FUNCTIONAL MAPPING

Elekta Neuromag®

# System Description

## Magnetoencephalographic and Electroencephalographic System

ELEKTA

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# 1. Overview

Elekta Neuromag® is a complete bioelectromagnetic measurement system for functional brain studies. The sensor system comprises 306 MEG-channels and 64, or optionally 128, EEG-channels, all registering the electromagnetic signatures of the intracranial ionic currents associated with the information processing. The MEG-sensor unit in it's floor-mounted gantry, the movable subject chair and bed together with the patient monitoring and stimulus delivery systems are contained in a magnetically shielded room. All hardware and software necessary to collect, analyze, display, archive and transport MEG/EEG data as well as to generate the necessary stimuli are included in the Elekta Neuromag®.

The 306 channel Elekta Neuromag® incorporates a unique vector sensor that comprises two orthogonal planar gradiometers and one magnetometer. The sensor combines the focal sensitivity of planar gradiometers with the more widespread sensitivity of magnetometers in an optimal fashion. This sensor is ideal for studies of local spontaneous neocortical activity and of deeper brain structures. Additionally, the magnetometer channels facilitate recordings of patients with small heads, such as young children, because the effect of the gap between the recording sensor and the sources of brain activity is minimized. The sensor element is manufactured with high precision on a silicon chip using thin-film technology, which provides the gradiometer coils superior immunity against ambient noise and outstanding uniformity of sensors. Owing to this geometric precision, the external disturbances sensed by the magnetometers can be eliminated using novel software based technique by which the magnetometers are gradiometrized up to arbitrary order. The quantitative performance criteria of Elekta Neuromag® sensor array are explained in detail in References 1 and 14 (*Nenonen et.al.)* of this technical description, and compared with other existing MEG arrays.

The integrated EEG-system consists of 60 single-ended channels and 4 differential channels, enabling recordings of EEG, EOG, EMG and ECG signals. The EEG-system includes a non-magnetic, MEG-compatible EEG cap. As an option, the number of both EEG-channels and the electrodes on the EEG cap can be increased up to 128 channels.

The Elekta Neuromag® system proposed here offers high spatial sampling of the magnetic field; the field is measured at 510 locations above the cortex by 510 coils configured into 306 independent MEG-channels. A high dynamic range up to 27 bits is obtained without flux splippage. The temporal sampling rate is 5 kHz as standard and 10 kHz as an option. All this is provided with extensive software capabilities for data acquisition, data manipulation, source modeling, anatomic visualization, and DICOM 3.0 based image transfer and retrieval.

The system and its predecessors are used extensively throughout the world, and have a proven track record in the areas of basic and clinical research; as of March 23$^{rd}$ 2005 altogether 38 such whole head units have been installed. Thus, Elekta is the worldwide market leader with its 36 % share of the installed base of the whole-head MEG devices.

The Elekta Neuromag® 306-channel MEG system represents the state-of-the-art of MEG/EEG systems, and a continuous upgrade-path will be provided to maintain parity with future generations of MEG systems. The installation of the system includes training of scientific and technical personnel in data acquisition and analysis as well as basic system maintenance and troubleshooting.

# 2. High performance sensor configuration

## 2.1 Optimal sensor configuration

The Elekta Neuromag® sensor configuration is radically different from the legacy MEG sensor arrays comprising of either axial wire-wound gradiometers or magnetometers. The design of the array is based on diligent studies and optimization using various performance criteria that have been presented over the last twenty years for evaluation of multichannel MEG devices.

In our design the field distribution is sampled by 510 pick-up loops at distinct locations over the cortex. The 510 independent pieces of information are combined into 306 data channels, 204 planar gradiometers and 102 magnetometers. This coil configuration optimally combines the focal sensitivity of the planar gradiometers (measuring the sideways gradients of the normal component $B_z$) and the widespread, spatially less specific, sensitivity of the magnetometers (measuring the normal component $B_z$). The shape of each of the two loops comprising a single planar gradiometer is a 26.8 mm x 10.0 mm rectangle, with a baseline of 17.0 mm. The magnetometer coil shapes are 21.0 mm x 21.0 mm squares.

With this geometry the Elekta Neuromag® sensor array offers the densest spatial sampling of biomagnetic field in the industry. The total sampling area of the pick-up loops is 1543 cm$^2$, 27% more than the total area covered by the array. This is possible because the pick-up loops in our triplet sensor element partially overlap. Owing to the ingenious combination of magnetometers and gradiometers, physical overlap provides true additional information. This feature is not feasible in wirewound axial gradiometer or magnetometer based arrays.

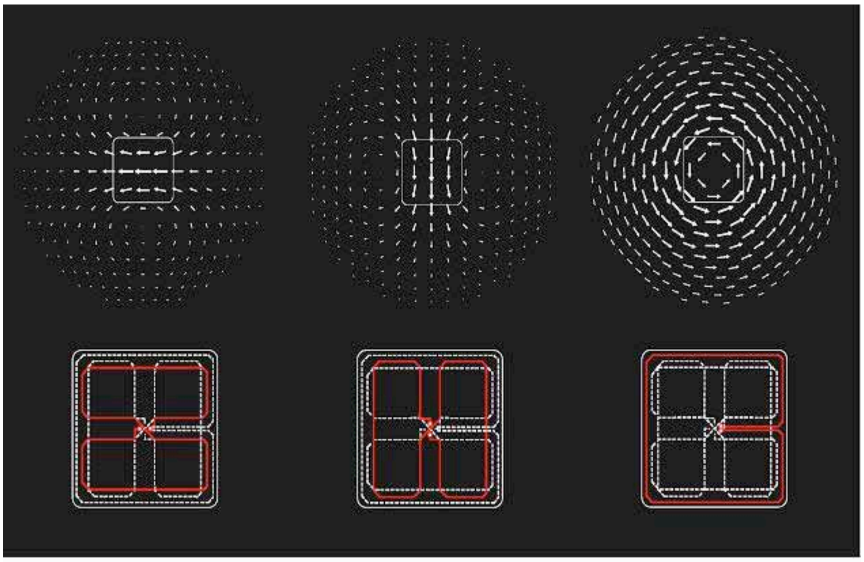

*Figure 1. Schematic presentation of the lead fields of the pick-up coils at the triple sensor unit.*

Figure 1 illustrates the lead fields (sensitivity patterns) of the two gradiometers and the magnetometer integrated on one Elekta Neuromag® sensor unit. The lead fields of the three channels in such a sensor element are orthogonal to each other. This means that despite of the overlapping pick-up loops the three channels of the sensor element convey orthogonal information: The signal in any one of the three channels can not be predicted from the signals of the other two.

In comparing the performance of various sensor arrays this orthogonality should be contrasted with the fact that the information conveyed by any group of three adjacent axial gradiometers, or magnetometers, in the competing sensor arrays is highly correlated: Given the signal of one of the channels the signals in the other two can be rather accurately predicted. This is because three adjacent axial gradiometers view the neural current distribution from nearly the same direction. Therefore, they do only slightly more than repeat the same measurement three times, especially in the densest arrays of such type. This means that the total amount of information obtained with the three channels is only slightly more than square root of three times the information obtained with a single axial channel, whereas, in the case of the triplet sensor, the three signals being independent due to the orthogonal lead fields, the three channels convey a total amount of information three times that of a single channel. This orthogonality of the information conveyed by the individual channels of the triple sensors of Elekta Neuromag® is crisply demonstrated in Figure 2.

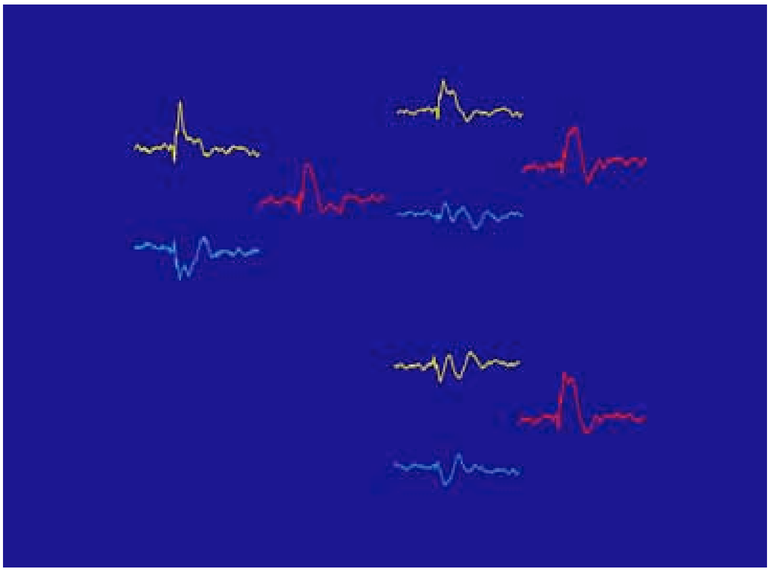

*Figure 2. Median nerve SEF responses from three adjacent Elekta Neuromag® triple sensor units demonstrating the orthogonality of the individual channels.*

The quantitative performance comparison between the entire whole head coverage sensor arrays can be put in exact mathematical form using Shannon´s theory of communication (Shannon & Weaver, 1949). In this calculation the geometry, sensitivity, and the noise of the channels are all taken into account in a consistent manner. The results of the comparison are presented in References 1 and 14 *(Nenonen et al.),* where it is shown (Fig. 5 of Reference 1) that the information conveyed by the Elekta Neuromag® 306-channel array, i.e. the channel capacity in bits per sample, is 30% higher than the information obtained by commercially available magnetometer (248 channels) and axial gradiometer (275 channels) based systems.

With this method we also find out that the placement of the three triple sensor pick-up coils concentrically on top of each other is *the optimal arrangement.* Shifting the centers of gravity of the three pick-up coils away from the common center actually leads to *lower degree of orthogonality and thus to reduced information transmission.*

In conclusion, the design of the Elekta Neuromag® MEG sensor array is based on a thorough study and optimization of the channel capacity. The superior performance of the triple sensor array resulting from this optimization is based on:

1) overlapping thin-film pick-up loops with low inductance and large total pick-up area, and a record low average sensor noise of 3 fT/√Hz on the average (see Figure 3), and
2) maximal degree of orthogonality between the lead fields of the individual channels.

In addition to maximized channel capacity the Elekta Neuromag® sensor array design offers other advantages that facilitate successful MEG recordings. Among the MEG users there is ongoing controversy on the advantages of gradiometers over magnetometers and vice versa. With the Elekta Neuromag® MEG system the advantages of both these basic sensor types are available. The triple sensor array optimally combines the focal sensitivity of 204 planar gradiometers and the widespread sensitivity of 102 magnetometers. Because arrays of both sensor types are available during all the recordings there is no need to speculate whether the phenomenon or signal seen/not seen would have been seen/not seen if magnetometers/gradiometers would have been available.

The number of each sensor type being lower than in the arrays containing only magnetometers or only axial gradiometers is more than compensated by the superior noise performance of the triple sensor channels: The amount of information obtained with a sensor array is roughly inversely proportional to the square of the average sensor noise. Therefore, 102 magnetometers having sensor noise of 3 fT/√Hz provide information at the same rate as (5/3)^2*102=283 magnetometers having average sensor noise of 5 fT/√Hz.

To demonstrate the ultimate performance of the Elekta Neuromag® sensor array reprints describing two exceptionally demanding MEG experiments are attached. The first experiment demonstrates the “hardware beamformer” property associated with the compact sensitivity pattern of the planar gradiometers, and the second experiment reveals the superior sensitivity of magnetometers to sources located extremely deep.

The first example is a cognitive study on cortical dynamics (Reference 2: *Nishitani, Hari*) where a rather complicated sequence involving consecutive, temporally overlapping activation of the cortex at five different nearby locations is observed. In this work the planar gradiometers with their compact lead fields well localized directly under the sensor element are at their best. Because the planar gradiometers show a single field maximum in the channels directly above the source the sequence of events on the cortex can be followed by merely observing these maxima of the averaged raw signals (see Fig. 3 in Reference 2: *Nishitani, Hari*). No signal processing or source modeling is necessary to figure out this dynamic cortical sequence. Source modeling – dipole fitting in this case – is necessary only for accurate localization of the active areas.

To our best knowledge no MEG work on phenomena involving this complicated sequences of cortical activity at near-by locations has been reported based on recordings done with conventional axial or magnetometer sensors. This is because the signal of axial gradiometer or magnetometer is a mix-up of superimposed maxima and minima of magnetic field on opposite sides of the active cortical area, rendering such straightforward analysis that would reveal sources this near-by in space and time not feasible. Because of their focal sensitivity pattern the planar gradiometers provide excellent signal-of-interest to background brain activity ratio, and have therefore been very successful in studies of the spontaneous activity of the brain as is evident from the list of publications, Reference 3.

The second example demonstrating the performance of Elekta Neuromag® sensor array is a paper on brain stem auditory evoked fields (Reference 4: *Parkkonen and Mäkelä*). In this case the signal of interest is at such a high frequency that the background activity of the brain has considerably decreased. The widespread sensitivity of the magnetometers can thus be fully exploited and the brain stem responses arising from very deep sources are resolved with a much better signal-to-noise ratio than with gradiometers. Without magnetometers an intolerably high number of averages would have been required. It should also be noted that the amplitude resolution of the Elekta Neuromag® data acquisition has been designed to resolve the extremely low signal of amplitude below 5 fT as demonstrated in Fig. 1 of Reference 4 (*Parkkonen and Mäkelä*).

In addition to seeing these very deep neural sources in adults the magnetometer channels also facilitate recordings of patients with small heads, such as young children, because owing to their far reaching sensitivity pattern the effect of the gap between the recording sensor and the sources of brain activity is minimized.

In situations less extreme than these two examples the information collected with the two different sensor types is automatically integrated by the analysis software. Especially, the novel Signal Space Separation method integrates the recorded information into a form that can be presented as signals of a virtual sensor array of any type. This method also works in a stable manner only when information from both “far sighted” magnetometers and “short sighted” planar gradiometers is available.

The performance of the Elekta Neuromag® sensor array is thoroughly studied and compared with the performance of conventional arrays in References 1 and 14 (*Nenonen et.al.*). The conclusion is that the Elekta Neuromag® sensor array design is superior in:

Channel capacity
Dipole detectability and localization accuracy
Resolvability of dipole sources.

With the development of new analysis methods, e.g. beamformer-like spatial filters, the superiority further increases(*Nenonen et.al.*).

**2.2 The sensor noise**

Typical averaged noise values in factory acceptance tests and at the final installation sites are:

For magnetometers: 3 fT/√Hz (white noise) and (6 Hz/f) fT/√Hz (1/f-noise)
For gradiometers: 3 fT/cm√Hz (white noise), and (6 Hz/f) fT/cm/√Hz (1/f-noise).

An example of the actual noise distribution of test data is shown in Figures 3 and 4.

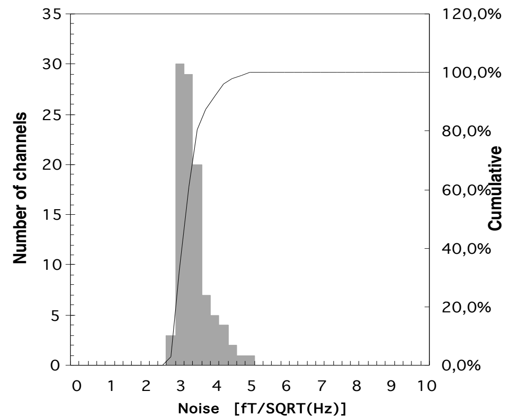


*Figure 3. Example of white noise distribution of magnetometer channels in a final factory inspection test.*

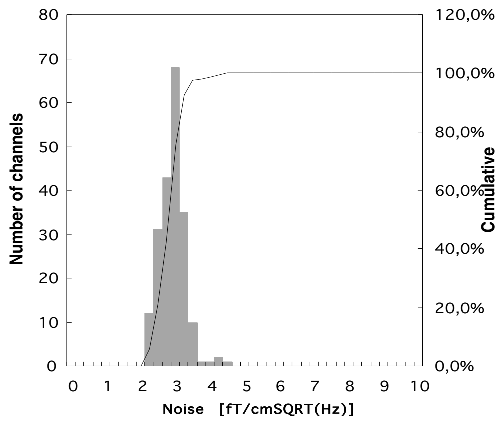


*Figure 4. Example of white noise distribution of gradiometer channels in a final factory inspection test.*

Characteristic spectral components of empty room test data from an actual MEG laboratory are shown in Figures 5 to 8.

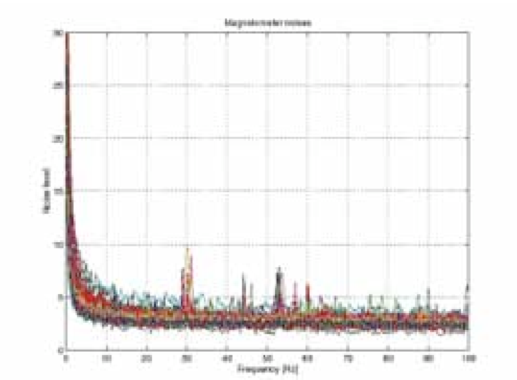

*Figure 5. Example of the spectral components of all magnetometer channels in an actual MEG-laboratory. The increased amplitudes around 30 Hz and its harmonics are due to vibrations in the walls and floor of the shielded room.*

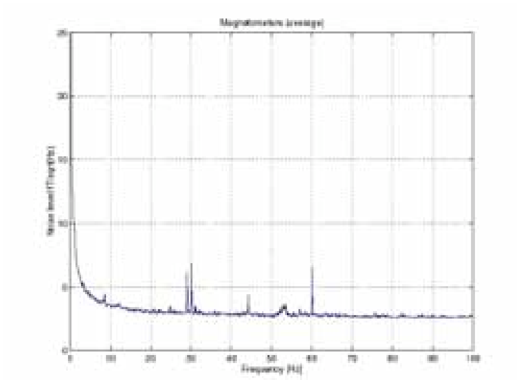

*Figure 6. Average of the spectral components of all magnetometer channels of Fig. 5.*

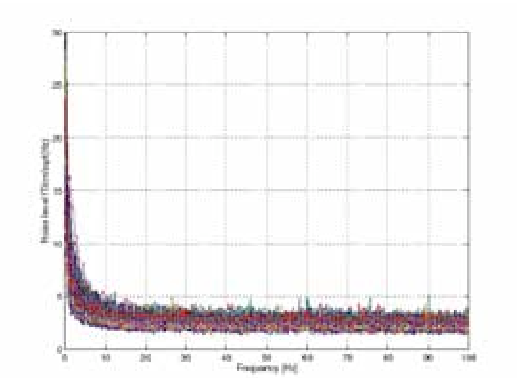

*Figure 7. Example of the spectral components of all gradiometer channels in an actual MEG-laboratory*

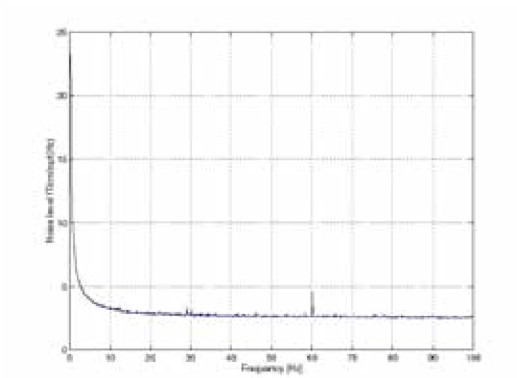

*Figure 8. Average of the spectral components of all gradiometers channels of Fig. 7.*

# 3. Sensor Coverage

The sensor coverage of the Elekta Neuromag® sensor array is illustrated in Figure 9. In the design, special attention has been paid to completely cover the temporal lobes. The average distance from the sensors to the room-temperature surface is 18 mm.

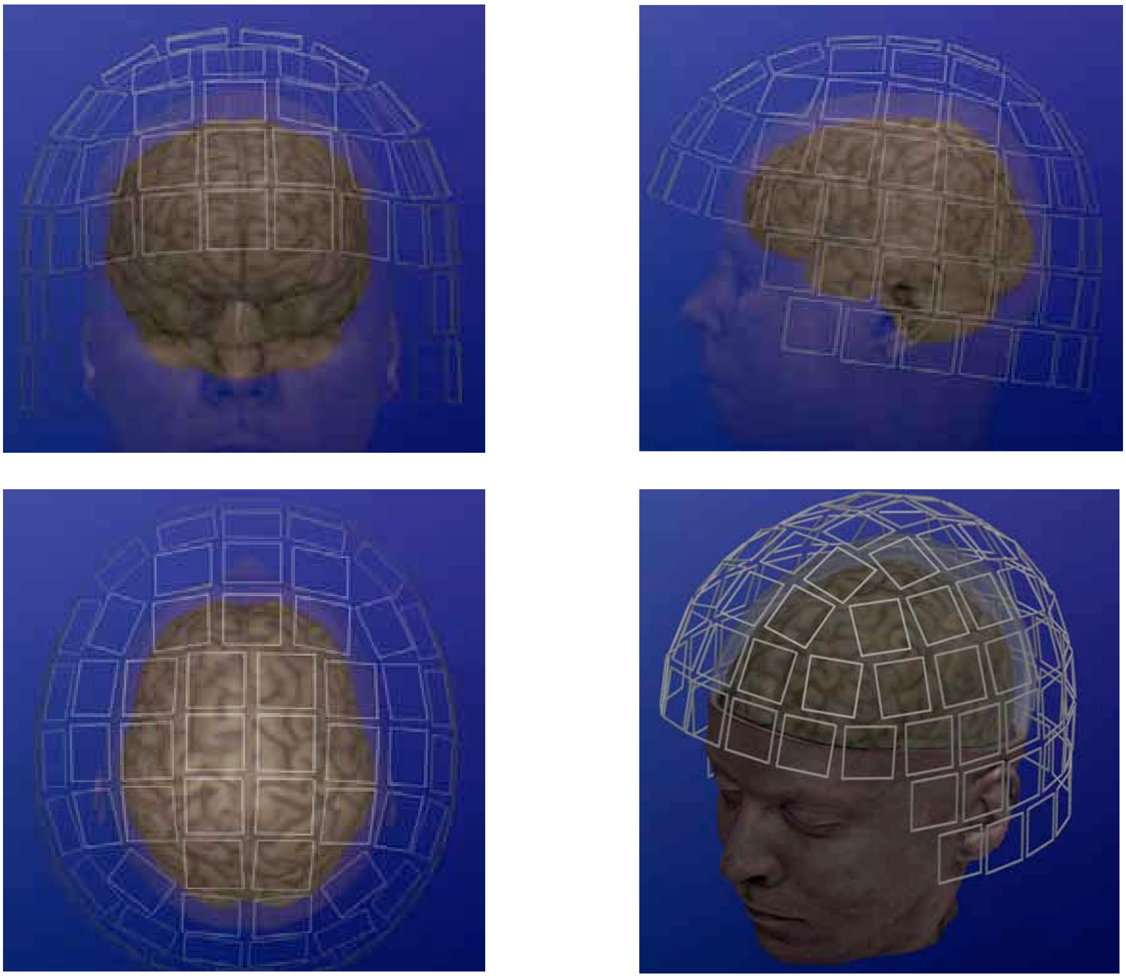

*Figure 9. Sensor coverage of the Elekta Neuromag® system*

The shape of the helmet is based on a realistic head shape according to the standard EN960:1994. The realistic shape minimizes the average brain-to-sensor distance, especially as compared to helmet shapes based on spherical and conical sections and shortens the measurement times. Patient comfort is thus improved  The maximum dimensions of the room temperature helmet are:

Length: 222 mm
Width: 181 mm
Depth: 210 mm

# 4. Electronics and data acquisition system

## 4.1 System configuration

The overall acquisition system configuration is shown as a block diagram in Reference 5. Digital Signal Processors (DSP) are used to read out the signals from the SQUIDs (Superconductive QUantum Interference Devices), EEG channels, miscellaneous channels and trigger lines. Single common clock is used to synchronize the events. The DSP's carry out also the filtering of the signals. Multiple parallel real-time computers are used to collect the data from the DSP units. The parallel real-time computers are connected to the Acquisition Workstation via a high-speed switch and an optical fibre link. Owing to the digital flux locked loop and the digital signal processing, all channels have an identical frequency response.

## 4.2 Resolution for digitization and the related usable signal bandwidth

The electronics of the MEG system incorporate 24-bit converters between the digital and analog signal domains. These converters sample the sensor signals at a rate of ~ 40 kHz; the data stream is subsequently downsampled by the digital signal processors to the rate chosen by the user, e.g. 600 Hz. This downsampling process increases the resolution at the small signal end of the dynamic range via averaging. With the rates given above, three more bits are added to the resolution, thus yielding in the majority of MEG-measurements a 27-bit effective resolution of the filtered output signal.

The data is transferred to the acquisition workstation as 32-bit numbers and, depending on user's needs, stored as 16 or 32-bit words. After removing the contributions of external magnetic noise sources, the remaining brain signal has a rather moderate dynamic range. Therefore, the signal can also be stored as a 16-bit number using range settings. This approach reduces the number of disk space needed and speeds up downloading and uploading of data files.

## 4.3 Maximum sampling rate

Maximum sampling rate for all channels is 5 kHz as standard and 10 kHz as an option. For all available sampling rates all channels are used. All channels, including MEG, EEG, trigger and analog input channels are sampled simultaneously.

## 4.4 ADC/DAC channels

The number and the specifications of analog and digital input lines excluding trigger lines, which are sampled synchronously with the MEG and EEG signals are:

8 auxiliary analog input lines with 16 bit resolution.
12 miscellaneous +/- 10V analog output channels with 24 bit resolution (optional).

# 5. Gantry, bed and chair

The up and down movement of the gantry can be operated by one person. Change between seated and supine measurement positions takes less than two (2) minutes with no stabilization time required. For ease and clarity of operations all patient related cables, except the SEF-stimulus delivery leads, are connected to the side panels of the gantry.

The bed and chair are on wheels so that the patient can be pulled out of the shielded room e.g. in case of a clinical emergency. The bed has a moving upper bed so that the patient's head can be quickly pulled out of the helmet in case of e.g. a seizure onset.

The height of the subject's head in the helmet is adjusted by elevating the chair. The chair is equipped with a removable table.

*Figure 10. Supine measurement position.* *Figure 11. Seated measurement position.*

A separate chair insert to facilitate pediatric measurements is provided. This chair is equipped with a neck support and a removable table.

*Figure 12. Chair insert for pediatric measurements.*

# 6. EEG system

## 6.1. General description

The Elekta Neuromag® system allows simultaneous recording of MEG and EEG data and storage of the data to a single data file.

The standard system includes an integrated 64 channel EEG-system. The system consists of 60 unipolar channels and 4 bipolar channels. The signal processing path used for the EEG signals is identical with that for the MEG-signals. The sampling of all the EEG channels is synchronized with the MEG data.

In the optional 128-channel EEG system an additional set of 64 unipolar channels are added to the system.

EEG noise over the band from 0.1 Hz to 100 Hz measured with a 10 k_ room temperature source impedance is less than 0.4   V RMS.

*Figure 13. The EEG-cap.*

The system delivery includes two EEG-caps. The sizes of the caps are S (46-52 cm) and L (52-58 cm). The customer can decide the number of electrodes to be attached to each of the caps prior to shipment of the system. Additional cap sizes are available as options including size XL (58-64 cm).

For loose-electrode setups the system provides a 32-channel head box with connectors for reference and ground electrodes.

## 6.2 EOG/ECG

To monitor eye movement, eye blinks and cardiac cycle four bipolar EEG-channels can be used. Typically, either one or two channels are assigned for this purpose (EOG: electro-oculogram). In rejection mode a threshold value is set for these channels. If the threshold value is exceeded the epoch is rejected from on-line averages (amplitude criteria). Additionally, if raw data acquisition has been activated the epoch will be stored into raw data file. Offline it is possible to remove the eye blink or eye movement artifact from the data using Signal Space Projection (SSP) method to project out the signals that elicit from the eye movement. For reference, see Reference 6 (*Hari et.al.*). The SSP package is an integral part of the Elekta Neuromag® software and it is applicable to both MEG- and EEG-data. It can be used to define the SSP vectors, e.g., during eye movement that is detected using EOG-channels. These SSP vectors can then be used in any of the source localization or data plotting to project out the signal caused by the eye-blink.

One of the bipolar channels is typically assigned as ECG channel to monitor the cardiac cycle. As in the EOG application above it is possible off-line to define one or more SSP vectors during the cardiac cycle and to project the cardiac fields out of the data.

Alternatively, the MaxFilter™ can be used to eliminate heart artifact since the heart signal arises from outside the MEG sensor.

# 7. Effective environmental magnetic noise cancellation

## 7.1 Noise reduction, gradiometers

The geometrical accuracy of the planar gradiometers is outstanding owing to the photolitography on silicon technology employed in the manufacture. This together with the relatively short baseline results in excellent inherent immunity to external interference.

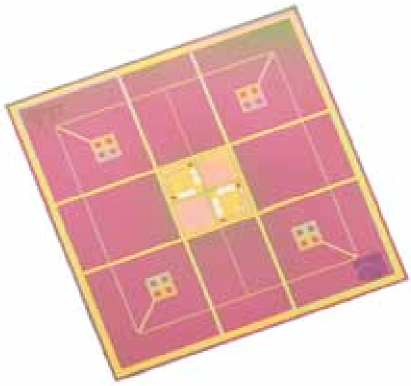

*Figure 14. Triple sensor element manufactured on silicon chip.*

In addition to the noise immunity achieved by precise geometry, the external interference in the planar gradiometers is further reduced by Signal Space Projection (SSP) and Signal Space Separation methods described in the following sections.

## 7.2 Noise reduction, magnetometers

The noise reduction for magnetometers is based on Signal Space Projection and Signal Space Separation methods.

## 7.3 Signal Space Projection (SSP) Method

The external noise cancellation for magnetometer channels is routinely done by the Signal Space Projection (SSP) method. In this method the noise cancellation is based on the signals from the MEG magnetometer array itself. *No separate reference sensor system is required.* During installation of the MEG system, the spatial interference patterns originating from external sources and penetrating the shielded room is determined from an “empty-room” recording made with the system itself. In all subsequent measurements, a noise cancellation factor exceeding 1000 (>60 dB) can be obtained by “projecting out” these spatial interference patterns (directions in the Signal Space) from the measured data.

The interference patterns are stable typically over several months, even years. The method introduces no bias to source localization, and does not add any noise to the signals. The SSP method can be applied to gradiometers also to increase their inherently outstanding noise immunity even further. For details of SSP, see Reference 7, and Reference 8 (*Uusitalo and Ilmoniemi*).

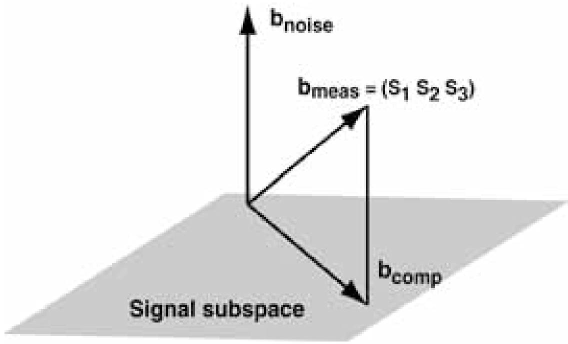


*Figure 15. 3-dimensional case illustration of the use of the SSP method. The measured signal is projected on a subspace orthogonal to the interference direction.*

### 7.4 MaxFilter™ for Noise Compensation

The magnetometers can be gradiometrized up to arbitrary order by MaxFilter™ that is based on Signal Space Separation method. In this method the biomagnetic and external interference signals are separated.

MaxFilter™ is based on the fundamental properties of magnetic fields (Maxwell´s Equations), and on the accurate geometry and calibration of the device. MaxFilter™ enables separation of artifacts from signals of magnetic origin. Furthermore, magnetic signals from sources inside and outside of the sensor helmet can be differentiated. Consequently, a "*software magnetic shielding*" effect is achieved which rejects the signals from sources outside of the helmet. The shielding factor is of the order of the calibration accuracy, that is, a 1‰ calibration accuracy leads to a shielding factor of about 1000. The shielding factor for even near-by external sources – like the heart of a small child within about 10 cm from the nearest channels – is considerable.


*Figure 16. The source areas of interest. The volume containing the sensors is assumed source free.*

For detailed description of the proprietary Signal Space Separation method, see Reference 9 (*Taulu et al.*). As described in the Reference 9 it is possible with this method also to eliminate the effect of the movement of the patient's head and display the data as if the head would have been stationary throughout the acquisition

(MaxMove™, works in progress, not cleared for US market). The interference due to ferromagnetic particles on the subject's head are also possible to eliminate using MaxMove™ (works in progress, not cleared for US market). The method greatly increases the robustness of the MEG-method by eliminating or reducing the most common artifacts.

# 8. Head position monitoring

The location of the head relative to the helmet is measured using 4 or 5 Head Position Indicator (HPI) coils attached to the subject's head. The locations of the coils with respect to the anatomy are digitized prior to the measurement with the Polhemus *Fastrak®* system (Colchester, Vermont, USA).

*Figure 17. Typical attachment of the HPI coils.*

## 8.1. Standard head position monitoring

In standard studies the coils are activated prior to the data acquisition. The head position is calculated from the measured signals.

## 8.2. On-line head position monitoring

The proprietary on-line head position monitoring system presently measures head position six times per second during the measurement. Head position is tracked by means of 4-5 marker coils that are continuously energized with high frequency AC-currents of different frequencies above the measurement bandwidth. The coil positions are continuously calculated from the measured distribution of the magnetic field. The method is currently works in progress (not cleared for US market).

## 8.3 MaxMove™ - Compensation of head position

Movement of the subject during the recording severely distorts MEG data. With cooperative healthy subjects this is not a problem but e.g. with small children and epilepsy patients head movements are unavoidable. The analysis of such data requires movement compensation which consists of dynamic recording of the head position and a method that takes the recorded movement into account in the analysis. In Elekta Neuromag® software this is accomplished by decomposing the measured data with Signal Space Separation method into a source model fixed to the head coordinate system, and the signals that would have been measured from a static subject are calculated. The field caused by magnetic impurities on subject's head will show up only in the DC-component of the MEG-field and is thus eliminated by removing DC from the data. Application of head movement compensation and elimination of the artifact caused by ferromagnetic impurity in a SEF-measurement are described in Reference 10 (*Taulu et al.*).

With the MaxMove™ software it is also possible to calculate the measured signals, e.g. averaged responses, on a virtual sensor array with an arbitrary location and orientation relative to the head.

The method is currently works in progress (not cleared for US market).

# 9. Co-registration with anatomical images

The co-registration of functional MEG data and MR images is carried out using MRI Integration software module (Mrilab) that is an integral part of the Elekta Neuromag® Software. The co-registration is based on three pieces of information. First, head digitization is carried out (see section 12 below) prior to the measurement. This includes anatomical landmarks as well as the locations of the head position indicator coils and digitization of any additional points. Second, the location of the head relative to the helmet is recorded during the MEG measurement by energizing the head position indication coils (see section 8 above). Third, the digitized anatomical landmarks are identified from MR images by the user. Also, in this step it is visually verified that the digitized additional points match with the MR image.

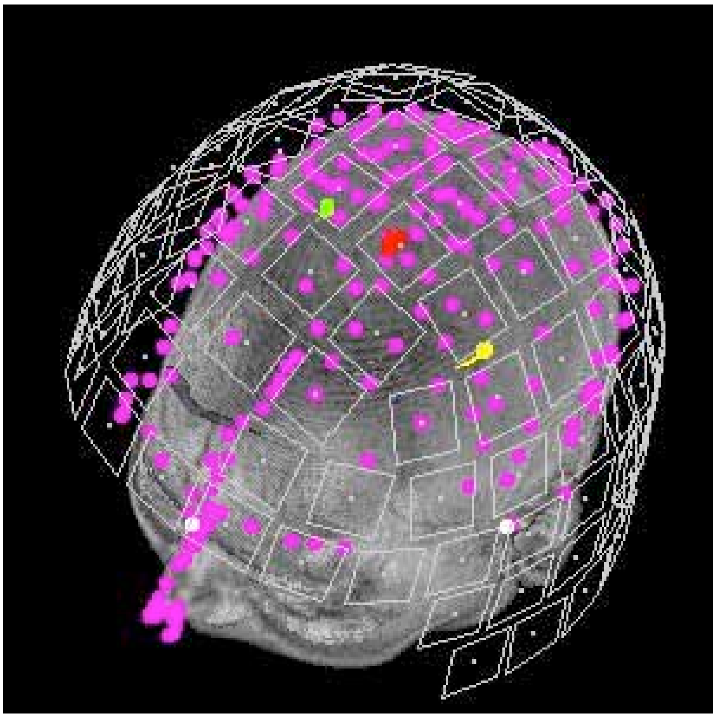

*Figure 18. Locations of the digitized anatomical landmarks at the coregistration.*

Anatomical landmarks – usually preauricular points and nasion are identified from orthogonal MRI slice sets and marked (white dots in Figure 18). Coordinate system is adjusted to ensure that the additional digitized points (purple dots in Figure 18) are matched to the surface of the scalp.

# 10. Stimulus delivery system

## 10.1 Auditory stimulus system

The auditory stimulus is generated with Neuroscan *Stim2* (El Paso, Texas, USA) software running on the stimulus delivery PC. Other audio sources can also be used, e.g. CD-players. The system is capable of delivering independent sounds to the two ears as well as delivering the same sound to both ears.

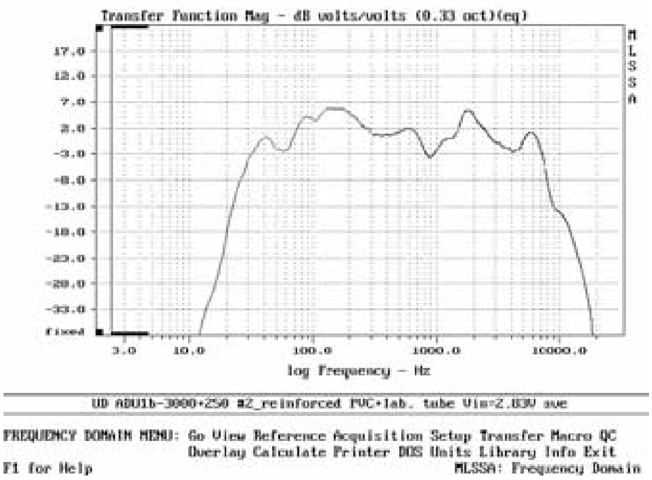


*Figure 19. Frequency response of the auditory stimulus system.*

The audio system can be provided with HiFi-quality artifact-free headphone system with wide frequency response; the frequency response measured from the subject headphones is flat within ± 3 dB to about 10 kHz (see Figure 19). The same stimulator has been used in fMRI studies.

## 10.2 Visual stimulus system

The visual stimulus is generated with Neuroscan *Stim2* (El Paso, Texas, USA) software running on the stimulus delivery PC. Other visual sources, e.g., VCR's and DVD's can also be used.

The video signal is split to the stimulus computer's screen and to a data projector. The data projector beams the optical image via an opening in the MSR wall to a non-magnetic back-projection screen. The diameter of the screen is 112 cm (44 inches). The angle, height, and viewing distance of the screen are adjustable.

The screen is equipped with wheels. The actual field of view can be changed by moving the screen inside the shielded room. For supine studies, a mirror can be attached to the screen to project visual stimulation on the ceiling of the shielded room.

Flat panel LDC display is provided as part of the stimulus delivery PC for generation and editing visual paradigms. The LCD display is outside of the shielded room. The image seen on the LCD display is directed into the data projector during the actual measurement.

*Figure 20. The back-projection screen.*

Two projector models are available: standard and premium. A typical delay for the premium data projector is 16 ms from trigger to presentation depending on the hardware configuration. Jitter of the projected image is less than 1 ms with 1024x768 resolution and 60 Hz refresh rate.

Triggering is controlled by the *Stim2* software. An indicator signal (trigger signal) for the exact timing of the appearance of the optical image can also be provided.

The brightness of the projectors well exceeds the need of any visual study. Neutral density filters are provided to reduce the luminance to desired level. The resulting luminance depends on the lens defining the image size, the geometry of the installation and the neutral density filters used.

### 10.3 Somatosensory stimulus system

Somatosensory stimulators with custom-made non-magnetic electrodes and leads are available. Stimulus parameters are controlled from the stimulator (amplitude) and acquisition software (sequence, timing). The non-magnetic electrodes and leads are designed to minimize artifacts.

### 10.4 Subject response device

Two independent, optical, single digit response pads for either finger lift or press are used to record subject/patient responses on line during data acquisition. Subject responses are available on-line for the stimulus presentation software and are recorded and displayed on the data acquisition monitors along with all stimulus triggers.

The delay between the activation of the response device and the external and internal triggers is less than 1 ms.

*Figure 21. Single digit response pad, activated by finger lift or press.*

### 10.5 Triggers for data acquisition/stimulus presentation

Two blocks of 16 bidirectional TTL-level trigger lines are included in the system. Each line is selectable as input or output. The blocks, equipped with two interface units, can be operated either independently (32 lines total) or in a mirroring mode where the operation of the two blocks is duplicated in two physically separate places, 16 lines total. The polarity of each input and output is user-selectable. Each input has also a user-selectable pull-up for connection of passive switches.

Trigger lines are connected to acquisition system by attaching BNC-cables from stimulators to the interface units (see Figure 22). The units are connected to the data acquisition system via an optical link.

*Figure 22. Interface to connect the trigger lines to the DACQ-system.*

The system also allows connecting printer ports of PC-computers directly to the i/o interface to deliver stimulus pulses. Serial port of the PC is used to feed in subject responses from, e.g. finger pads.

For on-line averaging up to 20 categories can be used. If data is averaged off-line the number of categories can be freely selected. For details, see section 20 Software, below.

The following trigger modes are supported:

External mode, where the stimulator masters the experiment, sending a digital event code and a trigger impulse for synchronization to the MEG/EEG-system.

Internal mode, where the acquisition system pilots the stimulator. Automatic generation of stimulus sequences for common paradigms.

The system allows to mix several types of stimuli (audio-visual, audio-somatosensory, visual-somatosensory, etc.) during the same recording session.

# 11. Computer system

## 11.1 Data acquisition workstation

The system is equipped with one H-P C8000 acquisition workstation. The workstation is configured with dual head graphics, 2 GB memory, a 146 GB hard disk and a built-in DVD+RW drive.

*Figure 23. A typical DACQ workstation with dual-head graphics and 20-inch flat panel displays.*

## 11.2 Data storage equipment

The available media for data storage are:

9.1 GB MOD (magneto-optical disk)
20 GB DAT (tape, per cartridge)

The data storage equipment is shared by both acquisition and analysis workstations.

## 11.3 Analysis workstation

The system is equipped with one separate H-P C8000 analysis workstation, and related data analysis software license. The workstation is configured with dual head graphics, 2 GB memory, a 146 GB hard disk and a built-in DVD+RW drive.

# 12. 3-D Digitization system

A Polhemus *Fastrak* (Colchester, Vermont, USA) system is used for digitization of the positions of the anatomical landmarks and the Head Position Indicator (HPI) coils. The system is also used to digitize the head shape and the locations of the EEG-electrodes. The system includes:

Polhemus Fastrak unit
Transmitter
Receiver
Digitizing pen
Non-magnetic goggles with an additional receiver to allow slight head movement during digitization

The Acquisition Software allows two digitization modes: individual points from subject's/patient's head surface, and continuous 'sweeps' of points from the subject's/patient's head surface.

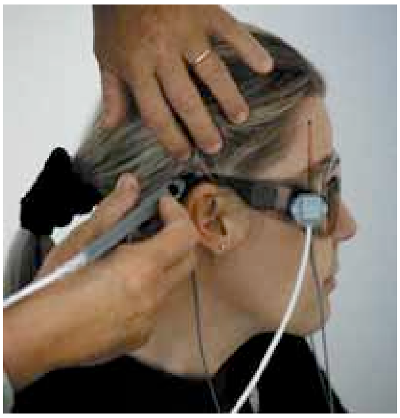

*Figure 24. Digitization of the HPI coils.*

The results are stored in data files together with the data and can be displayed using a utility program and extracted using import functions. Detailed description of the file format will be provided as part of the system delivery.

# 13. Cryogenics

## 13.1 Boiloff

The boil-off rate of the Dewar is 8 liters/day in both measurement positions. The liquid Helium volume is 78 liters. The refill interval is 7 days (once per week). The extra evaporation of helium during a seated/supine position change is neglible, about 0.04 liters.

For a refill helium transfer, a standard 100 liter storage container of helium is used. About 80 liters are consumed during the fill-up from 0% to 100%, and the rest 20 liters are a safety margin for non-optimal transfers and losses during transport or long storage times.

In an initial fill-up (cooldown) starting from room temperature a transfer of 100 liters will leave the system 50 ... 60 % full. The time required for this initial cool-down is two hours which is fastest in the industry. The down-time during service operations requiring a warm-up to room temperature is thus minimized.

### 13.2 Helium refill equipment

Flexible transfer siphon and helium pressurizing unit as well as necessary safety items are provided.

### 13.3 Helium exhaust line

The system is equipped with Helium exhaust line with a back-flow valve. All the Helium gas evaporating from the system, both in normal operations and during refill, is directed through the line. The line can be connected to Helium recovery systems.

### 13.4 Helium safety exhaust line

The system is equipped with Helium safety exhaust line. This line directs the Helium gas outside the building in the highly unlikely event that all the Helium suddenly evaporates from the system causing possible danger to the subject. Elekta Neuromag® is the only vendor to provide this safety feature.

## 14. Intercom system

An Intercom system between the subject and the system operator with both simplex and duplex modes is available.

## 15. Patient video monitoring

A video monitoring system with both visible light and infra-red capabilities is available.

## 16. Head phantom for MEG

MEG phantom with superior spatial precision and accuracy is included in the standard system configuration. The principle of the phantom is described in References 11 and 12.

*Figure 25. The phantom consisting of 32 equivalent current dipoles and 4 HPI coils.*

*Figure 26. The phantom with the cover in place.*

# 17. Test helmet

A transparent plastic model (scale 1:1) of the room temperature surface of the sensor helmet is provided. It can be used to test how subject's head fits into the helmet.

# 18. Printers

Black and white and color printers are available.

# 19. Magnetically shielded room (MSR)

The device can be operated either in a light magnetically shielded room (LMSR) based on Elekta Neuromag´s proprietary magnetic shielding concept, or in a conventional multi shell MSR provided by several vendors. The decision on the choice of MSR is made based on a survey including measurements of magnetic interference and noise levels at the proposed installation site. Further details on the site requirements can be found in the Elekta Neuromag Site Planning guide (Reference 13). LMSR is currently works in progress (not cleared for US market).

# 20. Software

## 20.1 Data Acquisition Software

The real-time data acquisition is controlled with the Acquisition Workstation. The workstation is equipped with two monitors. The raw data and the on-line averages are displayed simultaneously.

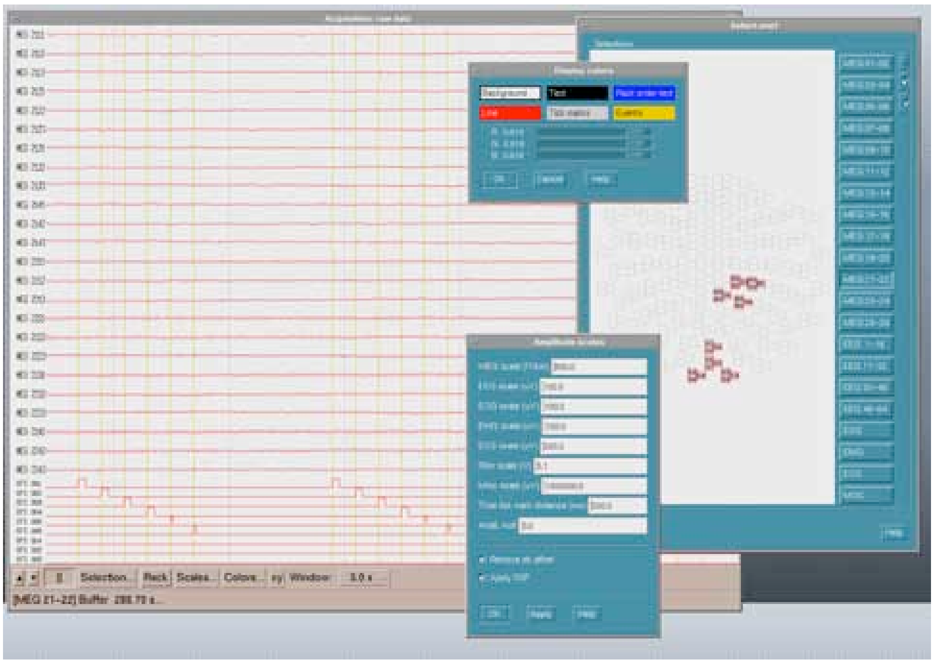

*Figure 27. A typical raw data display with a selection of MEG channels and all trigger channels.*

All raw data channels can be monitored on a strip chart style display in real-time and can be scanned through in sets of 32 at a time on the screen of the data acquisition monitor (see Figure 27). Multiple selections are provided including MEG-, and EEG-channels as well as trigger and behavioral response lines. The user can customize the selections. The noise levels of all MEG channels can be monitored. The system supports both automatic and manual tuning of the channels. Detrap-heating cycle of all the 306 channels takes 40 seconds.

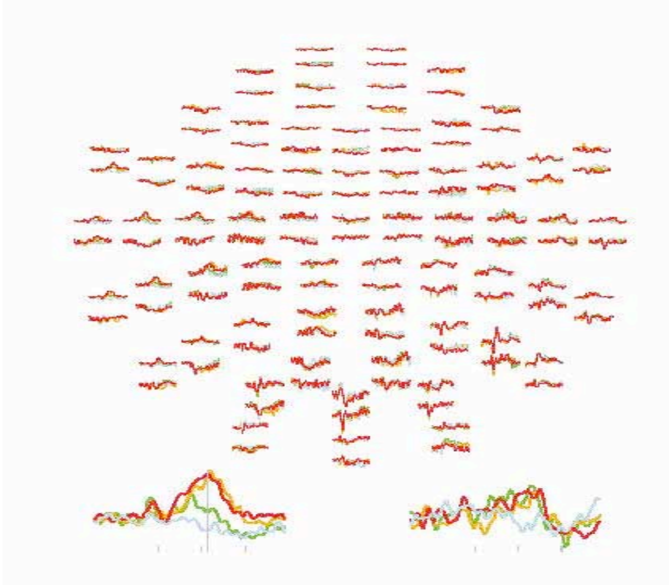

*Figure 28. Averaged data with 4 color coded categories.*

Up to 20 categories can be averaged on-line and monitored simultaneously. All categories are displayed by overlaying them on top of each other in a shared montage and applying different color for each category. In each category the number of averaged and rejected epochs are displayed and monitored continuously during the data acquisition. Categorization according to preceding and following events is possible.

The automatic rejection of signal epochs containing artifacts can use three kinds of artifact rejection criteria that can be activated for MEG and EEG channels:

> Amplitude-setting: The peak-to-peak amplitude within an epoch must not exceed this value.
> Spike: The absolute value of the difference between any sampled value in an epoch and the average of 20 previous values must not be larger than this.
> Slope: The epoch is subdivided into four equally long pieces. The averages over each piece are calculated. None of the three differences between subsequent partial averages must not exceed this value.

The above criteria are by default applied to all channels. If a channel not meeting the criteria is found, the epoch is rejected. The channels excluded from the artifact rejection during acquisition can be chosen freely.

EOG, EMG, and ECG rejection is only possible on the basis of the amplitude criterion. In addition to the above criteria, an epoch up to a given time interval after the reference event can be excluded from the rejection. This is useful if a strong stimulus artifact is expected.

## 20.2 Data Analysis Software

Filters

In data analysis software notch filters and low-, high-, and band-pass filters with freely selectable corner frequencies and widths can be used. The effect of the filters on the collected signals, and their frequency and impulse responses are shown on-line.

The applied filters are fft-based with time symmetric impulse responses. Thus, they do not generate phase errors. In frequency domain the leading and leaning edges have a length of a half cosine-window. The data is stored unfiltered and filtering is applied “on the fly”. It is always possible to refilter the data freely later if necessary.

Visualization of the evoked responses (Data plotting sw-module)

Visualization of the average evoked responses from all MEG- and EEG-sensors per type of stimulus: Multiple customer-selectable montages are available for both MEG and EEG channels.

Visualization of different responses by superposing the recorded responses corresponding to different stimulations: Implemented using different color codes as shown in Figure 28.

Other visualization and data manipulation tools

For example, the following features are included:

Calculation and visualization of the topographic maps showing the distribution of the magnetic fields and electrical potentials.

Possibility of manually eliminating of artifact signals from one or from several sensors before the calculation of the topographic maps has been performed.

Possibility of calculating differences between conditions. This feature of the software has been used very successfully, e.g., in the waveform and source localization analysis of Mismatch Negativity Field (MMF) data.

Possibility of simple scoring of the averaged waveforms (latencies, amplitudes, mean values over a time window, etc.)

Possibility to user-friendly export the results of the performed signal evaluations and re-importing of the user processed data (interfaces to C++ and MathLab programs).

Interface tool for preparing of high quality graphical output with the Cliplab software module. It facilitates report generation employing the drag and drop features. Layouts of the reports are user definable.

Dipole Fitting (Xfit sw-module)

Software provides tools for identifying the intra-cerebral current sources using a multi-dipole model. The time course of each source and their locations on anatomic MRI slices can be shown.

For example, following functions are included:

Single or multi-dipole time-varying model. Forward model supports also EEG.
Fitting single time points or time-varying modeling over time spans.
Multidipole fits can be run without constraints, or with the dipoles fixed in position or orientation.
Fit statistics and quality parameters are provided
Head model can be spherical (multilayer with EEG) or single/multi-layer realistic boundary element model.
PCA can be used to estimate the number of active sources.
The dipoles can be visualized on the MR-Images, on a schematic 3D viewer or on field contour images.
Source amplitudes and the goodness of fit are shown as a function of time.
The standard source localization program has also the capability of calculating the L2 minimum norm estimate of the source current distribution from any MEG-field distribution.

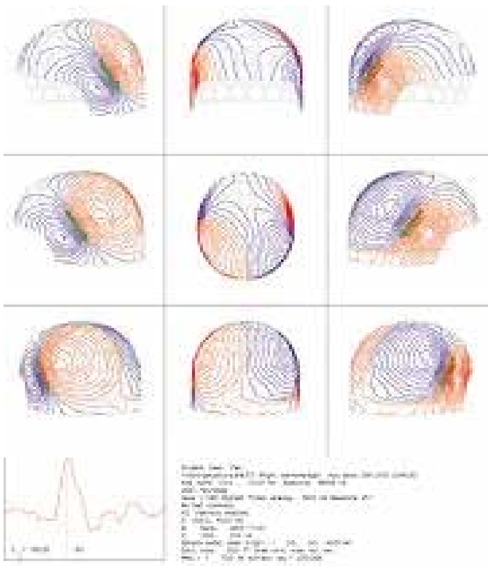

*Figure 29. Example of the field distribution visualization at a selected instant of an evoked response.*

<u>Minimum Current Estimation (MCE sw-module)</u>

L1-Norm based Minimum Current Estimation (MCE) is a software package for source localization of distributed sources. The package includes:

Signal preprocessing: low pass filtering, detrending, Signal Space Projection, decimation
Calculation of L1 Minimum Norm either on-line or as a batch job
Visualization of the calculated L1 Minimum Norm
Arrow display of source strength
Region of interest (ROI) display
Calculation of Region of interest (ROI) based on observed activities
Calculation of the activity in a ROI as a function of time (virtual channel)
Export of ROI as an ellipsoid to MRI

Visualization and documentation of the time dependence of the modeled source current distribution using mpeg-movies

Documentation of the data by exporting it in web-browser compatible file format

Minimum Current Estimation (MCE) software facilitates automatic source localization. No a-priori information is needed to identify the simultaneously active brain areas.

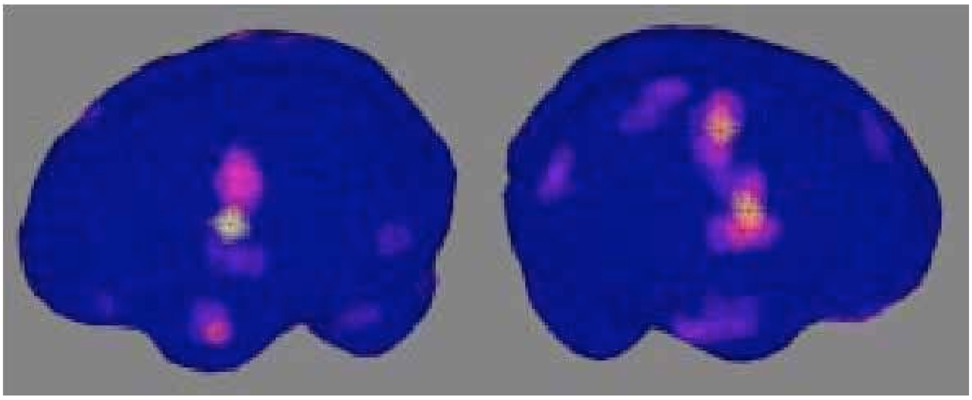

*Figure 30. Typical visualizations of MCE-current distribution at selected instant of time.*

Signal Space Projection (SSP) method for displaying temporal responses of virtual depth electrodes

The SSP technique can also be utilized in constructing virtual electrodes in the brain. An arbitrary number of virtual electrode points in the brain can be selected. The SSP method divides the measured signal *b(t)* into two components, $b_{||}$ and $b\_$, where the first part contains the contribution which is parallel to the signal vector of a source at the virtual electrode location and the second part represents the contribution from other sources. SSP in fact acts as a spatial filter passing only those signals that could have been generated by the given source locations.

Inter-subject averaging

Inter-subject averaging is possible using either Minimum Current Estimate software or Data Plotting software module. The waveforms of different patients can be superimposed with good precision by means of MaxMove™ software (works in progress, not cleared for US market): the data of each subject is first transformed to correspond to a standard head location (see section 8.3).

Signal processing (Graph sw-module)

Graph can be tailored according to the needs of both basic researchers and clinicians. A novice user invokes a predefined setup and interacts with the program solely through a standard graphical user interface. For an expert user, there are two additional levels available. First, a new setup can be constructed by creating new instances of predefined signal processor widgets corresponding to various elementary operations through a menu-based interface, and by linking them graphically to create a new signal processing sequences for the data. Second, user's own functions can be written to accomplish tasks which are not directly available. Results can be shown in "strip-chartrecorder" displays or saved to files for source modeling. Both electric and magnetic data can be analyzed with the graph software module.

The module offers several abstraction levels:

Windowing interface, menus, displays, configuration through flow graphs.
Additional functionality accessible through simple commands.
Full programmability in LISP programming language, which allows customization by software specialists and expert users.

Presently available operations include, e.g., bandpass filtering, baseline selection, FFT, power spectrum estimates, cross-spectrum estimation, thresholding, arithmetic operations, matrix operations, averaging, template matching, principal-component analysis (PCA), Signal Space Projection (SSP), wavelet analysis, and spike detection.

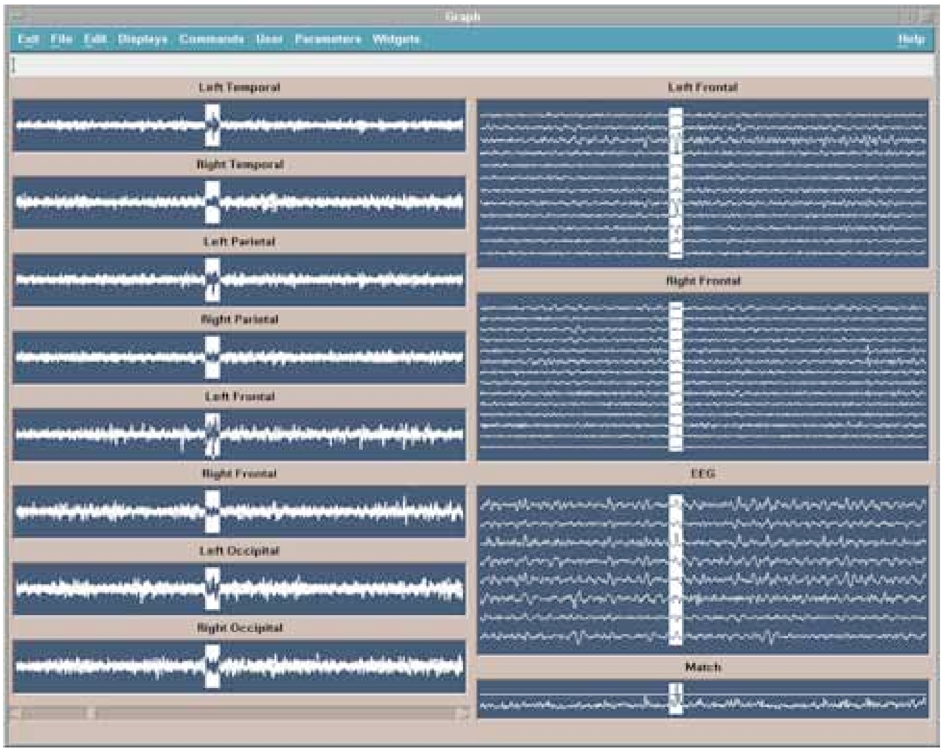


*Figure 31. Simultaneous Graph-display of MEG and EEG signals*

The spike detection is based on spatial filtering and thresholding that generates event lists. Amplitudes can be sorted and preferred range can be specified. The detected spikes can be automatically stored or fitted to generate dipole clusters. The method can be applied to slow wave activity. Additionally, it is possible to use template matching for automatic detection of spikes that share similar characteristics. The detected spikes in all the above cases can be averaged

Applications of the signal processing module:

Analysis of spontaneous activity including off-line averaging with complex averaging conditions
Recognition and categorization of epileptic spikes
Analysis of short-time changes in rhythmic activity

Integration with MR images

A comprehensive set of tools to handle MR images is provided, including:

MRI dipole overlay and fast browsing through the interpolated images with zooming and panning
MRI segmentation for 3-D surface rendering and for boundary element conductor models
Image fusion of functional information (simultaneous overlay of multiple dipoles) on 3-D rendered brain surfaces
Electronic ‘canvas’ for transporting graphics and illustrations from other software modules using drag-and-drop technique.
Dipoles can be differentiated from each other using different legends (triangle, dot, square, etc.) and colors
MRI import/export functions using DICOM 3.0

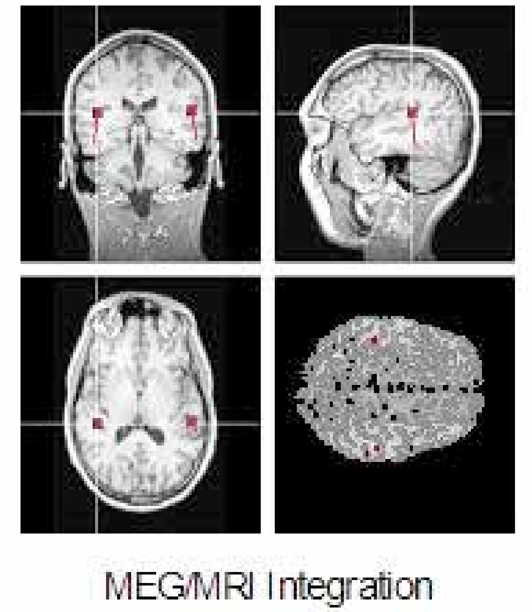


*Figure 32. Image fusion. Combining functional MEG data with anatomical MRI data. Source locations are overlayed on cross-sectional slices or on 3-D rendered surfaces.*

## 20.3 Software Licenses

The system delivery includes Site license for Elekta Neuromag Data Analysis Software. One License is provided for Data Acquisition software.

The site license (see above) covers the licenses that are connected to the local area network of the customer’s laboratory and that share the same domain name as the MEG system. Additionally, Elekta will provide licenses for workstations or portable computers that are used outside the laboratory by researchers that are collaborating with the customer and that have acquired data with the offered system at the site.

### 20.4 Operating system

The complete software is running on HP-UX Unix. Porting the software to Linux is works in progress (not cleared for US market).

## 21. Access to data

### 21.1 Data transfer

Image data can be transferred using either the standard DICOM 3.0 image transfer protocol or by sending the data files using FTP. This allows communication with, e.g. various medical imaging scanners, stand-alone image handling workstations, image guided treatment planning systems, and PACS-systems. For MRI and CT images, the system provides an image storage server and a Query/Retrieve client to access local or hospital servers.

### 21.2 File format

A detailed description of the file format is provided as part of the system delivery. Additionally, telephone and email support will be provided if requested during the warranty period.

Import/export libraries for HP-UX, Linux, and Windows are provided. Additionally, easy-to-use import/export functions for MatLab-environment are available.

Elekta promotes open systems and is working together with other software providers to allow input of Elekta's data files into their software programs. The vendors and research teams currently include Besa, Curry, ANT, Cortech, BrainStorm, Megan, and the Lyonnaise ELAN-software package.

## 22. Manuals

Three sets of manuals are included in the system delivery

## 23. References

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