Mejis et al., 1989) and the finite element method (FEM). Finally, realistic head models that account also for the effects of anisotropy in the electrical conductivity have been developed (de Munck, 1988; Zhou and van Oosterom, 1991).

12.3.3 Source Estimation Procedure

Initially, inverse source localization procedures were implemented on spherical models (Rush and Driscoll, 1978; Smith et al., 1993) and they were later extended to work on realistic geometry. In the case of a single-current dipole, to identify the intracranial sources that explain the fields recorded on the head surface, the procedure takes the measured values from all sensors at a given instant in time and searches, using iterative minimization techniques, for an equivalent dipole within the head that could generate such fields (Henderson et al., 1975; Kavanagh et al., 1978; Schneider, 1972; Sidman et
al., 1978). Techniques such as the brain electrical source analysis (BESA) (Jirsa et al., 2000) and CURRY (Neuroscan, El Paso, TX) are iterative with automatic picking of dipole sources and define one dipole for each point in time.

In more general cases, the localization procedure starts with some initial estimate of the distributed sources and then recursively enhances the strength of some of the elements, while decreasing the strength of the rest of the elements until they become zero. In the end, only a small number of elements will remain nonzero, yielding a localized solution. This method is implemented, for example, in the FOCUSS (Gorodnitsky et al., 1995) and LORETA (Pascual-Marqui et al., 1994) algorithms.

Another approach to source localization employs a spatiotemporal model, under the assumption that there are several dipolar sources that maintain their position and orientation fixed, while they vary only their amplitude as a function of time. Rather than fitting dipoles to measurements from one instant in time, dipoles are fitted by minimizing the residual least-square error over the entire time interval (Scherg and von Cramon, 1985). More advanced spatiotemporal approaches, such as the multiple signal classification algorithm (MUSIC) (Mosher et al., 1992), have also been developed, whereby the algorithm searches for a single dipole through the three-dimensional head volume. To localize the source, the user must search the head volume for local peaks. Extensions of this algorithm automate this search through a recursive approach (Mosher and Leahy, 1993).

12.4 Neurophysiological Recordings

12.4.1 Electroencephalography — EEG

The EEG is a record of the electrical aspects of neurophysiological activity. More specifically, a one-channel EEG represents the potential difference between two sites on the head, and requires two electrodes connected to the input of a differential amplifier — one active and one for reference. These electrodes are typically gold-plated or sintered Ag-AgCl, and they are attached to the scalp with a special glue (collodion) or electrolyte gel. Typically, the active electrode is placed close to the structures of interest, whereas the reference electrode is placed at a distant location (usually on the left or linked mastoids, behind the ears). This type of connection is called monopolar, or referential. When both the active and the reference electrodes are placed close to the structures of interest, the placement is called bipolar or differential. The advantage of this latter connection is that far-field activity common to both electrodes is cancelled and thus sharp localizations of events can be obtained. Alternatively, the reference electrode can be connected to a circuit that measures the average activity of all electrodes to obtain a recording with an average reference. The common electrical connection for the electrical circuitry of the recording equipment is called the ground, and all voltages are measured with reference to it. The patient is also connected to this point through a separate electrode typically placed on the patient’s forehead. The potential differences in each channel are amplified by high-gain, differential amplifiers, and then it is either displayed on a monitor, saved on a hard disk, or simply plotted on paper, depending on the technology used.

For clinical recordings, electrodes are arranged on the head in a montage that follows the 10–20 international placement system and its extensions. Routine clinical equipment employs about 21 electrodes, whereas more recent systems specialized primarily for research may include hundreds of electrodes. In this case, arrays of electrodes are arranged on a cap for convenience, and these densely sampled recordings provide the so-called dense-array EEG, or dEEG. A system that uses 256 channels is described next.

12.4.1.1 EEG Recording Device

The latest dEEG systems incorporate several unique features: they offer high spatial sampling with up to 256 recording channels; they are portable, and often the complete set of 256 amplifiers is battery operated and is about the size of a book; they can use active electrodes for noise cancellation, in which case each electrode incorporates a micropreamplifier that preconditions the EEG signals before transmission to the main amplifiers through the electrode leads, and this eliminates the need for a shielded room; and finally, they provide very high sampling rates of up to 5 kHz per channel.
The active electrode is a sensor with a very low output impedance. By integrating the first amplifier stage with a regular electrode, extremely low-noise measurements are now possible without any skin preparation. The noise levels achieved can be as low as the thermal noise of the electrode impedance, which is the theoretically minimum level. Active electrodes eliminate all problems associated with high electrode impedances, cable shielding, capacitive coupling between the cables, and sources of interference, as well as any artifacts due to cable or connector movements. The amplifiers of a dEEG system (ActiveTwo, BioSemi, the Netherlands) available in our lab, along with an active electrode and a cap with the electrode holders, are shown in Figure 12.2.

12.4.2 Magnetoencephalography — MEG

The MEG measures the extracranial magnetic fields produced by intracranial electrical currents. Neuro-magnetic signals are many orders of magnitude weaker than the ambient magnetic noise, which is due to the earth's field and to the presence of ferromagnetic objects and electrical instrumentation. Typical scalp-recorded magnetic fields have a peak amplitude of about 100 fT (Gomez-Tortosa et al., 1994; Lewine, 1990), whereas environmental electromagnetic noise in a hospital (power lines, elevators, MRI magnets, etc.) may be as high as 1 T $\left(10^{15} \text{ fT}\right)$ in extreme cases (Lewine, 1990). Therefore, to detect this kind of biological activity, it is necessary to use highly sensitive instrumentation and, at the same time, attempt to eliminate extraneous magnetic fields.

12.4.2.1 MEG Recording Device

MEG measurements were practically impossible before the introduction of superconductive instrumentation. The latest generation of biomagnetometers are composed of large arrays of pick-up coils, each of which is connected to a SQUID (superconducting quantum interference device) that acts as a very low noise, ultrahigh gain, current-to-voltage converter. The SQUIDs and induction coils are immersed in liquid helium to maintain a superconducting state. This type of device can detect even very small changes in magnetic flux, such as the one resulting from neurophysiological activity. Figure 12.3 shows a schematic diagram of a multisensor MEG system along with a detection coil and a SQUID of a single channel.

FIGURE 12.2 Active electrodes, electrode cap, and amplifiers of a portable dEEG system with 256 channels.
To reduce the amount of extraneous magnetic noise, MEG systems are operated in specially designed magnetically shielded rooms (Gallen et al., 1994). Additional improvements in the quality of the MEG signals are obtained by selecting an appropriate type for the detection coils. Coils can be single-loop magnetometers that measure the magnetic field directly, and first-, second-, or third-order gradiometers that consist of two or more loops that measure spatial changes of magnetic field (Flynn, 1994). Various examples of coils for both planar and axial geometry are shown in Figure 12.4.

A gradiometer (Figure 12.4d) can selectively cancel out environmental magnetic noise, depending on its “baseline,” i.e., the distance between the two coils; because the magnetic fields decrease very rapidly with distance from the source, fields generated by a neural source close to the gradiometer will be detected with different strengths in each loop, and therefore they will induce currents of different magnitude in the two loops, thus resulting in a nonzero net current in the gradiometer. On the other hand, fields generated far away from the gradiometer will be practically uniform in space and will result in zero net current.

Because of the sensitivity of MEG recordings to noise, patients implanted with electrically active medical devices such as cardiac pacemakers, neurostimulators, and infusion pumps cannot be studied with MEG, due to the electrical interference from the implanted devices. Also, equipment entering the room must be screened for large metallic components or electromagnetic activity that could introduce artifactual signals.

The cost and complexity of instrumentation led to the initial development of MEG systems containing only a few channels. Recently, however, whole-head systems with large arrays comprising 248 magnetometers have been developed (model 360WH, 4DNeuroimaging, San Diego, CA). An example of a 148-channel system is shown in Figure 12.5. The need for cryogenics, and for a shielded room and a rigid helmet-type sensor limit the scope of applications of the MEG-based mapping procedures.

**FIGURE 12.3** Schematic diagram of a multisensor MEG system (left) along with a detection coil and SQUID in a single channel (right).

**FIGURE 12.4** MEG detection coils include planar (a) magnetometers and (b) gradiometers, and axial (c) magnetometers and (d) gradiometers. In a gradiometer, a uniform field $B$ creates currents $J$ and $-J$ of opposite polarity a produces a zero net signal.
12.5 Data Analysis

12.5.1 Surface Maps
Since both EEG and MEG activity have a common basis, their analyses can be carried out using similar methods. During the last 30 years, new techniques, such as color mapping of activity distribution over the scalp (Desmedt et al., 1987; Duffy et al., 1979), have shifted the focus from an analysis of waveforms, derived at selected scalp sites, to the spatial distribution over the entire scalp, at particular points in time. The recording sensors typically span a two-dimensional surface over the skull, and each sensor measures a time series. When these measurements are interpolated and color-coded to provide a spatially continuous representation of the measurements, a so-called topographic scalp map is obtained at each time point. Figure 12.6 shows the location of the sensors on the head and a three-dimensional map of the electrical fields corresponding to the peak of the N1 auditory component.

Topographic analysis is either done qualitatively, by interpreting focal maxima and minima in the map, or quantitatively by dipole localization methods (Brandt, 1992). Alternatively, a combined spatiotemporal approach, where topographic information over different instances in time, called a space-time series, is taken for source localization.

Recently, much effort has been made in the development of source imaging techniques based on high-resolution or dense-array EEG (dEEG). For example, techniques such as scalp Laplacian mapping and cortical imaging attempt to restore the high-frequency content of brain electrical activity that is smeared and distorted by the low-conductivity skull (Babiloni et al., 1996; He et al., 1995; Hjorth, 1975; Le et al., 1994). These techniques can enhance the spatial resolution of the EEG by deconvolving the low-pass spatial filtering effect of the head volume conduction (Freeman, 1980; He et al., 1996; Sidman et al., 1992). Since a surface cortical map lies closer to the actual sources, its potential distribution may provide more direct view of the neural sources (Fender, 1991; Jayakar et al., 1991).
12.5.2 Source Imaging Procedure

The SI procedure consists of several steps that culminate in the display of functional information obtained using MEG or EEG onto high-resolution anatomic images typically obtained by MRI. For this final step, it is necessary to translate EEG/MEG locations into MRI coordinates.

The precise location of the measurement points on the scalp is determined electronically with reference to a Cartesian coordinate system anchored on three landmarks (fiducial points) on each subject’s head: two external ear canal points and the nasion. The line passing through the two pre-auricular points defines the y-axis of the system. The line perpendicular to the y-axis passing through the nasion defines the x-axis, and the line perpendicular to the x-y plane passing through the x-y origin defines the z-axis.

The EEG/MEG anatomic reference frame is established electronically: a set of three receivers triangulate the signal from a stylus-type transmitter placed successively at several reference points on the subject’s head (typically the three fiducial points, the vertex, and the inion). Additionally, small vitamin E-containing capsules visible on MRI are placed on the fiducials. The locations of the common markers on the MR images and the EEG/MEG measurements serve for translating EEG/MEG locations into the MRI reference frame. Validation studies have shown that the accuracy of this approach can be as high as a few millimeters (Gallen et al., 1994). The same stylus transmitter can be used to define the curvature of the head by tracing its surface.

After the anatomic reference frame has been established, the fiducial points registered, and the patient’s head digitized, the actual recordings are obtained. The latter consist of time-varying measurements at each detector position. The data undergo further analyses that allow the sources underlying the recorded activity to be localized.

The equivalent current dipole (ECD) model yields a description of the instantaneous current dipole in terms of its location, strength, and orientation, along with an estimate of its reliability (confidence volume). Even though there is some variation across labs regarding acceptance criteria for the dipole solutions, a high correlation between data and model and a small confidence volume are always desirable. It is, therefore, possible to select a set of “best-fitting dipoles” to describe the data.

Once the best fitting dipoles have been identified, they are co-registered onto the subject’s MRI scan. The resulting images are then printed on MRI films with different symbols and colors, each corresponding to a distinct type of neurophysiological activity.
12.5.3 Mapping-Based on EEG or MEG

Both theory and experiment suggest that the MEG offers no significant advantage over the EEG (Cohen and Cuffin, 1991). MEG systems, however, are very expensive (total cost about $3 million); they require special cryogenic equipment, a magnetically shielded room, daily monitoring and maintenance, and they are available only in a handful of places around the world. Thus, the clinical usefulness of MEG can be very limited. On the contrary, in addition to the unique features mentioned earlier, the latest EEG systems incorporate several advantages: they are readily available in practically all clinical settings, and even the most sophisticated systems are much less expensive than MEG (total cost about $150,000). Therefore, successful brain mapping based on EEG can have a significant impact on patient care.

12.6 Application Examples

In general, the neurophysiological signals recorded on the surface of the head can be separated into two categories, spontaneous and elicited. For instance, epileptogenic discharges, such as interictal spikes, are events of the former type. The latter type of activity, known as evoked potentials in the case of EEG and evoked fields in the case of MEG, results from external stimulation of a specific sensory pathway, such as the auditory, the somatosensory, or the visual.

In the next sections we give examples from our studies during the past few years that illustrate the process of measuring surface activity and localizing the underlying sources.

12.6.1 Auditory Evoked Responses

The most prominent component of an evoked response obtained from transient auditory stimulation is the N1, which occurs at approximately 100 msec after stimulus onset. Due to the magnitude and consistency of the response, the sources underlying the N1 can be easily localized. Typically, neurophysiological signals are collected in “trials,” each of which consists of a few hundred milliseconds of activity prior to and following the stimulus onset. Single-trial responses are contaminated by noise, and to improve the signal-to-noise ratio, many trials are collected and averaged (typically between 100 and 500), using the stimulus onset as a time reference. The averaging approach relies on the assumption that the neuronal responses to all stimuli are identical. Additionally, to eliminate artifacts from periodic events, such as arterial pulsations or the 60-Hz power line interference, the interstimulus interval is randomly varied within a predefined range.

A variety of stimuli can elicit this component. We used pure tones of 1-kHz frequency and 50 msec duration (10-msec rise/fall and 30-msec plateau) that were delivered binaurally at an intensity of 80 dB nHL, and a mean stimulus rate of 0.4/sec (Iyer et al., 2002). Figure 12.7 shows an example of the resulting evoked response. Each of the superimposed tracings represents the activity recorded on one of the 256 channels, while the highlighted area denotes the peak of the N1 component. The three-dimensional surface maps superimposed on the subject’s MRI were reconstructed at the N1 peak, while the two dipoles indicate the cortical areas activated at that time.

The estimated sources underlying the N1 component were consistently found to be on the floor of the Sylvian fissure, i.e., in the area of the primary auditory cortex, as shown in Figure 12.8. The sources depicted correspond to activity during the highlighted interval around the N1 peak, as shown in Figure 12.7.

12.6.2 Somatosensory Evoked Responses

Localization of the central sulcus and the adjacent precentral and postcentral gyri is a fundamental objective in most mapping studies involving patients, when brain lesions are located in the parietal or frontal cortex. In a recent MEG study (Zouridakis et al., 1999), we used tactile stimulation to map the somatosensory cortex. Stimuli, i.e., bursts of compressed air, were delivered to a plastic diaphragm clipped to the patient’s fingertip, lip, or toe (Benzel et al., 1993). Approximately 500 single trials were required,
each composed of 100 msec of prestimulus and 100 msec of poststimulus activity. The interstimulus interval was approximately 500 msec. The average responses were digitally filtered with a bandpass filter between 2 and 40 Hz to eliminate high frequency noise, low frequency artifacts, and baseline drifts. At each time point between 30 and 75 msec following stimulus onset, dipole coordinates were obtained using a single-dipole model, and the ones with the best correlation between the measured and predicted fields were selected as the source location. Following this approach detailed mapping of the sensory homunculus can be achieved. In the case of EEG-based mapping, evoked responses are typically obtained using electrical stimulation. Figure 12.9 shows an example mapping, where left cortical areas are activated after stimulation of the subject’s right toe, little finger, index finger, thumb, and lower lip. The topographic arrangement of the areas identified resembles the “homunculus” typically seen in textbooks.

FIGURE 12.7 The N1 evoked potential resulting from auditory stimulation as recorded from 256 channels around the head (left), surface distribution of potentials at the N1 peak, and cortical areas activated during the highlighted portion of the N1 (right).

FIGURE 12.8 Localization of the auditory N1 component in the primary auditory area resulting from 1-kHz tone stimuli.
12.6.3 Visual Evoked Responses

In cases in which a lesion involves the occipital cortex, visual evoked responses can be used to assess preoperatively potential postoperative complications. Figure 12.10 shows an example of the cortical areas activated after stimulation of a patient’s left hemifield of view with a checkerboard pattern (check size $1.4^\circ$, pattern reversal rate 1/sec). The maximum magnetic responses were obtained in the right hemisphere, at a latency of approximately 130 msec; this is indicated by a square in the figure.

12.6.4 Epileptogenic Spike Localization

Ictal events, such as spikes, are very important for localizing epileptogenic regions in the brain. During the past several years, MEG has been used in clinical settings as a noninvasive method for localizing the sources of ictal activity (Sutherling and Barth, 1989), and more recently, due to the availability of large-array sensors,
the sources of interictal spikes (Aung et al., 1995; Papanicolaou et al., 1999). Several studies have suggested that noninvasive source imaging may reduce dependence on invasive electrophysiology for localization of epileptic foci (Papanicolaou et al., 1999; Smith et al., 1993; Zouridakis et al., 1999). Most MEG epilepsy studies report localizations of interictal activity only, because the large artifacts from muscle activity typically associated with seizures make localization of ictal sources extremely difficult. As an example, 2 sec of simultaneous MEG and EEG activity is shown in Figure 12.11 where, in addition to the artifacts resulting from the electrical activity of the heart, an interictal epileptic spike can be seen in both modalities.

Source localizations of several spikes obtained during this study are overlaid on MRI scans in Figure 12.12, where they are shown as triangles. In this case, a focal area of interictal epileptic activity over the lateral surface of the left posterior temporal lobe can be seen.

12.6.5 Language Mapping

Identifying brain regions involved in language functions is often an integral part of the evaluation that brain surgery patients. At present, this task is accomplished mostly through invasive techniques (Ojemann et al., 1989), but recently noninvasive techniques based on MEG have also been used. For example, using a task for continuous recognition of either printed or spoken single words, evoked responses were recorded for 1 sec after the onset of a word and the corresponding intracranial generators were modeled as single-current dipoles. The number of dipoles obtained in each hemisphere was used to quantify the extent of cerebral activation (Breier et al., 2000; Zouridakis et al., 1998a). The areas thus identified included the posterior part of the superior temporal gyrus, and the supramarginal and angular gyri. A characteristic MRI slice with the localized sources superimposed is shown in Figure 12.13, where the circles and triangles correspond to two repetitions of the same experimental task.

12.7 Concluding Remarks

The previous paragraphs give some examples of how SI is used for research and clinical purposes. Both MEG and EEG large-array systems have received Food and Drug Administration (FDA) approval for
clinical use, and they are gradually becoming available in many centers around the world. As new technological and computational advances come into existence, the clinical relevance of this technique becomes more apparent. In particular, in the case of epilepsy surgery, the usefulness of SI as a noninvasive tool to preoperatively delineate the extent of a lesion (to be resected) and of the eloquent cortex (to be preserved) has already been recognized (Breier et al., 2000; Gallen et al., 1994; Hamalainen et al., 1993; Papanicolaou et al., 1999; Zouridakis et al., 1998a, 1998b).

With the development of larger sensor arrays and of general source modeling algorithms, it is possible that future clinical applications of source imaging may be extended to include brain injury and stroke assessment, dementias, developmental disorders, as well as further characterization of higher cortical

**FIGURE 12.12** A cluster of epileptic interictal spikes localized in the left posterior temporal lobe.

**FIGURE 12.13** Cortical areas involved with receptive language. The circles and triangles correspond to two repetitions of the same experimental task.
areas involved in attention, memory, and cognition. As a result, these procedures may lead to safer, faster, and more cost-effective clinical interventions.

References


