# STUDIES ON THE SPATIAL RESOLUTION IN MAGNETOENCEPHALOGRAPHY

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**Studies on the spatial resolution in Magnetoencephalography**



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**Abstract**

Functional neuroimaging is used in research and clinical settings to understand how the brain works when it is healthy and how to treat it when it is not. Magnetoencephalography (MEG) is a functional neuroimaging method that non-invasively detects brain activity via the magnetic fields generated by it. MEG samples brain activity with high temporal (<1 ms) and moderate spatial (~1 cm) resolutions. A challenge in MEG is how one defines spatial resolution; the aim of this work is therefore to determine if and how this can be done. To that end, a broad array of parameters were investigated that may affect spatial resolution in MEG. Five recent articles were used as key references to identify, understand, and interpret relevant parameters and metrics. Eight different metrics were identified that had clear and important relationships with spatial resolution, or encompassed quantities similar to spatial resolution. The parameters' relationship to MEG and spatial resolution were then further investigated. However, because none of the metrics could be directly related to spatial resolution, a universal definition of spatial resolution in MEG was left undefined in this work.

**Sammanfattning**

Funktionell neuroavbildning används i olika forsknings- och kliniska områden för att förstå hur hjärnan fungerar när den är frisk och hur hjärnan bör behandlas när den inte är frisk. Magnetoencefalografi (MEG) är en funktionell neuroavbildningsmetod som icke-invasivt detekterar hjärnans aktivitet genom de magnetiska fält som genereras i hjärnan. MEG samplar hjärnans aktivitet med hög temporal (<1 ms) och måttlig spatiell upplösning (~1 cm). En utmaning med MEG är hur spatiell upplösning defineras; syftet med detta arbete är därför att avgöra om och hur detta kan göras. För att undersöka detta studerades ett stort antal parametrar som skulle kunna påverka den spatiella upplösningen. Fem nyligen publicerade artiklar användes som referenser för att identifiera, förstå och tolka potentiella parameterar. Åtta olika parameterar fanns som hade ett tydligt och viktigt förhållande till spatiell upplösning, eller som hade kvaliteter likt spatiell upplösning. Parametrarnas förhållande till MEG och spatiell upplösning studerades sedan. Dock kunde ingen av parametarna direkt relateras till spatiell upplösning, därför definerades inte en spatiell upplösning i detta arbete.

**Acknowledgements**
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# Contents

# 1 Introduction

This Bachelor thesis is an analysis done on the spatial resolution in magnetoencephalography (MEG). MEG is a powerful tool when studying the brain, and has numerous clinical applications. But a challenge in MEG, among other neuroimaging systems, is how one defines spatial resolution. Spatial resolution depends on different assumptions as well as both hardware and software of the system. The aim of the project is to answer the following questions;

- What is spatial resolution in MEG?
- Which parameters and metrics affect and/or can be related to spatial resolution in MEG?

## 1.1 Anatomy

The brain is, and has always been, somewhat of a mystery. It is the heart of intelligence, and produces our thoughts as well sensations and stores information. The complexity and diversity of the brain makes it one of the most challenging organs to study. Different mechanisms are made to fulfill all various functions of the brain. Learning and emotions are typically slow processes in the brain, whereas consciousness happens in a timescale of hundreds of milliseconds [1].

The ability humans, and other vertebrates, have to act on information is dependent on the nervous system. The central nervous system comprises the brain and the spinal cord, and consists of specialized cells that can transfer information very quickly. The specialized cells are nerve cells (also called neurons) and glial cells. Neurons are electrically excitable cells, meaning that they communicate with each other by sending electric signals. This way they can send fast signals over long distances. The functions of neurons in the brain are to receive signals, i.e. information, as well as send information to target cells (e.g., other neurons or muscles). Neurons also determine whether the signals should be passed on to another cell or not [2]. The majority of neurons are in the gray matter on the surface of the cortex, which is the largest main part of the human brain. The cortex has a high surface area, with folds that almost triple its surface, and consists of billions of neurons. The neurons create electric signals in the brain all of the time. When an electric charge is moving, a circular magnetic field is generated [3]. Thus when a neuron sends its electric signals, a weak circular magnetic field is generated in the brain.

## 1.2 Magnetoencephalography

One of the biggest challenges in neuroscience is studying the brain non-invasively, since opening up the brain can lead to serious complications. Magnetoencephalography (MEG) studies the activity in the brain via the magnetic field generated by the neuron activity. MEG has gained a number of clinical applications in the field of neuroscience. For example, epileptic activity during seizures can be studied by MEG [4]. In Sweden, around 70 000 people suffer from epilepsy, making it a major neurological disorder [5]. Locating the part of the brain where the seizure starts is of great importance, because some of the individuals suffering from severe epilepsy could be candidates for surgery. For the seizure localisation MEG can be used before surgical treatment. Surgery involves taking out the specific area in the brain that is causing the seizure to start [4]. During a MEG-recording, specific sensors are placed on or around the head of the individual to detect the magnetic fields generated by the underlying neural activity i.e., neuromagnetic signals [1]. One of the advantages of MEG is that it is non-invasive, so the brain can be studied without surgery or other invasive procedures. Other advantages are that the procedure involves no radiation and has excellent temporal resolution.

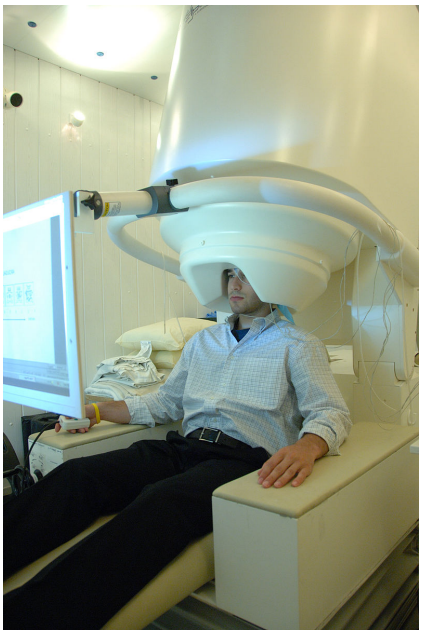

Figure 1: Person undergoing a MEG-recording [6].

The neuromagnetic signals generated in MEG are around 50-500 fT, making the signals 10 to 100 million times weaker then the earth's magnetic field [7]. In order to detect the very weak magnetic field outside the brain, extremely sensitive magnetometers are needed, like low critical-temperature superconducting quantum interference devices (low-$T_C$ SQUIDs). Low-$T_C$ SQUIDs do however require a cryogenic environment to operate. Often liquid helium is used to reach such low temperatures (boiling point T 4.2 K). Because of the low temperature, the thermal insulation between sensor and the scalp needs to be around 2

cm, which leads to weakened signal [8]. Other problems with using low-$T_C$ SQUIDs is that they can not be adjusted to individual head size or shape, again making the distance between sensor and scalp unnecessarily large. These restrictions have led to the birth of on-scalp MEG, where the sensors are placed directly on the scalp. The new sensors do not need to be cooled with liquid helium and can be placed in very close proximity to the head, theoretically improving signal levels and potentially spatial resolution [9]. On-scalp MEG has two leading sensor technologies: high critical-temperature (high-$T_C$) SQUIDS and optically pumped magnetometers (OPMs).

## 1.3 Neuroimaging

Images of the brain, or neuroimaging, are required in order to understand the brain better. Neuroimaging can be categorized as:

- Morphological imaging: An anatomical image of the structure of the brain. These are standard images that are wiedly used, e.g., to locate a lesion in the brain.
- Functional imaging: This is generally a more advanced technology that provides information about different functions of the brain. Live-recordings of neural activity fall under this category, the recordings can be used to generate a video of the neural activity coupled to a given brain function.

MEG measures the neural activity live, and therefore falls under functional imaging. The time-scale from when the event is happening in the brain, to when its shown in the recording, has to be small to provide accurate information. If the time interval is small, the temporal resolution is good. For MEG it is on the order of milliseconds, which is very fast comparing to other live-recording techniques. From the MEG-recording you should be able to distinguish from where in the brain the activity is coming. Spatial resolution is defined as the measure of the smallest discernible detail in an image [10]. The magnetic field decreases as roughly one over the distance squared, which means that the signal detected from deep sources (i.e., in the center of the brain) is much weaker than from the shallow sources (i.e., those close to the scalp). In MEG, spatial resolution for shallow sources is around 5 mm, whereas it is more like 1-1.5 cm for deep ones [8].

## 1.4 Magnetic field

For creating a measurable signal in the sensor in MEG, the magnetic field has to be larger than the signal from just one neuron. Approximately 50 000

neurons need to be active at the same time for there to be a signal in a sensor [7]. The magnetic field can be obtained by integrating all the currents, $\vec{J}$, in a volume, $\vec{V}$. For MEG the volume is the brain and currents are the electric signals generated by neurons. The magnetic field is given by:

$$\vec{B} = \frac{\mu_0}{4\pi} \int_V \vec{J}(r') \frac{\vec{r} - \vec{r'}}{\left|\vec{r} - \vec{r'}\right|^3} d\vec{r'}. \tag{1}$$

where $r'$ is the location of the current dipole, $r$ the location of the sensor and $\mu_0$ the permeability constant. The net currents of the neurons can be considered as a current dipole, $\vec{Q}$. The magnetic field can then be expressed as,

$$\vec{B} = \frac{\mu_0}{4\pi} \vec{Q} \frac{\vec{r} - \vec{r'}}{\left|\vec{r} - \vec{r'}\right|^3} \tag{2}$$

As shown in equations 1 and 2, the magnitude of the magnetic field decreases with the distance from the source as $\sim\frac{1}{r^2}$ [7].

## 1.5 Relating recording to neuron activity

The magnetic signals that are recorded in MEG need to be related to the neuron activity, i.e. from where in the brain the signal is coming. In essence, MEG only generates a map of the magnetic fields sampled from around the head and not an image of the brain; therefore a magnetic resonance image (MRI) of the subject's head is needed in order to accurately estimated the sources of the magnetic fields, i.e. neural currents in the brain. To be able to relate the location of the sensor signals to the subject's head, co-registration is needed. Co-registrations are done by placing small, magnetic dipole coils on the subject's head for the recording session. The coils will give a signal in the MEG-recording, which can be related to the MRI, enabling estimation of where in the brain the signals are being generated [9].

Co-registration only gives an indication of where the measured signals are coming from in the brain. One of the biggest challenges in MEG is to know the exact location, on the neural level, of the activity from the measured data. This problem is called the inverse problem. The inverse problem is to determine the unknown sources of magnetic fields in the brain based on MEG data [1]. The tricky part is that the inverse problem usually has infinite solutions, making it difficult to estimate which is the correct one. In

other words, different sources of magnetic fields in the brain may give the same measure in the sensors [1]. To solve the inverse problem different methods can be used, of which the most common are: minimum-norm estimates (MNE) and beamformers. However, all solutions only give an estimate and have some type of error.

Simulating MEG-data is essential in order for MEG to move forward and become more advanced. The simulations are, for example, needed when comparing different sensor technologies. To reconstruct the neural activity in MEG, the forward model is often used. The forward model connects the magnetic field generated in the brain (i.e., the neural sources/currents), to the magnetic field measured by the sensors outside the brain. The coupling between the neural current, $j$, and the recorded magnetic field, $b$, is called the lead-field. The lead-field defines how the sources couple to each sensor. The measured magnetic field in sensor $k$ can then be defined as:

$$b_k = \sum_{l=1}^{n} L_{lk} \cdot j_l \tag{3}$$

where $L_{lk}$ is the lead-field matrix and $j_l$ the current in the brain generated by the neural source $l$.

## 1.6 Dipole fields

The magnetic field detected outside of the head by the MEG system, as generated by a single neural current in the brain, can roughly be characterized as a pulse. The MEG-recording thus consists of the summation of such pulses with different heights and widths. When detecting radiation, for example gamma rays, the energy released in the detector can also be characterized as pulses. The pulses recorded from the gamma emitting source follow a Gaussian shape. Resolution can be quantified with the full width of half of the maximum amplitude of a pulse i.e., the full width at half maximum (FWHM), see figure 2 [11]. A role of thumb is that in order to spatially resolve two such pulses, they need to be separated by more than one FWHM. FWHM is therefore an easy way to measure the distance needed to distinguish two pulses. Unfortunately the pulses recorded in MEG do not follow a Gaussian pulse shape, and the FWHM of the pulses can not be used as a measure for resolution in MEG.

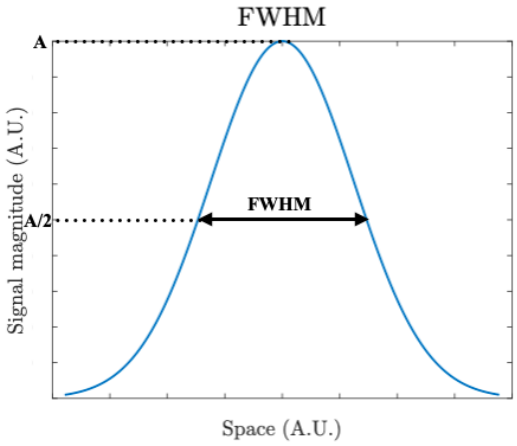


Figure 2: The full width of half of the maximum amplitude of a Gaussian pulse.

The sensors in most MEG systems only sample the radial component of the magnetic field (i.e., the component of the neuromagnetic field pointing directly out of the head/tangential to the head surface). Plotting the radial component of equation (2) over a distance will show how the dipole field would look like for a sensor array. Figure 3 shows the dipole field detected by high $T_C$SQUID and low $T_C$ SQUID. The high $T_C$ SQUID array is positioned 1 mm above the scalp and the low $T_C$ SQUID one is placed 2 cm above the scalp. As shown in figure 3, the dipole field from the high $T_C$ SQUIDs is high and narrow, compared to the low $T_C$ SQUIDs that is lower and smeared out. The difference in the dipole field is namely because of the scalp to sensor distance.

Roughly approximating one lobe (e.g., the positive one) of the dipole field as a Guassian can provide some insight regarding the difference in spatial resolution between low- and high $T_C$ SQUIDs in MEG. The FWHM for the high $T_C$ SQUID is much smaller than for the low $T_C$ SQUID. Two dipole fields close to each other would therefore be easier to separate when using the high $T_C$ SQUID sensor array. An approximate FWHM of the dipole pulses are shown in figure 4. The FWHM of the high $T_C$ SQUID is around 2 cm and the FWHM of the low $T_C$ SQUID is around 5 cm. The spatial resolution is therefore theoretically improved when using a high $T_C$ SQUID sensor. But the values of the dipole FWHM are much larger than the typically cited spatial resolution of MEG. As mentioned before, sources close to the scalp have a resolution of 5 mm, and sources deeper in the brain have a resolution of 1-1.5 cm with MEG. This indicates that the spatial resolution depends on

a lot more than just the dipole field. We therefore want to study metrics that could be affecting the spatial resolution in MEG.

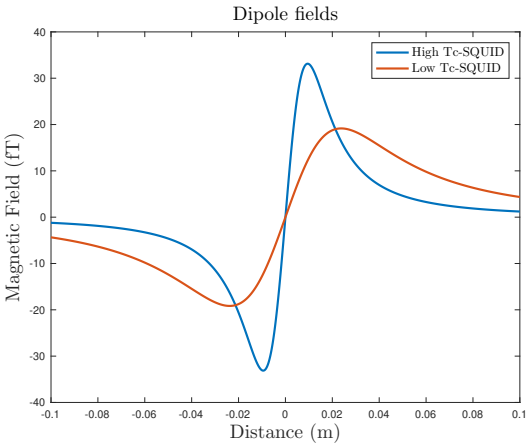


Figure 3: : Dipole fields detected by a high $T_C$ SQUID (blue) and low $T_C$ SQUID (red) array placed 1 mm and 2 cm above the scalp, respectively.

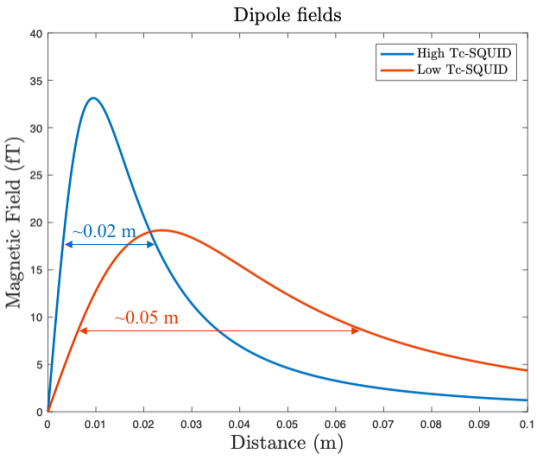


Figure 4: An approximate dipole-FWHM for a dipole field detected by a high $T_C$ SQUID (blue) and low $T_C$ SQUID (red) array placed 1 mm and 2 cm above the scalp, respectively.

# 2 Method

In order to define spatial resolution in MEG, articles were selected to find potential metrics. The articles that were used as key references in the analyzes were:

- Schneiderman, J. F. (2013) *Information content with low- vs. high-TC SQUID arrays in MEG recordings: The case for high-TC SQUID-based MEG*
- Riaz, B., Pfeiffer, C., Schneiderman, J. F. (2017) *Evaluation of realistic layouts for next generation on-scalp MEG: spatial information density maps*
- Schneiderman, J. F., Ruffieux, S., Pfeiffer, C., Riaz, B. (2019) *On-Scalp MEG*
- Iivanainen, J., Stenroos, M., Parkkonen, L (2016) *Measuring MEG closer to the brain: Performance of on-scalp sensor arrays*
- Boto, E., ..., Brookes, J. M (2018) *Moving magnetoencephalography towards real-world applications with a wearable system*

## 2.1 Selection of metrics

### 2.1.1 Definition of the metric

All the articles stated above were read, and all the potential metrics were assessed. The articles were mostly written for studying other things than image quality or spatial resolution; all metrics therefore needed a deeper investigation in order to relate them to spatial resolution. This was done by looking at the metric definition, to see if any of the metrics potentially could have any resemblance with spatial resolution. If the metric had a way of expressing the image quality or information about the image, it was selected in this process. An improved localisation of the activity could also lead to improved image quality. If the metric had any clear relationship to a MEG-recording, it was therefore also selected. The definition of the metric gave a first indication if the metric could have any relationship with spatial resolution, and it was therefore the first criteria for the metrics studied in this work.

### 2.1.2 Governing equation and parameters required

In order to further analyse the metrics, their governing equations and related parameters were studied. In this process it became clear whether the metric was explicit to simulated or recorded MEG-data, or if it could be used in both simulations and recordings. The study showed whether the metric could be duplicated or not, or if the metric was explicit to the study done in its article. It also showed if the metric was specific to MEG, or if it had more applications.

### 2.1.3 Relationship to MEG or spatial resolution

How the metric relates to MEG was later examined. The metric could have multiple applications, but only the relationship to MEG was further studied. If the metric had been used to study any functions or similar procedures in MEG, then it was taken into account for further study. Finally, the metric's relationship to spatial resolution was studied. How the metric relates to the image quality, if at all, was also examined.

## 2.2 Presentation of results

In order to summarize and aid in understanding of the various metrics discovered, a table was constructed. All the metrics were described in the table with their definition. The table also included the governing equation the metric had, as well as the parameters required for its equation; if the different parameters had to be defined or measured. The table also summarized each metric's relationship to MEG and spatial resolution.

# 3 Result

In order to analyze how the metrics relate to spatial resolution, different metrics with potential relationship to spatial resolution, were selected. The metrics that selected from the articles stated above were:

- Topography Overlap
- Peak position error (PPE)
- Cortical area (CA)
- Point-spread function (PSF)
- Signal power
- Total information capacity
- Spatial information density
- Shared Variance

The metrics stated are all based on simulated MEG-data except for *Shared Variance*, that is based on real MEG-data. The other metrics were all calculated from the lead-field matrix, see equation (3). Table 1 displays all the metrics definitions, governing equations and related parameters. Table 1 also shows the each metric's relationship to MEG and spatial resolution, if it exists. In section 3.1 - 3.6 the metrics are analyzed to a deeper extent than in the table.

Table 1: The selected metrics names, definitions, equations, and the metrics relationship to MEG and spatial resolution.

| **Name of metric** | **Definition** | **Governing equation** | **Parameters required** | **Relationship to MEG** | **Relationship to spatial resolution** |
|---|---|---|---|---|---|
| Topography overlap | Topography Overlap is a measure of how much the lead field from each source looks like one another. | Topography overlap can be measured with a correlation coefficient $CC_{ij}$, which is calculated between the topography of the reference source, $i$, and the topography of all the other sources, $j$. $CC_{ij} = \frac{\vec{t}_i - \vec{\bar{t}}_i}{\left\|\vec{t}_i - \vec{\bar{t}}_i\right\|} \cdot \frac{\vec{t}_j - \vec{\bar{t}}_j}{\left\|\vec{t}_j - \vec{\bar{t}}_j\right\|}$ where $t$ denotes the a column of the lead field matrix $\vec{L}$. | You need simulated MEG data and the lead-field matrix. | If the correlation coefficient is high, then it will be harder to distinguish where the signal is coming from. | A high topography overlap would worsen the spatial resolution, since a high topography overlap will make it harder to estimate the position of the source. |
| Peak position error (PPE) | PPE is the distance (i.e., in mm) between a "seed" source under study and the center of mass of the set of sources whose forward-calculated topographies are similar (90% or more) to it. | The distance between source $k$ and reference source $i$ is calculated: $\text{PPE}_i = r_i - \frac{\sum_k CC_{ik} \cdot r_k}{\sum_k CC_{ik}}$ where $r_i$ is the location of the reference source $i$ and $r_k$ is the location of the source $k$. | You need simulated MEG data, with the lead field matrix. The correlation coefficient needs to be calculated, as well as the location of the reference source and the center-of-mass of the sources that are highly correlated to it. | If the PPE is small, then it will be harder to estimate a source's position. | The PPE measures the distance between a sources and other parts of the brain from which that source can't be distinguished. PPE is therefore a measure of spatial resolution. |
| Cortical area (CA) | The surface area of a patch of the brain wherein the forward-calculated topography of the set of sources enclosed in the area is similar (90% correlated or more) to that of the "seed" source under study. | The cortical area is calculated as, $\text{CA}_i = \sum_k A_k$ for source $i$ that is giving the same output as the pack of sources $k$. $A_k$ is the relative cortical area associated with source $k$. | You need simulated MEG data, with the lead field matrix. To calculate CA you need the cortical area associated with the different correlated courses. | If CA is large, the spread of the correlated sources is high. | If the spread of sources is large, it will be harder to distinguish where the activity is coming from in the brain. A small value on CA thus indicates a good spatial resolution, as it will be easier to distinguish from which part of the brain the activity is coming from. |
| Shared Variance | Describes how well two sources can be distinguished from each other. | Shared variance measures the electrophysiological time-course (studies the electric signals over time) overlap between a 'seed' source and a source place randomly within 3 cm of that 'seed' source. A 50 % shared variance means that the 'seed' source and an another source produced a 50 % similar electrophysiological time-course. | The metric shared variance is based on recorded MEG-data. Beamformer was used on the MEG-data to estimate the source time-courses. | Shared variance has been used to compare different MEG-system's spatial resolution. | Shared variance has been used as a measure of spatial resolution in one article [12]. |
| Point-spread functions (PSF) | Describes how well an imaging system can describe a point source. | The PSF can be used, in MEG, to describe the change an image undergoes when using the inverse solution. The estimated current $\tilde{j}$ is derived by performing the inverse solution on simulated data. The real currents, $j$ are known. The estimated current can be described as, $\tilde{j} = \vec{K} j$ The resolution matrix, $\vec{K}$, indicates how "wrong" the inverse solution of the currents are. The values of $\vec{K}$ are the point-spreed functions. | You need simulated MEG data, with the lead-field matrix. As well as the estimated sources from the inverse solution, along with the original sources (the ones that have not undergone an inverse solution), the inverse solution and the resolution matrix. | The inverse solution is of central importance in MEG. A good inverse solution gives a better idea where the neural activations are in the brain. | Small PSFs means that the system does not smear a point source. In the case of MEG, the inverse solution has a significant impact on the image quality. A small PSF therefore means that the inverse solution is good. The PSF in this case, does not say anything about the image quality of the actual MEG system. Unless you are comparing the same inverse solution on two different systems, then the difference in PSF for them would say something about their relative resolutions. . |

| Name of metric | Definition | Governing equation | Parameters required | Relationship to MEG | Relationship to spatial resolution |
|---|---|---|---|---|---|
| Signal Power | The signal power in an array of sensors. | The signal power can be expressed as, $$S_i = \sum_k b_k^2$$ where $b_k$ is the measured magnetic field calculated from equation 3. | You need simulated MEG data, with the lead field matrix. | In order to detect neuromagnetic activity in MEG the signal power needs to be high. | If the signal power is on the same order or lower in magnitude than the noise level of the system, then the image quality will be very poor. |
| Total information capacity | Gives the maximum amount of information that can be transmitted from the brain to a camera/MEG sensor array without error. Measured in bits. | Based on Shannon's theory of communication. $I_{\text{tot}}$ is the total information from the entire array of the whole source. $I_{\text{tot}} = \frac{1}{2} * \sum(\log_2(P_k + 1))$ Where $P_k$ is the power signal-to-noise ratio (SNR) of the $k$-th orthogonalized channel of the array. The SNR can be calculated with the signal amplitude, the noise level, a matrix containing the lead-fields eigenvectors and a vector containing the lead-fields eigenvalues. Due to that a source will couple to different sensors, an overlap coefficient for each source is calculated. The overlap coefficient is taken into acount when calculating the power signal-to-noise. | You need simulated MEG data, with the lead field matrix. The matrix containing the eigenvectors is needed, as well as a vector with all the eigenvalues. The average signal and noise levels over the bandwidth are also needed to calculate the information capacity. The overlap coefficient is needed. | This metric has been used, among other things, to evaluate the performance of sensor arrays in MEG. | The metric provides information about the entire brain, but fails to look at any specific parts of the brain. The metric therefore fails to give us any information about the spatial distribution. |
| Spatial information density | Spatial information density (SID) checks the information capacity from every cortical source in the brain. This, unlike total information, looks at all the sources independently and thus gives the spatial information. Measured in bits per source. | The SID value for a single source is calculated as, $$\text{SID}_{\text{source}} = \frac{1}{2}\sum_k \log_2\left(\frac{\sigma^2_{\text{signal}}\lambda_k}{\sum_j U_{jk}\sigma^2_{\text{noise}}} + 1\right)$$ Just as in total information capacity the SNR is calculated to provide the information from each source, $\sigma_{\text{signal}}$ is the signal amplitude in a channel, $\sigma_{\text{noise}}$ is the noise amplitude in a channel and $U_{jk}$ the overlap matrix. | Same parameters as total information capacity. | Can be used to quantify e.g. the sensor layout to maximise the information that can be extracted from a source. | SID-maps represent the spatial distribution of information density, therefore taking the spatial dimension into account. However, it does not measure spatial resolution, since spatial resolution is measured as a distance and SID is in bits/area. |

## 3.1 Topography Overlap, Peak Position Error and Cortical Area

As stated in table 1, topography overlap is a measure of how much the lead field from each source looks like one another. The lead-field defines how the generated magnetic field from a source is coupled to each sensor. Because the sensors form an array around the head, a topography of the lead-field can be estimated. If the topography overlap is large, meaning that the lead field from two sources are similar, it will be harder to distinguish those two sources. A high topography overlap would therefore be bad for the spatial resolution, since it will be hard to identify where in the brain the signal is coming from.

If the topographical overlap for a given lead-field is high, then there are two metrics to describe how the overlap looks [8];

- Peak Position Error (PPE) - The distance between two correlated

sources. A small value of PPE means that sources that are highly correlated are very close to each other.

- Cortical Area (CA) - The area of the patch of the brain wherein sources are highly correlated. A high value of CA means that the source is effectively spread out.

If the PPE is small or the CA is large it will be harder to distinguish where the signal is coming from in the brain. PPE and CA are thus both measures of resolution. PPE measures the distance between sources that can't be distinguish from each other.

## 3.2 Shared variance

Shared variance has been used to measure spatial resolution. A 'seed' source is planted and 4 000 other sources are randomly distributed within 3 cm of the seed source. The overlap (correlation between electrophysiological time-courses) is then measured between all the sources and the 'seed' source. If the shared variance is over 50 % between the seed source and one other source, it will be further investigated. How different MEG-system can separate sources with a shared variance over 50 % was investigated in one article. [12] They claim to have better spatial resolution with one MEG-system (OMPs), as compared to a low-$T_C$ SQUID-based one, due to a better source separation of the shared variance with the OMPs.

## 3.3 Point-spread function

All image systems spread a point out to some degree, meaning that a point source could look like a blob in an image. [10] The point-source function (PSF) describes how well the image system can describe a point source. If the PSF is big, a point source in the image will look big and smeared out.

One study used PSF to measure how good the inverse solution for simulated MEG-data was. [8] They used PSF to compare the modeled currents (ground truth) to the estimated currents from the inverse solution, in order to see how much the inverse solution actually changes the currents. When the changes were small, the inverse solution was a good estimate. But when the changes were large, then the inverse solution was off and it did not give us the correct location of the activity in the brain. This indicates that the inverse solution has the biggest impact on the image and not the hardware or the image-system itself for MEG.

## 3.4 Signal Power

The signal power in an array of sensors should affect the spatial resolution, since a weaker signal would be harder to interpret/resolve. Without a strong signal it will be hard to determine where the signal is coming from, as well as to determine if the signal is background noise or an actual signal. The signal power is defined as the measured magnetic field in the array of sensors. The measured magnetic field depends on how the magnetic field generated from each source in the brain couples to the sensors, therefore signal power is also based on the lead-field matrix. [13]

## 3.5 Total information capacity

Total information capacity is a metric that can be used to evaluate the performance of a sensor array in MEG. [14] The metric gives the information that can be extracted in an array, when all the sources in the brain are active at the same time. It fails to give us any spatial information, as it gives the information from the entire brain and not specific parts of it. It does, however, give us a metric to work with, when comparing MEG-systems, that is not using any inverse solutions. As will be shown later, this metric can also be extended to another metric called spatial information density.

Information theory was originally formed by Claude Shannon in the end of the 1940's. 50 years later Shannon's theory of communication was used to estimate the information capacity of a noisy channel [13]. The information capacity, $I$, is defined as

$$I = \frac{1}{2}\log_2(P+1), \tag{4}$$

where $P$ is the power signal-to-noise ratio (SNR) of the channel.

The SNR has to be calculated in order to get the information capacity. To calculate the SNR for a single channel, a few assumptions are needed, and some of the equations stated above need to be rewritten. It is assumed that the neuron currents generated in the brain follow a Gaussian distribution, $j \sim N(0,\, \sigma^2_{\text{signal}})$. The noise for each channel is also assumed to be normally distributed, $n \sim N(0,\, \sigma^2_{\text{noise}})$ [13]. Rewriting equation (3) as an integral over the entire brain volume V,

$$b = \int_V \vec{L}(r) \cdot \vec{j}(r) dr. \tag{5}$$

Combining equation (5) with the assumption that the currents follow a Gaussian distribution make it possible to, once again, rewrite the expres-

sion for the measured magnetic field. The root mean square (RMS) of the measured magnetic field can be expressed as,

$$b = \sigma_{\text{signal}} \int_V |\vec{L}(r)| dr, \tag{6}$$

where $|\vec{L}(r)|$ is the magnitude of the lead-field matrix. The signal to noise ratio for a single channel can then be expressed as,

$$P = \frac{b^2}{n^2} = \frac{\sigma^2_{\text{signal}}}{n^2} (\int_V |\vec{L}(r)| dr)^2. \tag{7}$$

Unfortunately it is much more complicated for a multi-channel MEG system. The sensors do not receive signals from one source, but multiple, making it hard to distinguish where the signal is coming from. Since the lead-field describes how the source couples to each sensor, when different sensors receive signals from one source the lead-field is overlapping. The overlap can be described from an analytical viewpoint like,

$$G_{jk} = \int_V \vec{L}_j(r) \cdot \vec{L}_k(r) dr \tag{8}$$

where $G_{jk}$ is the overlap of the j-th and k-th lead fields.

Because of the lead-field overlap a set of virtual channels whose lead fields are independent of one another need to be constructed before evaluating the information they receive. [13] Therefore the vectors in the lead-field overlap matrix $G$ have to be orthogonalized. The orthogonalization of the vectors in $G$ is done via singular-value decomposition, so that $G = U\lambda U^T$, where $U$ is a matrix with the eigenvectors and $\lambda$ a vector with the eigenvalues of $G$. By the orthogonalized lead-field,

$$\vec{L}_k(r) = \sum_j U^T_{jk} \vec{L}_j(r), \tag{9}$$

the independent channels can be expressed. Finally the SNR can be expressed for an orthogonalized channel $k$,

$$P_k = \frac{\sigma^2_{\text{signal}} \lambda_k}{\sum_j U_{jk} \sigma^2_{\text{noise}}}. \tag{10}$$

Equation (10) shows that the sensor noise in the channel is mixed together with the orthogonalization from matrix $U_{jk}$, therefore taking the overlap

from the lead-field into respect. Equation (3) and (10) are brought together in order to calculate the information capacity for a multi-channel MEG system,

$$I_{\text{tot}} = \frac{1}{2}\sum_k \log_2\left(\frac{\sigma^2_{\text{signal}}\lambda_k}{\sum_j U_{jk}\sigma^2_{\text{noise}}} + 1\right). \tag{11}$$

As previously mentioned, information capacity fails to give any information about the spatial distribution. This is because the information extracted in the array is from the entire brain, consequently all information of certain regions of the brain is lost [14]. A new metric is therefore needed, one that can give the spatial information.

## 3.6 Spatial information density

Spatial information density (SID) was a metric shaped to evaluate the performance of sensors arrays in MEG. It, unlike total information capacity, gives us the maximum information from one individual source in the brain [14]. The metric looks at every source individually, and calculates the maximum information that could be extracted from that source. SID is calculated for every source in the brain. From the different values, a SID-map of the brain can be made.

Individual source will couple to multiple sensors within an array, just like in information capacity. The lead-field overlap is therefore as important for SID as it was for information capacity. The overlap is calculated for each individual source,

$$G_{\text{source}} = \int_{\text{source}} \vec{L}_i \vec{L}_k dv, \tag{12}$$

where $\vec{L}_i$ and $\vec{L}_j$ are the lead fields of sensors $i$ and $j$. The SID-values for each source are calculated in a similar way as total information capacity. Since a source might give information to different channels, a summation of the independent information from all channels is needed to calculate the SID-value for that source [14]. The SID value for a single source is,

$$\text{SID}_{\text{source}} = \frac{1}{2}\sum_k \log_2\left(\frac{\sigma^2_{\text{signal}}\lambda_k}{\sum_j U_{jk}\sigma^2_{\text{noise}}} + 1\right) \tag{13}$$

where $U_k$ are the eigenvectors and $\lambda_k$ the eigenvalues of matrix $G_{\text{source}}$.

# 4 Discussion

Due to the enormous amount of neurons that can create a signal in the brain, the localization of the activity is the toughest challenge in MEG today. Spatial resolution plays a major role in the localization of activity, and a spatial resolution of less than a millimeter is wished for in all parts of the brain. With new technology, using on-scalp MEG, the spatial resolution could be improved. The opportunity of measuring the magnetic field closer to the brain makes the signal stronger and easier to interpret. The signal measured with on-scalp MEG has a more narrow and high-amplitude dipole field, as compared to conventional MEG (see figure 4). Two dipole fields close to each other should therefore be easier to distinguish using on-scalp MEG. However, the same problem remains for on-scalp and conventional MEG: the sources deep in the brain are challenging to image and localize, as the amplitude of the magnetic fields they generate decreases with distance between them and the sensor (be it on the scalp or a few cm from it). The magnetic field generated deep in the brain will give a dipole field that is weaker and more spatially diffuse as compared to the ones generated close to the sensors.

Spatial resolution in MEG is tricky. Even a broad and widely used term as full width half maximum (FWHM) cannot be directly applied to MEG. A metric that could reflect spatial resolution is therefore needed in MEG. From the analysis done in this work, a few metrics were found that could be related to the spatial resolution.

## 4.1 Topography Overlap (PPE and CA) and Shared Variance

At first sight, the metrics topography overlap and shared variance look a lot alike. Topography overlap is a measure of how much the lead field (i.e., the coupling between sources and sensors) from a source looks like the lead field from another source. If the correlation coefficient is over 0.9 for a source, the article defined two other parameters; PPE and CA. Both PPE and CA are measures of the spatial resolution in an image, but both are limited to simulated MEG-data. Shared variance measures overlap in electric signals over time between a 'seed' source and 4000 other sources. With this metric, an article claims OMPs sensors have a better spatial resolution than low $T_C$ SQUID sensors [12]. If one source has a 50% or higher overlap with the seed source, it was used to define the spatial resolution. The article studies how well the sources, with a 50% overlap, can be separated from each other with different sensor technologies. Unlike measures related to topography overlap,

shared variance is based on real MEG data, and the data used has undergone a beamformer.

The lower threshold (50%) with shared variance is a more conservative approach than the 90% threshold for topography overlap. Using a lower threshold results in a larger portion of sources that are correlated. Using the higher threshold could instead be an overestimation, as a lot of highly correlated sources that do not satisfy the threshold are ignored. If the article that used the lower threshold instead would had a threshold at 90% the results would probably differ. Using such a high overlap would lead to that some of the sources that are now used to define spatial resolution, would be ignored. The spatial resolution would therefore change with the threshold, and would probably be much worse with a higher threshold.

Both topography overlap and shared variance measure the overlap between sources. But due to that the metrics use different data, the results they give are very different. When using an inverse solution to localise the source positions, it has become clear that the inverse solution has a significant impact on the image generated (i.e., different inverse solvers provide different source distributions) [8]. Using a beamformer, or any other inverse solution, on the data will therefore change the image: because the inverse problem does not have a unique solution, the localisation of the sources can never be completely accurate. Shared variance therefore has this disadvantage over topography overlap, since the metric is based on data from a beamformer.

A limitation to the results posited in Boto, et al.'s work is the number of sensors. The standard approach to MEG source analysis is to use well-developed statistical methods to estimate the activity of 1 000 - 10 000 sources from a roughly 300 sensor recording [15]. Sampling more than 10 000 sources only leads to a high correlation between the sources, and generally does not give any new information about the activity. When claiming higher spatial resolution with the OMPs sensors than low $T_C$ SQUIDs sensors in the article, it should be emphasized that the OMP system was only using 13 sensors [12]. The 13 sensors were not evenly distributed around the head, but gave a high coverage to a specific area of the brain. For the low $T_C$ SQUIDs sensors, they were using 275 sensors and compared the result to the 13 OMPs. Using only 13 sensors, but 4000 sources for the OMP system, makes the results in the article unlikely. They should, at most, get reliable results from around 450 sources when one considers the 'standard' 300 sensors/10 000 sources ratio. For comparison, Iivanainen et al. describe topography overlap with around 300 sensors for their OMP system [8]. The article also claims a better

spatial resolution even for a full-head system. If they were to use a full-head system with around 100 sensors, they would not be able to extract hundreds of thousands of source activations. The oversampling of the source space does not lead to any more information, and the 100 000 sources would have a high correlation with each other. Shared variance was therefore in this work not considered as a metric that could describe the spatial resolution. Topography overlap is however a more accurate description of spatial resolution, mainly because it is not using any inverse solutions. Topography overlap did a better job at giving a description of the spatial resolution in an image, but as stated before, it does have its limitations to simulated data.

## 4.2 Point-spread Function

At first sight the point-spread function could be a great measure for spatial resolution in MEG. For other image systems the PSF can be used to give an indication of how well the system handles a point source. In MEG, however, the PSF has only been used to investigate the behaviour of the inverse solution. This is logical because the inverse solution has such a large impact on image quality. Specifications of a given MEG system (i.e., sensor coverage, sensitivity, packing density, etc.) have a profound impact on the lead-fields, which, in turn, are central to any inverse solution. As such, it would be of interest to compare PSFs with the same inverse solution across MEG systems. Such an investigation would be enlightening regarding the relative spatial resolutions of different technologies (e.g., on-scalp vs. conventional MEG). An idea would be to measure how well a MEG-system handles a single dipole. If the single dipole had a known magnitude, the PSF can be used to describe how well the MEG-system handles that dipole field. The MEG-system that would measure a dipole field most similar to the "real" dipole would have the smallest PSF. From figure 3 it seems apparent that an on-scalp MEG-system would have a more accurate description of the dipole field than conventional MEG-systems.

## 4.3 Signal Power, total information capacity and spatial information density

Compared to all other metrics, signal power is the metric that could most easily be described in real-life MEG. This gives the metric a strong advantage, as it can be both simulated and measured in a recording. A high source power improves the recording, as the signals recorded are higher and easier to interpret. The signal power must be higher than the noise level for there to be a signal in the sensors. Signal power could therefore directly be related

to total information capacity and spatial information density, as it depends on where in the brain the signal could be detected. The signal power could be further investigated with total information capacity and spatial information density, to map out where in the brain the signal power is the highest. However, the relationship between signal power and spatial resolution in an image has not been deeper investigated in MEG.

The metrics total information capacity and spatial information density (SID) have been used to estimate the performance of different sensor arrays. Spatial resolution is a measure of distance, and total information capacity and SID are measured in bits and bits/area, respectively. Talking about the spatial distribution in bits per area is a new approach for describing the image. However, it does make the metric a bit harder to grasp, compared to spatial resolution. The metric SID is therefore not widely used in the field, even though it gives a representation of the spatial differences from all the sources in the brain, without using any inverse operators. SID is a good metric for checking the spatial distribution, but is not as popular for describing the spatial qualities as spatial resolution is. Another metric is needed, one as straightforward as SID and with the same advantages, but one that results in a distance measure of some kind.

One way to go further with the analyzes done in this work, would be to look at more metrics. The metrics found could be evaluated via simulations on a realistic head, together with the metrics that were discussed in this work. The metrics that could use a deeper study would be topography overlap and shared variance. Both metrics are on the right track to measuring spatial resolution. Topography overlap combined with shared variance could be a way of measuring the spatial resolution in a real MEG-system. Using a standard approach to MEG source analysis with shared variance could give interesting results, and it is worth looking into. Topography overlap also has the two measures PPE and CA. Both are a measure of spatial resolution, but PPE is measuring in length, just as spatial resolution. Therefore the PPE concept could be of interest when combining topography overlap with shared variance. Measuring the distance between sources that are highly correlated but still resolvable would give different values of the smallest resolvable distance. This could later be calculated for different parts of the brain, to see if the distance is changing.

## 4.4 Conclusion

The aim of this work was to identify what spatial resolution is in MEG, and to find potential metrics that could be affecting the spatial resolution. Unfortunately, the parameters that were analyzed could not define the spatial resolution in MEG. Most of the parameters found had their limitations to simulated MEG-data. However, a deeper understanding of the spatial resolution in MEG was obtained and new ideas of how to present the spatial resolution in MEG were introduced.

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