NEMOlab

2020 - 2021

by Sarang S. Dalal

New frontiers with optically pumped magnetometers (OPMs) for MEG and other biomagnetic signals

MEG systems are based on ultrasensitive sensors that can detect extremely small magnetic field changes. SQUIDs – superconducting quantum interference devices – have been the prevailing MEG sensory technology, but they require supercooling with liquid helium. This requires both cryogenic infrastructure as well imposes physical limitations on MEG system design. Effectively, they are responsible for the size of MEG systems and the requirement for volunteers and patients to remain still during an MEG measurement.

Figure 1
In early 2020, we received a starter set of 16 OPMs from FieldLine Inc. (Boulder, Colorado) for measuring MEG and other biomagnetic signals from the human body.

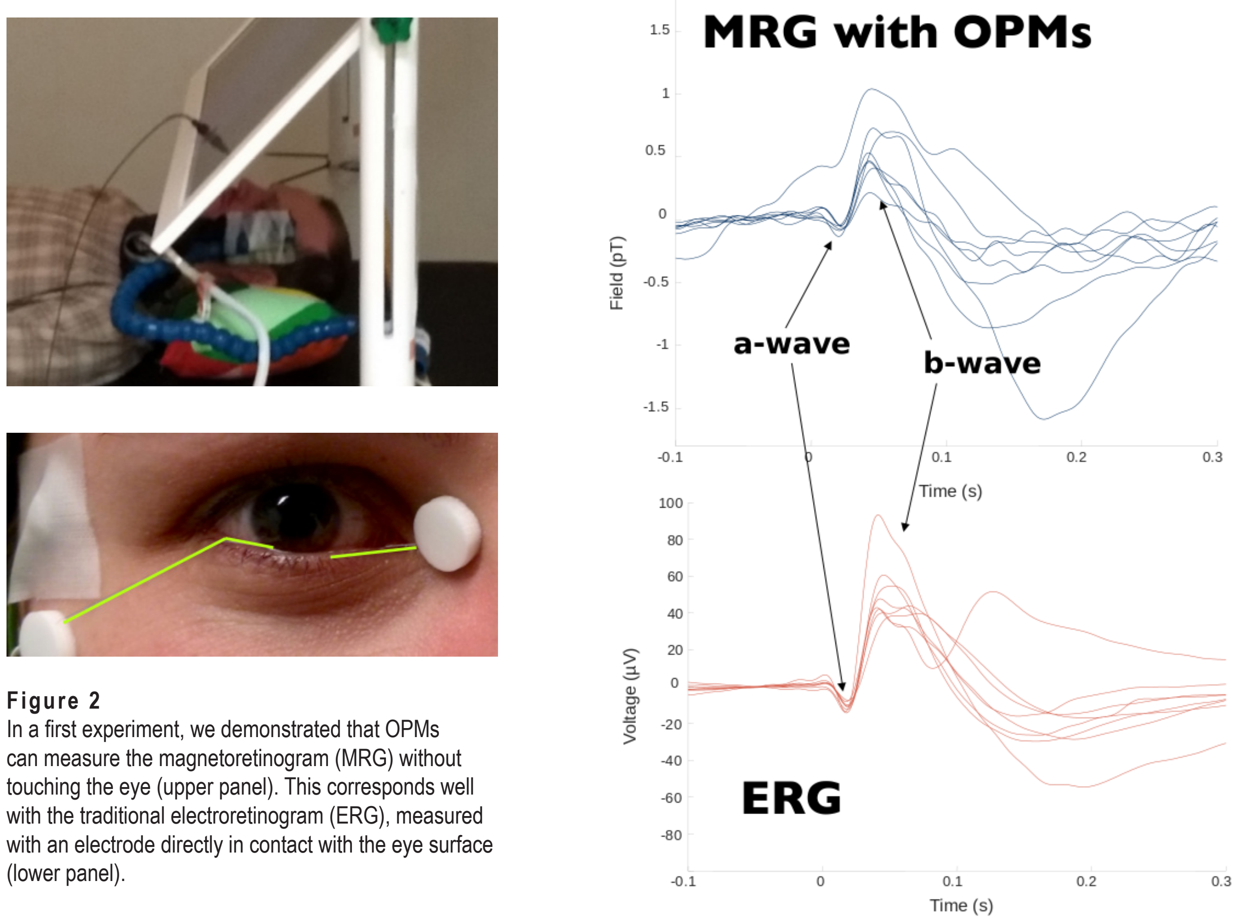

Figure 2
In a first experiment, we demonstrated that OPMs can measure the magnetoretinogram (MRG) without touching the eye (upper panel). This corresponds well with the traditional electroretinogram (ERG), measured with an electrode directly in contact with the eye surface (lower panel).

However, a recently developed quantum technology, optically pumped magnetometers (OPM), is poised to become the basis for next-generation MEG systems. OPMs have similar sensitivity to the super SQUIDs, but work near room temperature, using a vapor that absorbs light in proportion to magnetic field strength. They are similar in size to EEG electrodes and wearable, opening up a variety of new possibilities. The configurability of OPMs allows the same system to measure signals from neural structures that are poorly captured or impossible to measure with conventional MEG systems that are designed for the adult head. For example, the cerebellum suffers from poor coverage (Andersen, Jerbi, Dalal, 2020) but with appropriate positioning, its responses may be well-captured by OPMs.

We acquired a small 16-channel OPM system in early 2020 to gain experience with this technique and develop new applications that were previously impractical or impossible with our SQUID-based MEG system (see Figure 1).

OPM-based Magnetoretinography

In a project led by postdoc Dr. Britta Westner and PhD student James Lubell, we quickly demonstrated that OPMs placed next to the eye capture standard evoked responses from the retina (see Figure 2; Westner et al., 2021).

Such a magnetoretinogram avoids the discomfort of the electroretinogram (ERG) that requires electrodes directly on the eye, but the conventional MEG helmets are not optimal for measuring it. Apart from its use in the eye clinic, ERG can be informative in the investigation of retinopathies arising from diabetes and multiple sclerosis, particularly when combined with measurements of visual cortex. Our group has been using ERG together with MEG to investigate how the retina and cortex communicate in healthy vision. However, the nature of ERG is off-putting to many, discouraging wider use; the OPM-retinogram provides a comfortable alternative.

FACTS

Group members:

- Sarang S. Dalal
- Britta Westner
- Alexandra Vossen
- Lau Møller Andersen
- James Lubell
- Jordan Alves
- Tamas Minarik
- Barbara Berger

Publications 2020-2021:

- Petras K, ten Oever S, Dalal SS* / Goffaux V* (2021). Information redundancy across spa-tial scales modulates early visual cortical processing. NeuroImage, 244:188613.
- Tiihonen M, Westner BU, Butz M* / Dalal SS* (2021). Parkinson's disease patients benefit from bicycling - A systematic review and meta-analysis. npj Parkinson's Disease, 7:86.
- Westner BU, Lubell J, Jensen M, Hokland SC, Dalal SS (2021). Contactless measurements of retinal activity using optically pumped magnetometers. NeuroImage, 243:118528.
- Andersen LM & Dalal SS (2021). The cerebellar clock: predicting and timing somatosenso-ry touch. NeuroImage, 238:118202. 12pp.
- Jaiswal A, Nenonen J, Stenroos M, Gramfort A, Dalal SS, Westner BU, Litvak V, Mosher JC, Schoffelen J-M, Witton C, Oostenveld O, Parkkonen L (2020). Comparison of beam-former implementations for MEG source localization. NeuroImage. 216:116797.
- Andersen LM, Jerbi K, Dalal SS (2020). Can EEG and MEG detect signals from the human cerebellum? NeuroImage, 215:116817.

Invited talks by NEMOlab members:

- **Sarang Dalal**
  Baby steps towards fetal MEG with optically pumped magnetometers. MEG UK, 2021.

  Our vision – and a little heart – with OPMs. MEG Nord, 2021.
- **Britta Westner**
  Contactless measurements of retinal activity using OPMs, MEG UK, 2021.
- **James Lubell**
  Measurement of low- and high-frequency retinal activity using optically pumped magnetometers, Workshop on Optically Pumped Magnetometers, 2021.
- **Lau Møller Andersen**
  Cerebellar MEG - investigating the timing capabilities of the cerebellum, presented at the University of Münster at the Institute of Biomagnetism and Biosignal Analyses, 2020.

  The cerebellar clock – predicting and timing somatosensory touch, presented at the Karolinska Institute at the Swedish National Facility for Magnetoencephalography, 2021.

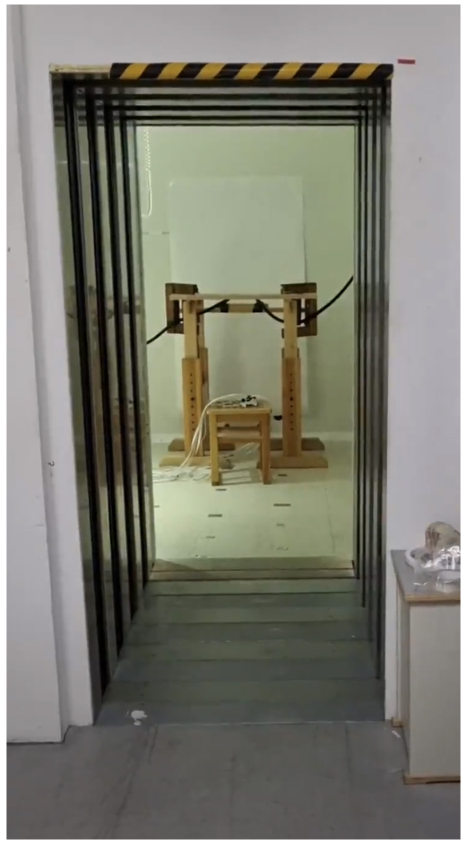

Figure 3
James Lubell visited the Physikalisch-Technische Bundesanstalt in Berlin with our OPMs to make use of their BMSR2 facility, the most magnetically quiet place on Earth. This allowed him to investigate the upper frequency limits of OPMs for measuring human neural activity in a virtually noise-free environment.

James Lubell later spent 1 month at the Physikalisch-Technische Bundesanstalt in Berlin, which has the most heavily magnetically shielded room in the world. In this environment, high-quality OPM performance can be achieved without active magnetic compensation coils, allowing James to test the limits of OPM sensitivity in a virtually noise-free environment (see Figure 3).

He succeeded in demonstrating that OPMs can measure robust high-frequency responses from the human retina, up to at least 150 Hz. This implies that, with sufficient noise cancellation, OPMs should also be suitable for measuring high gamma band activity from the cerebral cortex.

In addition, he was able to place several sensors around the eye and investigate the spatial distribution of these retinal signals. It turned out that the timing of the high-frequency oscillations varied by 2-3 milliseconds depending on measurement location, consistent with the propagation of retinal ganglion cell activity from the stimulated retinal patch to the head of the optic nerve (see Figure 4).

The precise cellular origin of the retinal oscillatory potential commonly measured with ERG has been debated. This data provides preliminary evidence that it indeed arises from retinal ganglion cell activity, the neurons which effectively commnicate retinal output to visual cortex via the thalamus. We are now planning follow-up experiments to confirm this finding.

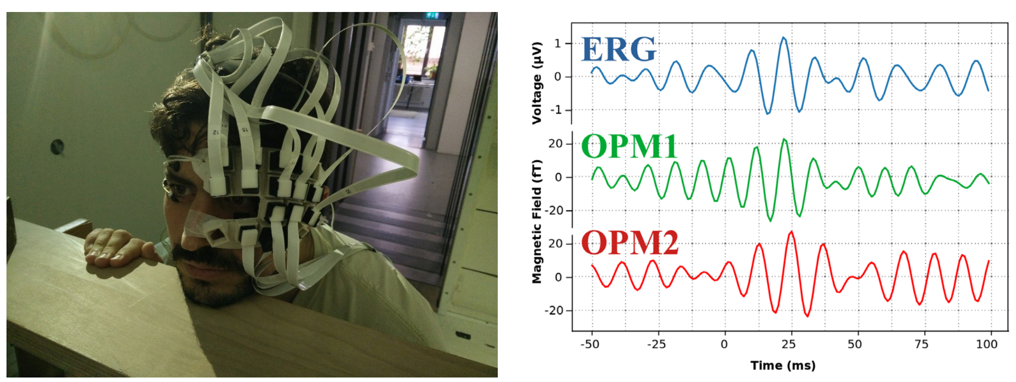

Figure 4
By placing OPMs around the eye, James Lubell was able to confirm that retinal signals up to at least 150 Hz were detectable and comparable to ERG measured from the eye, suggesting that OPMs should also be suitable for measuring high gamma band activity from the brain. Even more compelling, some OPMs captured similar signals with a delay of 2-3 milliseconds, suggesting that they may be able to disentangle local retinal activity from responses arising from the optic nerve head.

OPM-based fetal MEG

The developing brain of the human fetus generates tiny magnetic signals that can be measured from the mother's abdomen. Fetal magnetoencephalography (MEG) gives insight into how the healthy fetal brain begins to function as well as potential abnormalities in high-risk pregnancies. However, the technique has been limited to only three labs in the world that have SQUID-based MEG systems appropriately shaped for pregnant women. Measurement of fetal MEG with OPMs would greatly expand the availability of fetal MEG, since any OPM-MEG lab would be capable of it.

Together with obstetrician and clinical researcher Dr. Lars Henning Pedersen at Aarhus University Hospital, we set out to demonstrate whether OPMs can indeed capture brain signals from the developing fetus. Classic stimulation techniques involve delivery of light or sound onto the mother's abdomen. In this initial proof of concept, however, we instead relied on an acoustic signal intrinsic to the mother's body – the sound of her own heartbeat. The two major heartbeat sounds coincide with the QRS complex and T wave of the cardiogram that is readily visible in OPM sensors placed on the torso.

We recruited 2 women in the 36th week of pregnancy and placed OPMs on the abdomens. The mothers were allowed to rest or sleep for the duration of the recording. Heart signals – the magnetocardiogram – from both the mother and fetus were readily observed in the raw data. The two heart signals could be perfectly isolated with independent components analysis (ICA) (see Figure 5). This also allowed the heart signals to be removed from the data to potentially reveal any signals from the fetal brain – fetal MEG.

In both participants, this revealed waveforms consistent with two consecutive auditory evoked responses, each commencing 170 ms after the maternal QRS complex and T wave (see Figure 6 next page). This corresponds well with known fetal auditory response latencies from SQUID-based fetal MEG studies, and therefore represents the first OPM-based fetal MEG measurements.

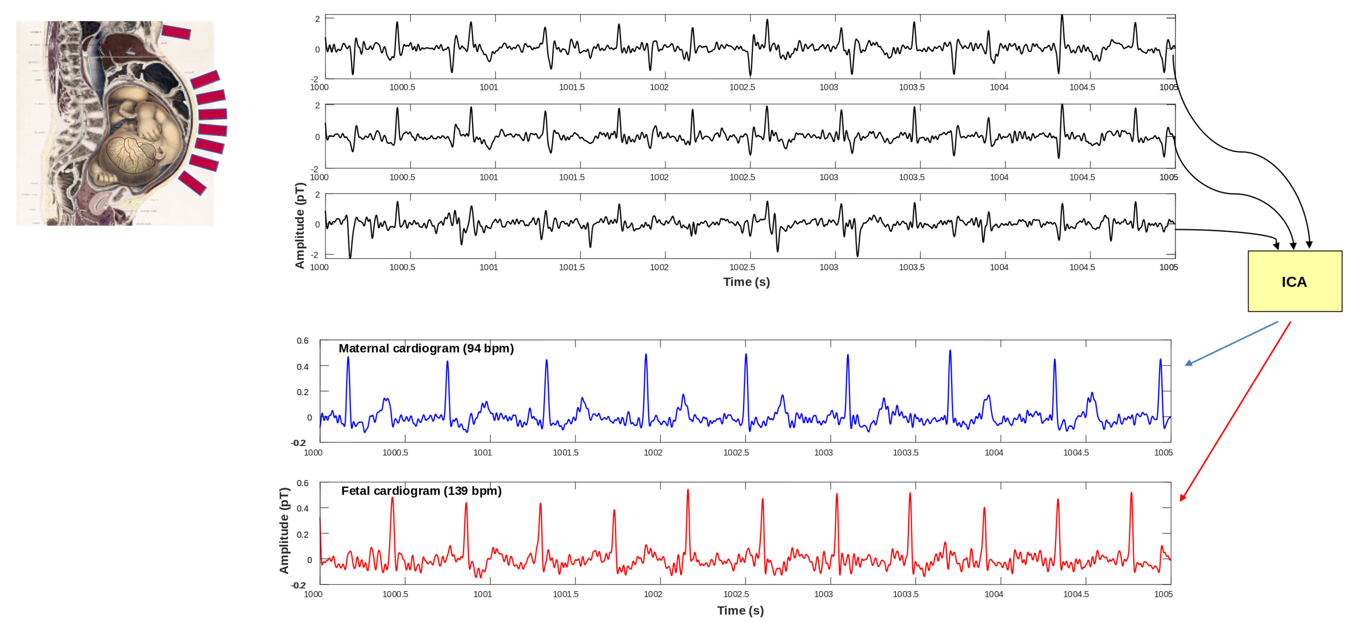

Figure 5
An example of fetal measurements in our lab, with OPMs placed over the abdomen of a mother at 36 weeks of pregnancy. By processing the signal with ICA, we are able to clearly distinguish the maternal cardiogram (blue) and fetal cardiogram (red).

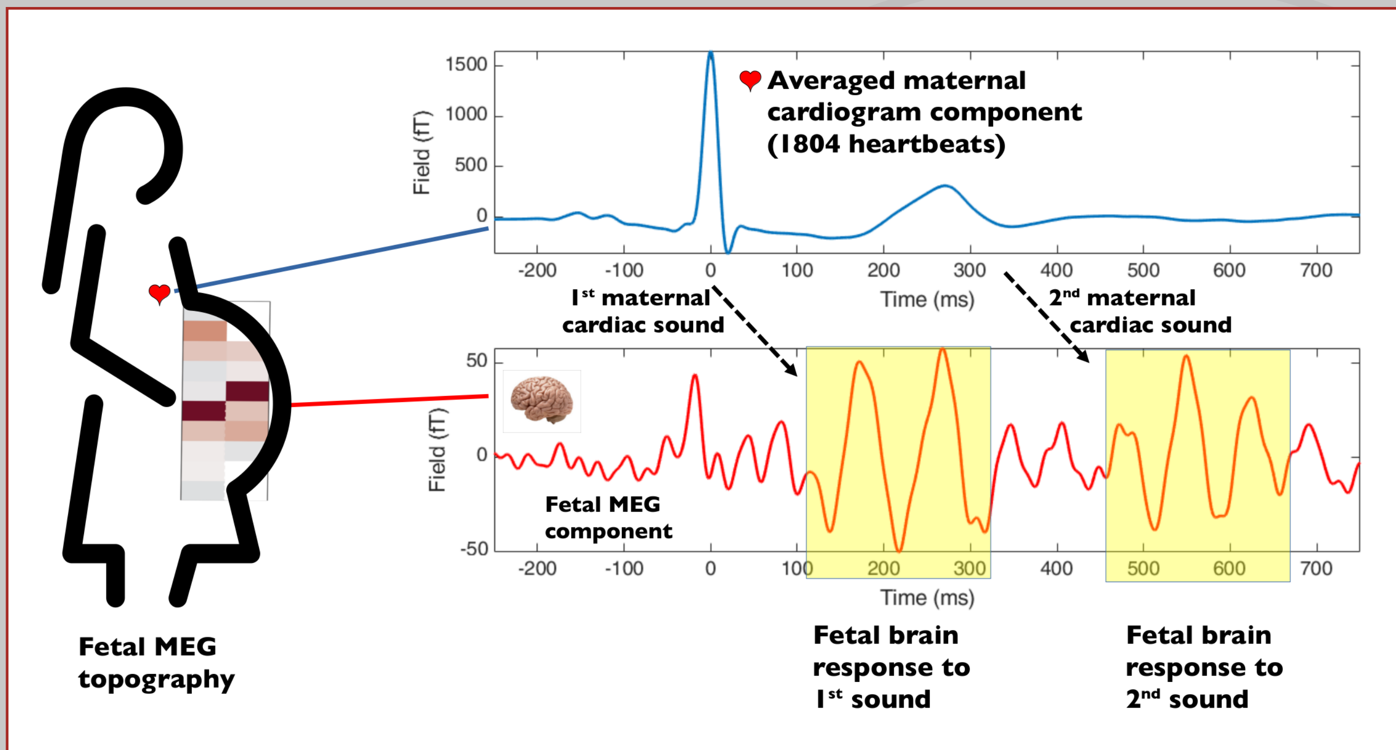

Figure 6
In a pilot experiment and the first ever proof-of-concept for OPM-based fetal MEG, we leveraged the sound of the mother's heartbeat as an auditory stimulus for the fetus. The fetus should hear two major sounds on each beat of the mother's heart; fetal brain responses (red) were observed 150-300 ms after each sound, consistent with latencies expected in week 36 of gestation. These responses were well-distinguished in location and timing from the maternal cardiogram (blue), with the highest amplitudes over the center of the maternal abdomen. These measurements demonstrate the feasibility and high-fidelity of OPM-based fetal MEG.

A fresh look at the cerebellum

In a project led by postdoc Dr. Lau Møller Andersen, we investigated a potential internal clocking mechanism that monitors predictable, temporal patterns and builds sensory expectation based on these patterns. We found suggestive evidence of the cerebellum involved in this clocking and decided to test this directly. We found strong evidence of the cerebellum being this internal clock, with cerebellum creating precise temporal predictions when patterns were regular and less so when patterns were irregular (Andersen and Dalal, 2021).

To show how this cerebellar clock might be informative to behaviour, Lau conducted another study that is to be presented at the BIOMAG conference in Birmingham 2022. Lau also led the writing of an influential review (Andersen et al., 2020) that shows that it is feasible to record the electrophysiological signals of the human cerebellum non-invasively, despite beliefs to the contrary. Lau here also showcased the breadth of cerebellar function showing its function to reach far beyond mere motor coordination, as is otherwise believed by many in the scientific community.

Lau's next study will focus on the potential role of the cerebellum in Parkinson's disease - as more and more evidence suggests that not only the basal ganglia are involved in Parkinson's disease but that also the wider connections to the cerebellum may play a role.

Another area of focus of his is how optically pumped magnetometers can be utilised to optimise recordings of the cerebellum (see Figure 7).

NEW FACE at CFIN

Barbara Berger, is a COFUND Research fellow hosted by AIAS and joined CFIN in 2022. She is affiliated with Sarang S. Dalal's group.

Barbara completed her MSc in Psychology with Wolfgang Klimesch in Salzburg (AT) and obtained her PhD in Cognitive Neuroscience at the University of Surrey (UK) supervised by Paul Sauseng. She previously held a Marie Sklodowska Curie Fellowship (Horizon2020) at Ole Jensen's lab at the University of Birmingham (UK).

Her research focuses on the brain oscillatory correlates of Executive Functioning – top-down control of attention and Working Memory – using MEEG/OPM in combination with non-invasive neurostimulation (TMS). Currently she is investigating the electrophysiological expression of the link between visual percepts and Working Memory maintenance.

NEW FACE at CFIN

Tamas Minarik, joined CFIN in February 2021 as postdoc at the Nemo lab of Sarang S. Dalal.

He obtained a Marie Sklodowska Curie Felloship (Horizon Europe) in 2022 and is investigating the role of the Thalamus in selective attention and how it interacts with relevant cortical structures. The project is using MEG in conjunction with rhyhmic visuo-auditory stimulation.

Tamas is further working on improving source modelling of MEEG signals.

Previously he has been working with Paul Sauseng at the LMU Munich (DE) and Ole Jensen at University of Birmingham (UK).

Figure 7
Dr. Lau Møller Andersen seated in the magnetically shielded room with optically pumped magnetometers over his cerebellum.