

# 1 **In vivo magnetic recording of neuronal activity**

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## 17 **KEYWORDS**

18 Magnetic fields, magnetoencephalography, MEG, spin electronics, magnetic sensors.

## 19 **SUMMARY**

20 **Neuronal activity generates ionic flows and thereby both magnetic fields and**  
21 **electric potential differences, i.e. voltages. Voltage measurements are widely**  
22 **used, but suffer from isolating and smearing properties of tissue between**  
23 **source and sensor, are blind to ionic flow direction, and reflect the difference**  
24 **between two electrodes, complicating interpretation. Magnetic field**  
25 **measurements could overcome these limitations, but have been essentially**  
26 **limited to magnetoencephalography (MEG), using centimeter-sized, helium-**  
27 **cooled extracranial sensors. Here, we report on in vivo magnetic recordings of**  
28 **neuronal activity from visual cortex of cats with *magnetodes*, specially**  
29 **developed needle-shaped probes carrying micron-sized, non-cooled magnetic**  
30 **sensors based on spin electronics. Event-related magnetic fields inside the**  
31 **neuropil were on the order of several nanoteslas, informing MEG source models**  
32 **and efforts for magnetic field measurements through MRI. Though the signal-**  
33 **to-noise ratio is still inferior to electrophysiology, this proof of concept**  
34 **demonstrates the potential to exploit the fundamental advantages of**  
35 **magnetophysiology.**

## 36 **HIGHLIGHTS**

- 37 • Spin-electronics based probes achieve local magnetic recordings inside the  
38 neuropil
- 39 • Magnetic field recordings were performed in vivo, in anesthetized cat visual  
40 cortex
- 41 • Event-related fields (ERFs) to visual stimuli were up to several nanoteslas in  
42 size
- 43 • ERFs could be detected after averaging less than 20 trials

## 44 **IN BRIEF**

45 Caruso et al. report in vivo, intra-cortical recordings of magnetic fields that reflect  
46 neuronal activity, using magnetodes, i.e. micron size magnetic sensors based on spin  
47 electronics.

## 48 INTRODUCTION

49 Neuronal activity entails ionic flows across the cell membrane and along dendrites.  
50 This electrical activity can be measured extra-cellularly or intra-cellularly by  
51 microelectrodes (Kandel et al., 2000) which are either thin metallic micro-wires, or  
52 glass pipettes containing an ionic solution, to realize a conductive interface between  
53 the local brain tissue and the recording instrumentation. Intracellular recordings  
54 directly reveal the transmembrane voltage or current of an isolated neuron, but  
55 intracellular recordings in vivo are difficult in practice and often only brief  
56 measurements of single neurons are feasible. Extracellular recordings, on the other  
57 hand, measure the aggregate fluctuations in voltage arising from the net neuronal  
58 activity around the electrode's tip, with respect to a reference electrode (Buzsáki et al.,  
59 2012). Microelectrodes inside the neuropil record action potentials and local field  
60 potentials (LFPs), electrocorticographic electrodes provide mesoscopic LFPs, and  
61 scalp electrodes deliver the electroencephalographic (EEG) signal. Combining many  
62 electrodes into planar (Maynard et al., 1997) or laminar arrays (Lewis et al., 2015)  
63 allows for the study of whole brain networks and their dynamics in the intact brain  
64 (Buzsáki, 2004).

65 The electric currents flowing through the active neuropil also give rise to a magnetic  
66 signature. Magnetoencephalography (MEG) (Cohen, 1968, 1972; Hari and Salmelin,  
67 2012) is a non-invasive method to measure the magnetic fields of active neuronal  
68 populations during perceptual or cognitive tasks in the healthy or diseased human  
69 brain. This technique uses Superconducting Quantum Interference Devices (SQUIDS)  
70 cooled down to the temperature of liquid helium (4.2 K). The apparatus necessary for  
71 this cooling imposes a distance to the cortical surface of 3 to 5 cm in in vivo  
72 configurations. The spatial resolution is typically better than for EEG recordings, but  
73 even under optimal conditions still lies in the order of several mm<sup>3</sup>, with signal  
74 amplitudes in the femtotesla ( $10^{-15}$ T) to picotesla ( $10^{-12}$ T) range.

75 Local magnetic recordings of the neuronal activity could be a complementary  
76 technique to electrophysiology, because the magnetic signal provides interesting  
77 properties in addition to those realized by the electric signal. Contrary to electric fields,  
78 which strongly depend on the dielectric properties of the tissue between neuronal  
79 sources and the recording electrode, magnetic fields travel through tissue without  
80 distortion, because the respective permeability is essentially the same as free space

81 (Barnes and Greenebaum, 2007). Therefore, magnetic fields are only attenuated by  
82 the distance to the current source. Ionic flows and the corresponding magnetic fields  
83 are likely largest inside neurons. As those magnetic fields pass through the cell  
84 membrane without attenuation, extracellular magnetic field measurements might  
85 provide functionally intracellular measurements without impaling the neuron.  
86 Moreover, while electrophysiological recordings yield scalar values, local magnetic  
87 recordings yield information about both amplitude and direction of current sources.  
88 Thereby, they might allow the precise localization of the source of neuronal activity at  
89 a given moment in time in the 3D volume of the brain. Furthermore, electrodes always  
90 measure the electric potential relative to a reference electrode, and the position and  
91 type of reference can substantially influence the measured signal. Moreover, in multi-  
92 electrode recordings, all channels typically share the same reference, which poses a  
93 problem for analyses of functional connectivity, because the resulting signals are not  
94 independent. Magnetodes, presented in this work, provide an elegant solution,  
95 because the recorded magnetic signals are reference-free, and therefore allow for an  
96 unbiased measure of connectivity and information flow throughout the brain. In  
97 addition, these magnetodes can be used to perform magnetic resonance  
98 spectroscopy (Guitard et al., 2016).

99 In order to minimize tissue damages, magnetic probes for insertion into the brain  
100 require a needle shape and the miniaturization of the magnetic sensors, while  
101 maintaining a very high sensitivity at physiological temperature. Approaches to record  
102 the magnetic biological signal closer to the sources than MEG have been successfully  
103 realized by using small SQUIDs (Magnelind, 2006), atomic magnetometers (Sander  
104 et al., 2012) or winded coils (Roth and Wikswo, 1985) and very recently with nitrogen-  
105 vacancy centers in diamond on a living invertebrate (Barry et al., 2016). However,  
106 limitations due to the millimeter size of the sensors or to its operating conditions never  
107 allowed penetration into the neuropil nor recording at distances of merely tens of  
108 microns from active cells.

## 109 **RESULTS**

### 110 **Development and fabrication of micron-size magnetic sensors based on spin** 111 **electronics for in vivo recordings**

112 Spin electronics (Baibich et al., 1988) offers the capability to reduce magnetic sensors  
113 to micron size and to reach sensitivity in the sub-nanotesla range while working at  
114 body temperature and thereby avoiding bulky vacuum isolation (Reig, 2013). We have  
115 designed Spin Valve (Dieny et al., 1991) Giant Magneto-Resistance (GMR) sensors  
116 consisting of 5 segments of  $4 \times 30 \mu\text{m}^2$  arranged in a meandering configuration on  
117 silicon substrate that was ground to a thickness of  $200 \mu\text{m}$  and etched to form a needle  
118 shape for tissue penetration (Fig. 1A). The sensors have been electrically insulated by  
119 a dielectric bilayer of  $\text{Si}_3\text{N}_4/\text{Al}_2\text{O}_3$ . We refer to these probes as ‘magnetodes’, for a  
120 magnetic equivalent of electrodes (see STAR Methods for details of manufacturing  
121 and characterization).

122 GMR sensors are magnetic-field dependent resistors. To measure magnetic field  
123 strength, an input voltage is applied to the GMR, and the output voltage is recorded  
124 (Fig. S1). The GMR output voltage varies sigmoidally as a function of the in-plane  
125 component of the magnetic field (Fig. 1B). The sensor is configured such that very  
126 weak magnetic fields, around zero, result in outputs constrained to the steep linear  
127 part of the curve, thereby maximizing the dynamic range in the region of interest. In  
128 the linear part, the slope is  $1.8\%/m\text{T}$ , corresponding to a sensitivity of 10 to  
129  $25 \text{ Volt}_{\text{out}}/(\text{Volt}_{\text{in}} \times \text{Tesla})$ . The noise spectrum at a typical input voltage of 0.5 V leads  
130 to sensitivities of  $7 \text{ nT}/\sqrt{\text{Hz}}$  at 10 Hz,  $2 \text{ nT}/\sqrt{\text{Hz}}$  at 100 Hz and  $370 \text{ pT}/\sqrt{\text{Hz}}$  in the  
131 thermal noise regime above 1 kHz (Fig. 1C).

### 132 **Experimental setup**

133 We performed in vivo recordings in primary visual cortex of anesthetized cats (see  
134 STAR Methods). Figure 2 shows a schematic representation of the experimental  
135 setup. A magnetode was inserted into the tissue to a depth of less than 1 mm from  
136 the cortical surface using micromanipulators under microscope inspection. The  
137 magnetode was sensitive to fields orthogonal to the tip, that is, parallel to the cortical  
138 surface. A tungsten electrode was targeted to be less than 1 mm from the magnetode,  
139 to simultaneously obtain an independent electric recording. Recordings were  
140 performed without shielding. To physiologically activate the recorded brain area, a  
141 flash of light was presented directly to one eye of the cat. The duration of light

142 stimulation was either 100 ms or 500 ms, with a variable inter-stimulus interval of 0.9  
143 to 1.5 s to avoid adaptation or entrainment. The stimulus was presented 1000 times.  
144 The output signals from the tungsten electrode and the magnetrode were  
145 preprocessed and averaged with respect to stimulus onset, to calculate the event-  
146 related potential (ERP) for the electrode and the event-related field (ERF) for the  
147 magnetrode (see STAR Methods).

### 148 **Estimation of the expected field strength**

149 We estimated the field strength that we could expect, when recording magnetic fields  
150 inside the neuropil. As a starting point, we used the well-established magnetic fields  
151 recorded with MEG. When MEG signals are recorded from human subjects presented  
152 with visual stimuli, event-related fields (ERF) can be obtained with typical amplitudes  
153 in the range of 50 fT (Salmelin et al., 1994). For these MEG sensor-level field  
154 strengths, detailed models of the underlying sources estimate dipole strengths in the  
155 range of 10 nA\*m (Hämäläinen et al., 1993; Murakami and Okada, 2006). We  
156 constructed a model of an ensemble of neurons, which can produce such dipole  
157 strength, to then calculate the field strengths expected for magnetrode measurements  
158 very near or inside this neuronal ensemble. We simulated a square array of 10,000  
159 aligned neurons with a mean center-to-center separation of 5  $\mu\text{m}$ . In each neuron, a  
160 current was simulated, such that the ensemble of neurons appeared as a dipole of  
161 10nA\*m, when recorded from a large distance. The corresponding difference in  
162 electric potentials was simulated to occur over a distance of 200  $\mu\text{m}$ . This distance  
163 was estimated from current-source density measurements in cat visual cortex in  
164 response to visual stimuli (Mitzdorf, 1985). The currents in the neuronal ensemble  
165 gave rise to a magnetic signal of 50 fT at a distance of 6 cm, 800 fT at 1.5 cm, 126 pT  
166 at 1 mm, 1.3 nT at 100  $\mu\text{m}$  and 2.3 nT inside the neuronal ensemble. Thus, these  
167 simulations predict that magnetic field measurements within or in close proximity to  
168 the activated neurons will give ERFs in the range of a few nano-Tesla.

### 169 **Separation between magnetic signal and electrical contamination**

170 When magnetrodes are introduced into the neuropil, they might face direct capacitive  
171 coupling to electric currents flowing in the neuropil. Therefore, we developed a  
172 measurement scheme that suppressed this capacitive coupling. In this scheme, the  
173 GMR sensors were fed with alternating current (AC, Figure S2) with frequencies in the  
174 range of 20-80 kHz, and the sensor output was demodulated separately for

175 components that were in-phase with the AC modulation and those that were out-of-  
176 phase.

177 The currents fed to the GMR during the AC measurement scheme are not expected  
178 to directly influence neurons in the vicinity of the magnetode. We estimated, for a  
179 typical AC current, the resulting magnetic and electric field intensities induced in the  
180 neuropil, and they were several orders of magnitude below thresholds for neuronal  
181 stimulation (see STAR Methods).

182 We used two phantoms, one to generate purely magnetic fields, and another one to  
183 generate purely electric fields. When the input to the GMR was a time-varying  
184 magnetic field, the GMR output reflected this almost purely on the in-phase component  
185 (Fig. 3A). By contrast, when the input to the GMR was a time-varying electric field, the  
186 GMR output reflected this primarily at higher frequencies and then primarily in the out-  
187 of-phase component (Fig. 3B). Electric fields also induced a small in-phase  
188 component, presumably due to a mixing in the silicon substrate.

### 189 **Validation of the magnetic nature of in vivo recordings**

190 The phantom measurements provided GMR in-phase and out-of-phase outputs for all  
191 physiologically relevant frequencies of electric or magnetic field input. Thereby, they  
192 provided a transfer function for electric fields and a transfer function for magnetic  
193 fields.

194 In order to estimate contamination from electric field in vivo, we used the ERP recorded  
195 in one session (cat 2B) and convolved it with the transfer function estimated for electric  
196 fields in the phantom measurements. This provided an estimate of the GMR output  
197 that would be expected if the input were purely an electric field with the waveform of  
198 an ERP (Fig. 4A). In this case, the GMR out-of-phase component (green line) was  
199 larger than the in-phase component (red line).

200 Subsequently, we convolved the same ERP waveform with the transfer function for  
201 magnetic fields. This provided an estimate of the GMR output that would be expected  
202 if the input were purely a magnetic field with the waveform of an ERP (Fig. 4B). In this  
203 case, the in-phase component (red line) was substantially larger than the out-of-phase  
204 component (green line). We used the ERP waveform for both simulations, to aid direct  
205 comparison and to avoid circularity, when we compare, in the next step, the simulated  
206 GMR outputs to the experimentally observed GMR output.



207 The observed GMR output (Fig. 4C) showed a substantially larger in-phase  
208 component (red line) than out-of-phase component (green line). This pattern  
209 corresponds to the pattern estimated for magnetic field input (Fig. 4B), which suggests  
210 that the GMR output is mainly determined by the neuronally generated magnetic fields.  
211 The magnetic field input is primarily reflected by the in-phase component of the GMR  
212 output. Therefore, in the following, we refer to the in-phase component of the GMR  
213 output as event-related fields (ERFs), and we compare them to the event-related  
214 potentials (ERPs) recorded simultaneously through the tungsten electrode.

### 215 **Comparison between simultaneously recorded event-related fields (ERFs) and** 216 **event-related potentials (ERPs)**

217 Figure 5A shows the ERF and Figure 5B the simultaneously recorded ERP for the  
218 recording in the first animal (cat 1) with a visual stimulus duration of 100 ms. Figure  
219 5C shows a magnification of the data with the ERF (red) and ERP (green) scaled and  
220 superimposed to facilitate comparison. The ERF showed a magnetic response starting  
221 20 ms after stimulus onset, corresponding to the conduction delay between the retina  
222 and the primary visual cortex. The ERF was characterized by a strong negative  
223 component at 36 ms and a positive peak around 61 ms. The peak-to-peak amplitude  
224 was 2.5 nT. The onset of the ERP was comparable to the magnetic one, with a trough  
225 at slightly shorter latency and a peak at similar latency as the magnetic signal.  
226 Figure 5D shows the Pearson correlation coefficient between ERF and ERP as a  
227 function of time lag, with positive lag values indicating that the ERF lagged the ERP.  
228 The correlation function peaked at a value of approximately 0.55, for a lag of  
229 approximately 2 ms. The side peaks and troughs are due to the partially rhythmic  
230 nature of the ERP and ERF.

231 Similar results were obtained in two separate recordings from another animal (cat 2A  
232 and cat 2B). Figure 5E-H shows the results for one recording site and a visual stimulus  
233 duration of 100 ms. Figure 5I-L presents the data from another recording site later in  
234 the experiment, with a visual stimulus duration of 500 ms. With the longer stimulus  
235 duration, the on and off responses were clearly separated, as evident in the magnetic  
236 and electric recordings. The signal amplitude of the magnetic (and of the electric)  
237 recordings was larger in cat 2, with peak-to-peak amplitudes of approximately 10 nT.  
238 Similar to cat 1, the electric signal had a shorter latency than the magnetic signal, but  
239 in cat 2 the difference was only a few milliseconds. The cross-correlation functions



240 between the ERFs and ERPs of cat 2 showed peak values around 0.85 at a lag of  
241 2-3 ms.

### 242 **Evaluation of signal quality**

243 To further characterize the magnetic responses, we determined two metrics of signal  
244 quality. In a first approach, we calculated a simple metric of signal-to-noise ratio  
245 (SNR), based on the mean squared ERF or ERP (see STAR Methods for details).  
246 When this SNR was determined for ERFs based on averaging all 1000 trials, it reached  
247 values between 12 and 17 (Fig. 6A). When ERFs were based on averaging increasing  
248 numbers of trials, they reached significance at 229, 103 and 95 trials, for recording  
249 sessions cat 1, cat 2A and cat 2B, respectively (Fig. 6B; bootstrap test, see STAR  
250 Methods). For ERPs, it reached maximal values between 30 and 36 and was  
251 significant for single trials (Fig. 6C).

252 While the SNR metric is simple, it is not very sensitive. Therefore, in a second  
253 approach, we quantified how many trials had to be averaged for the ERF or ERP to  
254 assume its final shape. We first selected a random half of all trials to calculate a  
255 template shape. We then averaged increasing numbers of the remaining trials and  
256 calculated the correlation between the resulting shapes and the template shape. When  
257 the correlation was determined for ERFs based on averaging all remaining 500 trials,  
258 it reached values between 0.92 and 0.97. The correlation reached significance for 31,  
259 18 and 16 trials, for recording sessions cat 1, cat 2A and cat 2B, respectively (Fig. 6E;  
260 bootstrap test, see STAR Methods). For ERPs, it reached maximal values of 0.99 and  
261 was significant for single trials (Fig. 6F).

## 262 **DISCUSSION**

263 In summary, we have shown that magnetodes based on spin electronics can be used  
264 to record in vivo magnetic signals originating from neuronal activity. This was possible,  
265 because GMR sensors combine a small size of a few tens of microns with sufficient  
266 magnetic field sensitivity. Magnetic field recordings inside the tissue offer unique  
267 opportunities, because they are reference-free, they measure the direction of magnetic  
268 fields and thereby of the underlying (intracellular) current flows, and because these  
269 magnetic fields are not smeared by intervening neuropil. In vivo magnetic field  
270 measurements might contribute to a better understanding of the commonly recorded  
271 extracranial MEG signal. There are also efforts to record neuronally generated

272 magnetic fields by means of magnetic resonance imaging (MRI) (Bandettini et al.,  
273 2005; Körber et al., 2013), and our magnetrode recordings provide ground-truth  
274 measurements for this.

275 We would like to highlight the potential utility of GMR-based sensing of neuronal  
276 activity for recordings from untethered implanted devices. Implanted recording probes  
277 play an important role in many neurotechnological scenarios. Untethered probes are  
278 particularly intriguing, as they avoid connection wires and corresponding limitations  
279 (Seo et al., 2016). Yet, for untethered probes to be maximally useful, they need to be  
280 tiny, and this results in a fundamental problem for electrical recordings. Electrical  
281 recordings require two electrochemical interfaces with sufficient distance, such that  
282 the electrical potential difference does not become vanishingly small. The necessary  
283 distance restricts the size to which untethered devices based on electric recordings  
284 can be reduced. Magnetic field recordings do not suffer from this problem, because  
285 they require merely a singular GMR. Thus, magnetrode-based untethered recordings,  
286 while challenging, might provide a unique combination of recording and transmitting  
287 modalities for future neurotechnology.

288 We revealed visually evoked magnetic fields by averaging over multiple stimulus  
289 repetitions. This was possible, because the underlying postsynaptic potentials (PSPs)  
290 are long-lasting compared to their temporal jitter across trials. Thereby, PSPs  
291 temporally superimpose in the cross-trial average. This holds not only for PSPs of one  
292 postsynaptic neuron, but for PSPs of many neurons in the vicinity of the magnetrode.  
293 Thus, the ERF became detectable due to effective summation of the PSP-related  
294 magnetic fields across neurons and across trials. ERFs in the different recording sites  
295 reached significance after averaging 16-31 trials (Fig. 6E). Thus, moderate  
296 improvements in sensitivity and shielding will likely enable detection of ERFs on single  
297 trials. If the detection of single-trial ERFs will succeed, also the detection of magnetic  
298 fields corresponding to single action potentials (APs) appears realistic. AP amplitudes,  
299 when recorded with electrodes close to the cell body, substantially exceed ERP  
300 amplitudes. This is likely due to the fact that each AP reflects massive transmembrane  
301 currents that move the transmembrane voltage across the cell body from -60 mV to  
302 +30 mV. Whether these strong currents generate detectable magnetic fields crucially  
303 depends on their spatial symmetry and temporal simultaneity. If all involved currents  
304 flew simultaneously and with spherical symmetry, they would generate no detectable

305 magnetic field. However, it is known that APs emerge in the axon hillock and  
306 retrogradely invade the cell body and sometimes the dendrites (McCormick et al.,  
307 2007; Stuart et al., 1997). Thus, APs are likely magnetically visible.

308 Single extracellular metal microelectrodes typically record spikes from merely a  
309 handful of neurons, because insulating cell membranes isolate them from the  
310 hundreds of neurons in their immediate vicinity (Buzsáki, 2004). Magnetic fields  
311 corresponding to action potentials, that is “action fields” or AFs, should travel from  
312 neurons to the magnetrode without attenuation. This might enable AF recordings from  
313 tens or even hundreds of neurons from the vicinity of the magnetrode. The separation  
314 of spikes originating from these many neurons would be a challenge.  
315 Electrophysiological recordings allow separation of a handful of spikes, based on the  
316 relatively stereotypical spike waveform of a given neuron and the fact that millisecond-  
317 precise spike coincidences of neighboring neurons occur with a very low probability of  
318 0.01 – 0.001 (Jia et al., 2013; Kohn and Smith, 2005). Magnetic recordings would be  
319 able to benefit from the same factors, and in addition from the vectorial nature of  
320 magnetic sources and the corresponding vectorial sensitivity of the sensors. Sensors  
321 specific for the three spatial dimensions could be combined on a single magnetrode  
322 to estimate the 3D position of each neuronal source relative to the magnetrode.

323 Importantly, the magnetrode as presented here, without further modifications or  
324 improvements, can provide useful ERF measurements even in an unshielded  
325 environment after averaging over merely 16-31 stimulus repetitions. These values are  
326 similar to the number of 30 stimulus repetitions, which has been estimated as the  
327 minimum to obtain a consistent visually evoked ERP from human EEG recordings  
328 (Thigpen et al., 2017). Thus, for event-related experimental designs, the fundamental  
329 benefits of magnetic in vivo recordings can now be exploited. ERFs can be used to  
330 localize the underlying ionic currents, without smearing by intervening cell  
331 membranes. In fact, ERFs are most likely dominated by intracellular currents, rather  
332 than by the extracellular return currents measured as ERPs. Thereby, magnetic field  
333 recordings could greatly refine current-source density estimates, measurements of  
334 increasing importance (Lakatos et al., 2016). The vectorial nature of the ERF  
335 recordings allows the identification of the current flow direction after combination of  
336 merely three GMR sensors. Obtaining similar information from ERP recordings  
337 requires measurements with a dense 3D grid of electrodes.

338 Magnetodes also allow for an elegant combination of magnetic field recordings with  
339 magnetic resonance imaging (MRI). Modern high-field MRI can provide structural  
340 images of the living brain with sub-millimeter resolution. The spatial information in MRI  
341 is based on spatial gradients in magnetic field strength and the corresponding spatial  
342 gradients in the Larmor frequency, that is, the frequency at which protons re-emit  
343 radio-frequency energy. This frequency can be easily obtained from magnetode  
344 measurements, and will thereby permit very precise co-registration of the magnetode  
345 with the position in the MRI that corresponds to the measured Larmor frequencies.  
346 Finally, the magnetode can be used to perform MR spectroscopy of the immediate  
347 magnetode surround (Guitard et al., 2016), thereby combining the recordings of  
348 rapidly changing neuronal currents with recordings of neurotransmitters and  
349 metabolites.

350 The in vivo magnetic field measurements presented here have a sensitivity that is still  
351 below the conventional metal microelectrode. We would like to compare this situation  
352 to the early days of MEG measurements in humans, when its sensitivity was probably  
353 far below EEG. Today, EEG is preferred, when e.g. large cohorts of subjects are  
354 measured (Dikker et al., 2017) or when combined with fMRI (Scheeringa et al., 2011);  
355 MEG is preferred, when spatial localization and measurements of deep sources is  
356 essential (Gross et al., 2002). Similarly, electrophysiological and  
357 magnetophysiological in vivo recordings will be complementary. Conventional  
358 microelectrodes and modern MEMS-based multi-contact electrodes will continue to be  
359 indispensable workhorses for neurophysiology. At the same time, magnetodes will  
360 allow recordings that are different in nature and thereby offer distinct advantages for  
361 answering specific questions.

## 362 **AUTHOR CONTRIBUTIONS**

363 Conceptualization, M.P.L., C.F. and P.F.; Methodology: L.C., J.T.R., J.P.A., J.V. and  
364 V.T.; Investigation: T.W., C.M.L., J.N., P.J., L.C., J.P.A., J.V., S.C., P.P.F., C.F., P.F.  
365 and M.P.L.; Analysis: T.W., V.T., J.N., C.M.L. and P.F.; Writing – Original draft: M.P.L.,  
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477  
478

## 479 **FIGURE LEGENDS**

### 480 **Figure 1. Magnetode description and magnetic characteristics.**

481 (A) Scanning Electron Microscopy picture of a magnetode containing 2 GMR elements, each  
482 with a meandering configuration. The elements are deposited on a 200  $\mu\text{m}$  thick silicon  
483 substrate that is 150  $\mu\text{m}$  wide before narrowing at an 18° angle towards the tip. The sensitive  
484 direction is in the plane of the elements and orthogonal to the long axis of the tip. A platinum  
485 electrode (blue square) has additionally been deposited, but no recordings were achieved with  
486 it. Scale bar 100  $\mu\text{m}$ . (B) Output voltage of the GMR sensor as a function of the magnetic field.  
487 The sensor is used for very weak magnetic fields around zero, which lead to outputs within  
488 the steep linear part of the curve. In the linear part, the slope is 1.8%/mT. (C) Equivalent-field  
489 noise spectral density  $S_B$  from 1 Hz to 10 kHz of the corresponding probe for 500 mV and 1 V  
490 peak-to-peak AC voltage of the GMR element. To obtain  $S_B$ , the output voltage is converted  
491 in field-equivalent by applying a calibrated magnetic signal at 30 Hz.

### 492 **Figure 2. Experimental setup.**

493 Recordings were performed in primary visual cortex of the anesthetized cat. To activate the  
494 area, a visual stimulus was applied directly to the contralateral eye using blue LED light. The  
495 magnetode, containing the GMR sensor, was positioned within visual cortex. A tungsten  
496 electrode was targeted to be less than 1 mm from the magnetode, to simultaneously obtain  
497 an independent electric recording. The zoomed-in inset illustrates the expected configuration  
498 of the magnetode and electrode in the neuropil. The output signal from the GMR sensor was  
499 demodulated. Subsequently, the GMR and the electrode signal were amplified, filtered and  
500 digitized.

### 501 **Figure 3. GMR output in AC mode to electric and magnetic field inputs.**

502 (A) The black line shows in arbitrary units the magnetic field input to the GMR, generated by  
503 a respective phantom. The input signal was an exponential chirp, i.e. a sinusoidal current with  
504 frequency varying exponentially from 1 Hz to 2 kHz. The GMR output was demodulated, and  
505 the in-phase output is shown in red, the out-of-phase output in green. Magnetic input is  
506 expected to be reflected primarily in the in-phase output, which is confirmed. (B) Same as (A),  
507 but with an electric field input (black line, in arbitrary units). Electric field input is expected  
508 to be reflected more in the out-of-phase output, which is confirmed, particularly for higher  
509 frequencies.

### 510 **Figure 4. Validation of the magnetic nature of in vivo recordings.**

511 (A) GMR output after in-phase (red) and out-of-phase (green) demodulation, which would be  
512 expected (based on the phantom measurements shown in Fig. 3), if the input were a purely  
513 electric field with the waveform of an ERP (black). (B) Same as (A), if the input were a purely

514 magnetic field with the same waveform. (C) Experimentally observed GMR output after in-  
515 phase (red) and out-of-phase (green) demodulation. The ERP recorded simultaneously from  
516 an independent tungsten electrode is shown in black. The ERP and the GMR outputs are  
517 averages over 1000 stimulus repetitions.

518 **Figure 5. Comparison between simultaneously recorded event-related potentials**  
519 **(ERPs) and event-related fields (ERFs).**

520 (A) ERF obtained in cat 1 by averaging the GMR in-phase output over 1000 stimulus  
521 repetitions. The dashed vertical lines indicate onset and offset of the 100 ms long visual  
522 stimulus. (B) ERP obtained simultaneously by averaging the signal from an independent  
523 tungsten electrode, over the same 1000 stimulus repetitions. For both the ERF and the ERP,  
524 the gray shaded regions show  $\pm 1$  SEM. The error region of the ERP can be visually  
525 appreciated by magnifying the figure. (C) Direct comparison of the waveforms of the ERF (red)  
526 and the ERP (green). (D) Pearson correlation coefficient between the ERF and the ERP as a  
527 function of time lag. (E-H) Same as (A-D), but for a recording session in cat 2. (I-L) Same as  
528 (E-H), but for a separate recording session in cat 2, using a 500 ms long visual stimulus.

529 **Figure 6. Evaluation of signal quality.**

530 (A) Signal-to-noise ratio (SNR) of the ERF as a function of the number of trials that were  
531 averaged. As specified in the color legend, different colors refer to different recording sessions,  
532 and color saturation indicates significance. (B) Same as (A), but zoomed in on the transition  
533 to significance. (C) Same as (A), but for the simultaneously recorded ERP. (D) Pearson  
534 correlation coefficient between a template ERF averaged over 500 trials and a subset-ERF  
535 averaged over the number of trials specified on the x-axis. Template and subset ERF always  
536 averaged non-overlapping sets of trials. (E) Same as (D), but enlarged around the transition  
537 to significance. (E) Same as (D), but for the simultaneously recorded ERP. Note that metrics  
538 for ERFs and ERPs are shown with different y-axis scales. The correlation values for ERPs of  
539 cat 2A and cat 2B (F) are very similar and largely overlap.

## 540 **STAR Methods**

### 541 **CONTACT FOR REAGENT AND RESOURCE SHARING**

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### 544 **EXPERIMENTAL MODEL AND SUBJECT DETAILS**

545 The animal experiments were approved by the responsible government office  
546 (Regierungspräsidium Darmstadt) in accordance with the German law for the  
547 protection of animals. Two adult cats (1 male, 1 female) were used for visual  
548 neuroscience experiments, after which magnetrodes were tested.

### 549 **METHOD DETAILS**

#### 550 **Probe fabrication process**

551 The GMR stack is deposited by sputtering on a commercial silicon substrate of  
552 700  $\mu\text{m}$ , insulated by a 1  $\mu\text{m}$  thick  $\text{SiO}_2$  layer. The deposition is made by DC sputtering  
553 at a partial Argon pressure of  $5 \cdot 10^{-3}$  mbar. The GMR stack has the following  
554 composition (starting from the top and with thicknesses indicated in nm in  
555 parenthesis):

556 Ta(3)/PtMn(18)/CoFe(2)/Ru(0.85)/CoFe(2.1)/Cu(2.3)/CoFe(1.5)/NiFe(3.5)/Ta(3)/ $\text{SiO}_2$   
557 /Si.

558 This structure contains on top the pinned layer, composed of an artificial  
559 antiferromagnet (PtMn/CoFe/Ru/CoFe).

560 The wafer is annealed at 300°C in a field of 1 T applied along the wafer plane and  
561 meant to set the magnetization of the PtMn/CoFe layer, which is the magnetic  
562 reference layer. After deposition and annealing, the wafer substrate is ground down to  
563 200  $\mu\text{m}$  by mechanical grinding (GDSI, USA).

564 The GMR stack is patterned by optical lithography. Shipley 1813 resist has been used  
565 for the entire process except the deep reactive ion etching (DRIE) process. Spin  
566 coating is realized at 5000 rpm in a clean room (which leads to a resist thickness of  
567 1.3  $\mu\text{m}$ ) and soft baked at 110°C for 3 min on a hot plate to evaporate the coating  
568 solvent and harden the resist. The UV exposure process is realized on a MJB3 or

569 MJB4 (Karl Süss, Süss Microtec, Germany) mask aligner that makes physical contact  
570 between photomask and sample. Both aligners have a wavelength of 365 nm and  
571  $5 \text{ mW/cm}^2$  and  $10 \text{ mW/cm}^2$  power respectively. Exposure time depends on the steps  
572 (etching, contacts, passivation) and are detailed in Table 1. After exposure, the sample  
573 is rinsed in a developer to remove the exposed parts and submitted to a second bake  
574 on a hot plate. All parameters for the photolithography processes (etching of the GMR,  
575 contact deposition, passivation layer and silicon etching by DRIE) are given in Table  
576 1. In a first step, the GMR element is etched by ion milling under Argon gas at  $10^{-4}$   
577 mbar, for a beam current of 7 mA and 90 W RF powered for 20 min.

578 Contacts are realized by a lift off process where a bilayer of Ti (15 nm)/Au (150 nm) is  
579 deposited by electron beam evaporation at  $10^{-8}$  mbar base pressure, and 65 mA beam  
580 current for Ti and 330 mA beam current for Au.

581 Each GMR element is contacted on its short end (Fig. 1), along the entire height and  
582 width, with the current running in the plane of the stack.

583 An electrode made of Platinum (thickness 200 nm) was also deposited by evaporation  
584 at the tip of the probe (Fig. 1A), but could not be used during the in vivo recordings on  
585 AC mode, because of a saturation of the electrode amplifier by the AC current feeding  
586 the GMR.

587 Passivation of the structure is insured by sputtering  $\text{Al}_2\text{O}_3$  (150 nm)/ $\text{Si}_3\text{N}_4$  (150 nm)  
588 across the entire probe surface, except for the contact pads on the opposite side of  
589 the probe. Deposition of the passivation bilayers is done at  $5 \cdot 10^{-3}$  mbar, with 200 W  
590 RF power. After passivation, resistance leakage is quantified and only probes with  
591 infinite resistance are used.

592 Finally, DRIE was used to define the tip-shape of the overall probe. Deep etching uses  
593 the Bosch process (Laermer and Schilp, 1996), also known as time-multiplexed  
594 etching that alternates repeatedly between etching and passivation modes to create  
595 deep vertical penetration with a highly anisotropic profile. DRIE is a plasma etching  
596 mode with a gas mix of  $\text{SF}_6$  and  $\text{O}_2$ , after a prior  $\text{CHF}_3$  etch used to remove the  $\text{SiO}_2$   
597 layer. 400 cycles were used to etch down the silicon and define the final shape of the  
598 probe.

599 The probe was then mounted on a printed circuit board (PCB) by gluing its upper side  
600 and then contacted to the copper lines by wire-bonding. Wire-bonds were 50  $\mu\text{m}$  thick  
601 and were protected by encapsulation in thin araldite glue.

602 The magnetoresistance ratio  $\Delta R/R_0$ , where  $\Delta R$  is the maximum resistance variation as  
603 a function of field and  $R_0$  is the mean resistance, is 6.1% for this stack at room  
604 temperature.

### 605 **Transport and noise characterization**

606 Probes were characterized through magneto-transport and noise spectral density  
607 measurements at room temperature. For the magneto-transport experiments, a DC  
608 current of typically 1 mA was applied to the GMR element, whose output voltage was  
609 amplified and low-pass filtered at 30 Hz (Stanford Research SR560). An external  
610 magnetic field generated by two air coils mounted in Helmholtz configuration was  
611 applied along the sensitive axis of the GMR (i.e. parallel to the Pinned Layer main  
612 axis).

613 Noise spectral density measurements were performed in a Magnetically Shielded  
614 Room. Voltage supply was provided by two 9 V batteries in series to the GMR element  
615 and to an equivalent adjustable resistance. Both outputs were sent to the inputs of a  
616 low-noise amplifier (INA 103) in differential mode. The amplifier output was further  
617 amplified and filtered (SR 560 fed by battery). The total gain of the acquisition line was  
618 typically between 10,000 and 100,000, and the bandwidth was [0.1 Hz; 3 kHz]. An  
619 external magnetic field, in the  $\mu\text{T}$  range at 30 Hz, generated by an air coil, was used  
620 for calibration purposes.

621 The signal was Fourier transformed to obtain the noise spectral density over the  
622 chosen frequency band. The measured voltage signal together with the known signal  
623 generated by the calibrated coil resulted in the factor that was subsequently used to  
624 convert the voltage signal into an equivalent magnetic field signal.

### 625 **Electronics schemes for GMR measurements**

626 For general GMR characterization, the GMR was fed with a DC current, and the output  
627 voltage was measured through a low-noise amplifier and a band-pass filter from 0.1 Hz  
628 to 3 kHz.

629 For in vivo GMR measurements, we used a measurement scheme that suppressed  
630 capacitive coupling to the neuropil, which may occur in DC measurements (Amaral et

631 al., 2011). In this scheme, the GMR sensors were fed with alternating current (AC,  
632 Fig. S1) with frequencies in the range of 20-80 kHz, and the sensor output was  
633 demodulated separately for components that were in-phase with the AC modulation  
634 and those that were out-of-phase. The in-phase signal is linked to the resistive part of  
635 the bridge (i.e. the GMR), and the out-of-phase signal relates to the capacitive coupling  
636 to the neuropil. Thus, the AC mode is designed such that magnetic fields are detected  
637 on the in-phase channel and electric fields on the out-of-phase channel.

638 Total gain of the acquisition line typically ranged from 500 to 1000. The frequency  
639 band for recordings was [0.3 Hz; 3 kHz] or [0.3 Hz; 1 kHz].

### 640 **Phantom experiments**

641 Phantom experiments were developed to separate between magnetic signal and  
642 potential electrical contamination. The setup contained two sources, one source  
643 generating a magnetic field and a second source generating an electric field. The  
644 magnetic field source consisted of an isolated wire immersed in saline solution,  
645 connected to a current source. The electric current source consisted of two wires with  
646 exposed ends in the bath, connected to a separate current source. A magnetrode was  
647 placed close to both sources within the saline bath.

648 Sweep signals ranging from 1 Hz to 3000 Hz were used to drive either the magnetic  
649 or the electric phantom separately. On the basis of those measurements, the transfer  
650 functions of the system to electric or magnetic inputs were calculated. The transfer  
651 functions allow to calculate the responses of the sensor to any given electric or  
652 magnetic field input (as long as the input is constrained to the 1-3000 Hz range).

### 653 **Magnetic and electric fields generated by the AC current in the GMR**

654 To evaluate the possible impact onto the neuropil, of the GMR feeding current in the  
655 AC mode, we performed an estimate of the magnetic and electric fields generated in  
656 close vicinity to the probe, to compare it with excitability thresholds as reported for  
657 Transcranial Magnetic Stimulation. The electric field induced in the medium when the  
658 GMR is supplied by an AC current  $I$  can be estimated by a simple model. Considering  
659 a gold contact line longer than the dimensions of interest, the magnetic field can be  
660 written as follows:

$$661 \quad B = (\mu_0 I) / (2 \cdot \pi \cdot r) \approx 20 \mu\text{T}$$



662 where  $I = 1$  mA, and where  $r = 10$   $\mu\text{m}$  is the distance between the contact line and the  
663 point of interest in the bath,  $\mu_0$  being the permeability of the tissues. The equation of  
664 induction links the time variations of  $B$  through a surface  $S$ , to the induced electric field  
665  $E$  along the edge of this surface. If we consider a circular loop of radius  $R = 1$   $\mu\text{m}$ , then  
666 the electric field intensity is approximated by

$$667 \quad E = (\mu_0 I f R) / (2r) \approx 10^{-5} \text{ V/m}$$

668 for a frequency  $f = 10^5$  Hz. This electric field intensity is several orders of magnitude  
669 below the typical values used for neuronal stimulation (100 V/m as reported in  
670 (Ilmoniemi et al., 1999)).

### 671 **In vivo recording procedures and data analysis**

672 Anesthesia was initiated intramuscularly with 10 mg/kg ketamine hydrochloride  
673 (Ketavet, Zoetis, Germany) and 0.05 mg/kg dexmedetomidine (Dexdormitor, Orion  
674 Pharma, Germany) supplemented with 0.04 mg/kg atropine sulfate (Atropin, B.Braun,  
675 Germany). Anesthesia was maintained after tracheotomy by artificial ventilation with a  
676 mixture of  $\text{N}_2\text{O}/\text{O}_2$  (70/30%) with 0.8% isoflurane. Analgesia was maintained by  
677 intravenous infusion of sufentanil (2  $\mu\text{g}/\text{kg}/\text{h}$ , Sufentanil-Hameln, Germany) together  
678 with electrolytes (3 ml/kg/h, Sterofundin, B.Braun, Germany) and glucose (24 mg/kg/h,  
679 bela-pharm, Germany). After all surgical procedures had been terminated, the animals  
680 were paralyzed by intravenous infusion of vecuronium bromide (0.25 mg/kg/h,  
681 Vecuronium-Inresa, Germany). Atropine (Atropine-POS 1%, Urspharm, Germany)  
682 was topically applied to the eye in order to dilate the pupil. Depth of anesthesia was  
683 controlled by continuously monitoring the electrocardiogram and  $\text{CO}_2$  level.  
684 Dexamethasone (Voren, Boehringer Ingelheim, Switzerland) was administered every  
685 48 h and if needed. A craniotomy was performed around the central part of the primary  
686 visual cortex area 17 (homologue to V1 in primates, Horsley–Clarke coordinates AP -  
687 2 to -10, ML 0 to +6). The dura mater was removed in a small window to allow easy  
688 insertion of the recording probes.

689 No shielding was used for the recordings, neither a mu-metal shield as in MEG, nor  
690 an aluminum shield as in a Faraday cage. This led to substantial line-noise artifacts at  
691 several frequencies (Fig. S3 and S4). Nevertheless, we reasoned that a shielding  
692 would have complicated experimentation, while its benefits would have been partly  
693 counteracted by the requirements of life support. Specifically, the animal was

694 connected to an ECG monitor, it received intra-venous infusions, it's body temperature  
695 was recorded via a rectal thermo probe, which was connected to a control unit, which  
696 in turn drove a heating pad. These limitations can be overcome by appropriate  
697 modifications in life support equipment or through experiments in awake animals. For  
698 the present proof of principle, averaging over multiple stimulus repetitions was  
699 effective in revealing the stimulus evoked responses even in the presence of strong  
700 noise.

701 Electrical recordings were performed with tungsten electrodes (1 M $\Omega$  impedance,  
702 FHC, USA). The electrode and the magnetode were held by separate  
703 micromanipulators (David Kopf Instruments, USA) allowing for a precise positioning  
704 and careful insertion into the cortex under microscope inspection. The magnetode  
705 was inserted first, about 1 mm below the cortical surface, and angled such that the  
706 probe penetrated the cortex as perpendicularly as possible. Subsequently, the  
707 tungsten electrode was inserted in close vicinity to the magnetode. Given the cortical  
708 thickness of the cat, the sensors were expected to be located near cortical layer 4, the  
709 input layer. Signals from the magnetode (after demodulation) and the electrode were  
710 recorded with a standard acquisition system (Tucker Davis Technologies, USA). To  
711 this end, signals were buffered by a unity gain headstage, high-pass filtered at 0.5 Hz,  
712 low-pass filtered at 300 Hz and digitized at 1017 Hz.

713 For visual stimulation, a brief (100 or 500 ms) flash of light was applied directly to the  
714 contralateral eye of the cat. This light flash (470 nm wavelength) was generated by an  
715 LED (Omicron-Laserage, Germany) and applied through a polymer optical fiber (2 mm  
716 diameter) ending close to the cornea, with an output intensity of about 2-10 mW at the  
717 end of the fiber. The fiber and the animal's forehead were shielded with aluminum foil,  
718 to ensure that no light reached the magnetode. This is important, because the  
719 magnetode's silicon substrate could be directly influenced by the light flash, i.e. by  
720 the photovoltaic effect (Mikulovic et al., 2016). However, the detected magnetic signals  
721 have a sharp deflection with a latency of 20-40 ms, which corresponds to the  
722 conduction delay from the retina to the cortex, ruling out a direct effect of the light flash  
723 on the magnetode. To generate the light flash, the LED was controlled by the same  
724 unit that also controlled data acquisition (RZ2, Tucker Davis Technologies, USA).  
725 Several recording sessions were performed, each comprising 1000 light flash  
726 repetitions. The light flash had a duration of 100 or 500 ms depending on the session.

727 The inter-stimulus interval was 0.9 s plus a random time between 0 and 0.6 s to  
728 prevent adaptation or entrainment of the cortex to the repeated visual stimulus.

729 Offline data processing and analysis was done by custom written software and the  
730 FieldTrip toolbox (Oostenveld et al., 2011) coded in Matlab (The Mathworks, USA).  
731 Line noise artifacts at 50 and 100 Hz were removed by a second-order Butterworth  
732 bandstop filter applied in the forward direction. Additional artifacts that showed up as  
733 lines in the power spectra of the magnetic signal were removed by a DFT filter as  
734 implemented in FieldTrip. To this end, each analyzed data epoch was padded with  
735 surrounding data to a length of 10 s, a direct Fourier transform (DFT) was calculated  
736 for the specified frequencies, and the corresponding sine and cosine components  
737 were subtracted. The DFT filtering frequencies and the filtering effects are visible in  
738 Figure S4. To allow direct comparison, the same filtering routines were applied to  
739 magnetic and electric signals, even if the electric signals did not show some of the line  
740 noise components. For calculation of ERFs and ERPs, signals were low-pass filtered  
741 at 90 Hz with a 6<sup>th</sup> order Butterworth filter applied in the forward direction. For the  
742 evaluation of signal quality, this was replaced by a 50 Hz Butterworth low-pass filter  
743 applied in both forward and backward direction.

744 Subsequently, data were segmented into trials starting 0.2 s before and ending 0.8 s  
745 after the light flash. For each trial, the mean was subtracted. Subsequently, trials were  
746 averaged to extract the stimulus-locked (i.e. evoked) brain activity. For electric  
747 recordings, these averages are referred to as event-related potentials (ERPs); for  
748 magnetic recordings, they are referred to as event-related fields (ERFs). To address  
749 both response types, we refer to event-related responses (ERRs). For the evaluation  
750 of signal quality, trials were further segmented into epochs containing the ERRs. We  
751 choose an analysis window starting 20 ms after stimulus onset and having a width of  
752 100 ms to capture most of the response energy. To quantify the noise, for each trial,  
753 an equally long window was chosen at a random time between -500 to 0 ms relative  
754 to stimulus onset. For each epoch, a linear de-trending was performed by fitting and  
755 subtracting a linear regression. Signal processing was identical for post-stimulus  
756 (signal) and pre-stimulus (noise) epochs.

## 757 **QUANTIFICATION AND STATISTICAL ANALYSIS**

### 758 **Signal quality estimation**

759 To assess the quality of ERRs, we used two approaches, namely a metric of signal-  
760 to-noise ratio (SNR) and a correlation to a template response.

761 In the SNR approach, we defined:

$$762 \text{SNR}(dB) = 10 \times \log_{10} \left( \frac{P_S}{P_N} \right)$$

763 where  $P_S$  is the power of the ERR and  $P_N$  the power of the noise. The power was  
764 quantified as the mean squared ERR in the specified epochs. Note that this definition  
765 of stimulus and noise is different from previous studies, which assume a model of  
766 additive (Gaussian) noise on top of a constant stimulus (Turetsky et al., 1988). SNR is  
767 then calculated from an estimation of the signal and noise components of the recorded  
768 stimulus evoked signal. However, we think that using the ongoing brain activity  
769 (baseline) as a measure of ‘noise’ is more intuitive because the SNR then quantifies  
770 the amount of stimulus locked activity, without making assumptions about the nature  
771 of different sources of noise. For simplicity, we keep the nomenclature of ‘signal’ and  
772 ‘noise’ for ‘stimulus evoked’ and ‘baseline’ activity, respectively.

773 We investigated how many trials had to be averaged to obtain a signal power, i.e. ERR  
774 power, that significantly exceeded the noise power. Starting with a single trial, we  
775 averaged increasing numbers of trials. For each number of trials, we performed the  
776 following procedure 1000 times: We randomly selected a respective subset from all  
777 1000 available trials, and then calculated a bootstrap estimate of the 95% confidence  
778 interval (CI) of its SNR (based on 1000 bootstrap resamples of this subset).  
779 Subsequently, the upper and lower limits of the CIs from the 1000 subsamples were  
780 averaged, and the observed SNR was considered significant, if its lower average CI  
781 was larger than zero.

782 In a second approach, we calculated the correlation between, on the one hand the  
783 ERR obtained from a subset of trials, and on the other hand a template ERR. The  
784 template ERR was the average over 500 randomly selected trials. We tested how  
785 many of the remaining trials had to be averaged to obtain a subset-ERR that was  
786 significantly correlated to the template-ERR. Starting with a single trial, we averaged  
787 increasing numbers of trials. For each number of trials, we performed the following

788 procedure 1000 times: We randomly selected a respective subset from the remaining  
789 500 trials (excluding the ones used for the template), averaged them to obtain the  
790 subset-ERR, and then calculated the bootstrap estimate of the 95% CI of its Pearson  
791 correlation with the template-ERR (based on 1000 bootstrap resamples of this subset).  
792 Subsequently, the upper and lower limits of the CIs from the 1000 subsamples were  
793 averaged, and the observed correlation was considered significant, if its lower average  
794 CI was larger than zero.

795 **KEY RESOURCES TABLE**

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Chemicals, Peptides, and Recombinant Proteins		
Developer AZ400K	AZ electronic materials	Cat#AZ400k
Developer MF 319	Microposit	Cat#021079
Primer HMDS	Microposit	N/A
Photoresist AZ4562	AZ electronic materials	Cat#AZ4562 250ml
Photoresist Shipley 1813	Microposit	Cat#021838
Ketamine hydrochloride	Zoetis	N/A
Dexmedetomidine	Orion Pharma	N/A
Atropine sulfate	B. Braun	N/A
Isoflurane	CP-Pharma	Cat#1214
Sufentanil	Hameln pharma plus	N/A
Vecuronium bromide	Inresa	N/A
Dexamethasone	Boehringer Ingelheim	N/A
Experimental Models: Organisms/Strains		
Domestic cat ( <i>Felis catus</i> )	Own breeding facility	N/A
Software and Algorithms		
MATLAB	MathWorks	<a href="https://www.mathworks.com/">https://www.mathworks.com/</a>
FieldTrip toolbox	Oostenveld et al., 2011	<a href="http://www.fieldtriptoolbox.org/">http://www.fieldtriptoolbox.org/</a>
Other		
Tungsten microelectrodes	FHC	Cat#UEWMEGSECN3M
RZ2 BioAmp Processor	Tucker Davis Technologies	Cat#RZ2-8
PZ2 Preamplifier	Tucker Davis Technologies	Cat#PZ2-256
LED module (470 nm)	Omicron-Laserage	Cat# LEDMOD470.400.OEM
Polymer optical fiber (2 mm diameter)	Omicron-Laserage	Cat#LEDMOD.FASY.OEM

796

## 797 **SUPPLEMENTAL INFORMATION**

### 798 **Table S1. Photolithography parameters.**

### 799 **Figure S1. Schematic representation of DC acquisition mode.**

800 The sensor, having a resistance  $R_{\text{gmr}}$  is mounted in a Wheatstone bridge, with two identical  
801 resistances ( $R$ ) of 500  $\Omega$ ; a variable resistance  $R_{\text{pot}}$  is used to balance the bridge. The output  
802 of the bridge is sent through a low noise amplifier (INA 103) to a filter-amplifier (SR 560). The  
803 output voltage is collected on an acquisition card.

### 804 **Figure S2. Schematic representation of AC acquisition mode.**

805 The GMR is fed with sinusoidal current of a typical carrier frequency between 20 and 80 kHz.  
806 The GMR output is a modified version of this feeding current, after amplitude modulation by  
807 the time-varying magnetic field that impinges onto the GMR. The GMR output is pre-amplified  
808 (INA 103) and demodulated by multiplication (AD633 mixers) with two carrier frequency  
809 signals, one with 0° and another with 90° dephasing. The resulting signals are low pass filtered  
810 (typically at 3 kHz) to eliminate the carrier signal contamination. Both demodulated signals,  
811 called “in-phase” and “out-of-phase”, are collected. A pure resistance change of the bridge  
812 resistance, due to magnetic field dependent changes in GMR resistance, gives an in-phase  
813 signal, whereas a capacitive change of the bridge, induced e.g. through a coupling to silicon  
814 or to the bath, induces an out-of-phase signal.

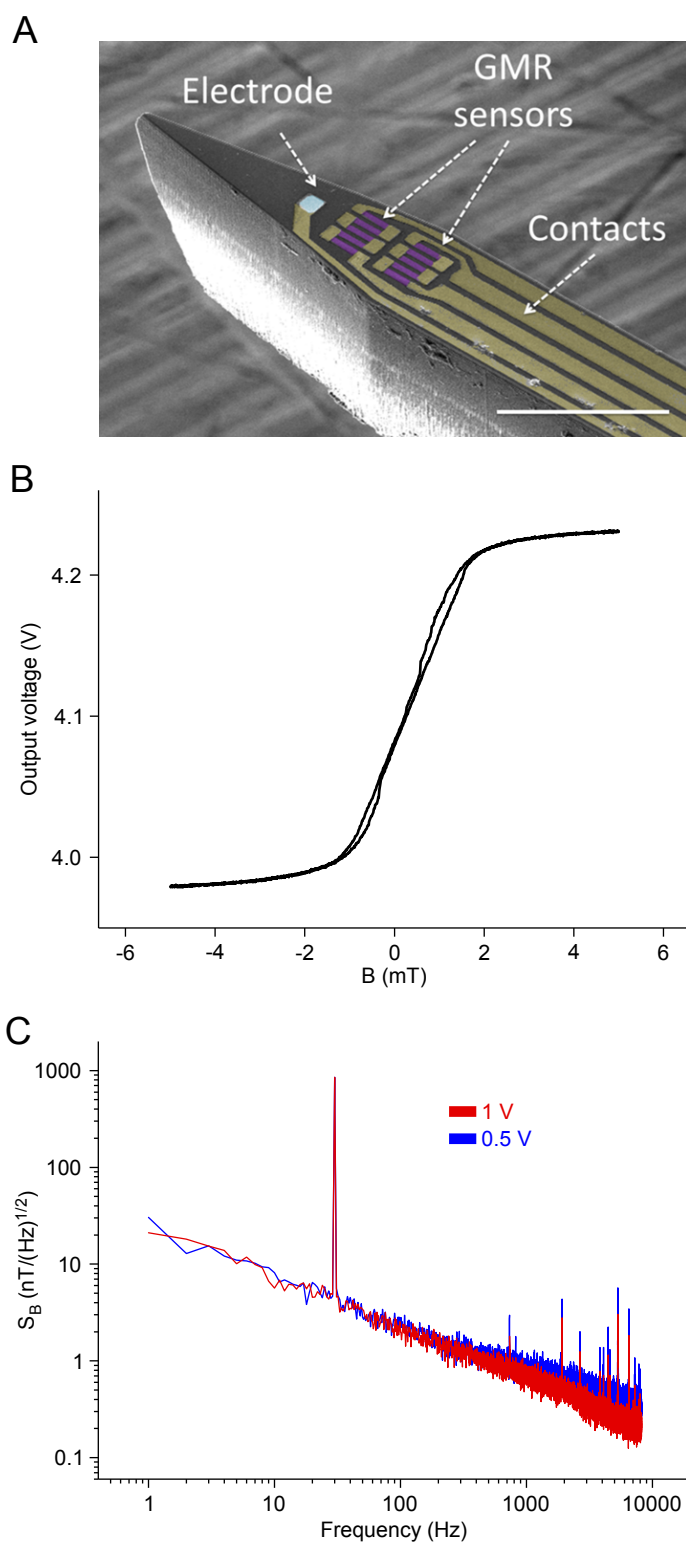
### 815 **Figure S3. Example recordings of electric and magnetic recordings.**

816 Example traces of simultaneously recorded electric and magnetic signals, with and without  
817 filtering, as specific in the panel titles. Details of the filtering are specified in the STAR Methods  
818 section.

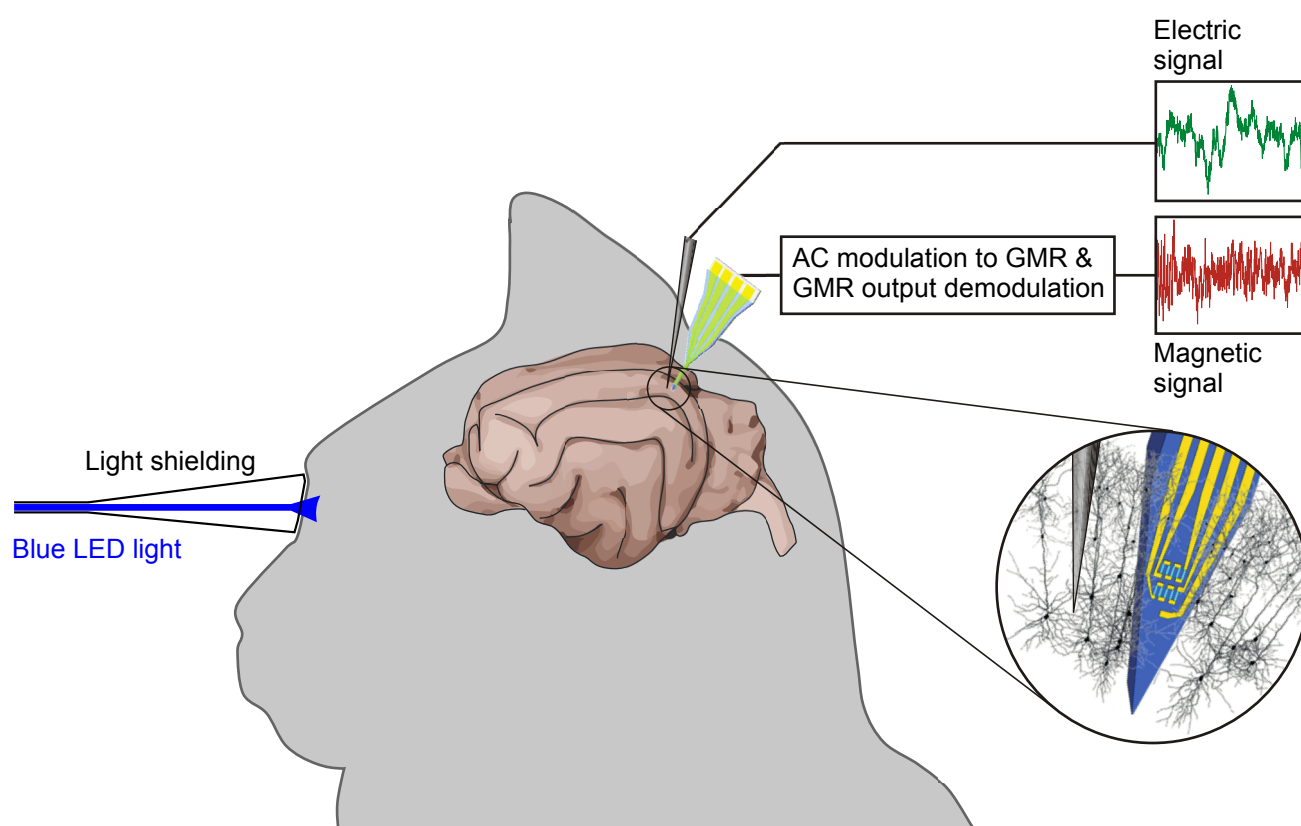
### 819 **Figure S4. Average power spectra of electric and magnetic recordings.**

820 Average power spectra of simultaneously recorded electric and magnetic signals for the three  
821 recording sessions indicated on the left. Each panel shows in black the spectrum without noise  
822 subtraction and in red the spectrum after noise subtraction. Details of the noise subtraction  
823 are specified in the STAR Methods section.

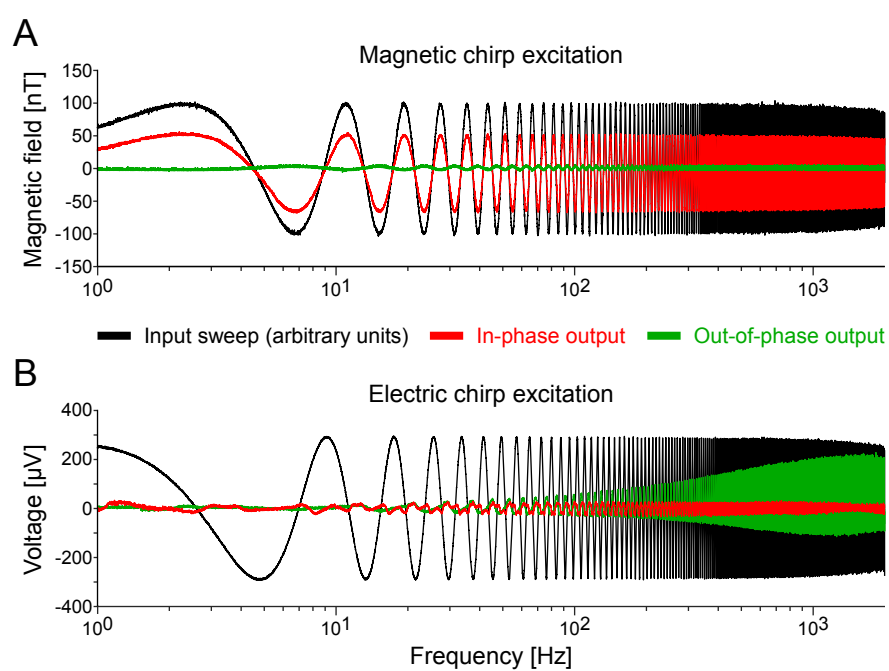




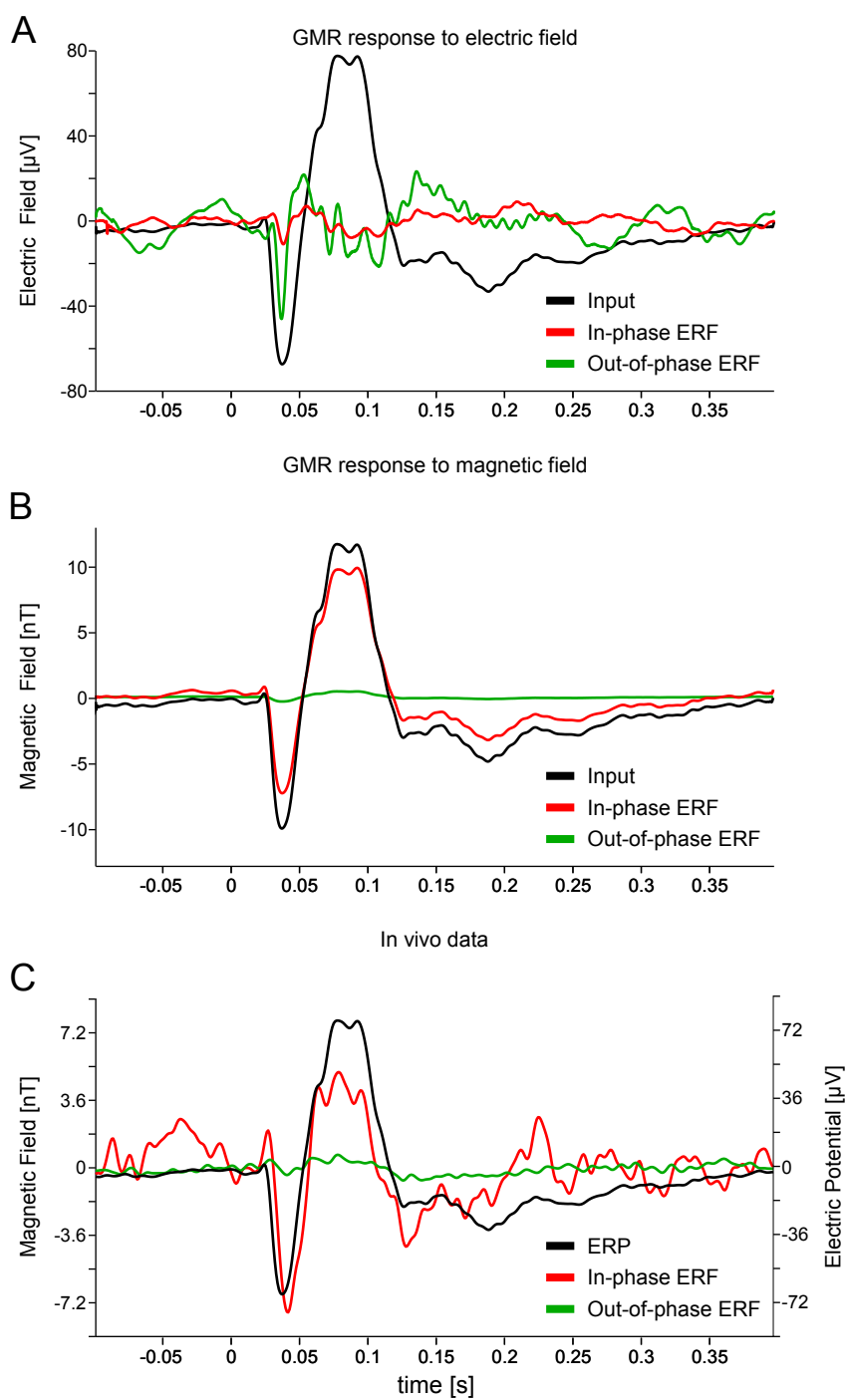
Caruso et al., Fig. 1



Caruso et al., Fig. 2

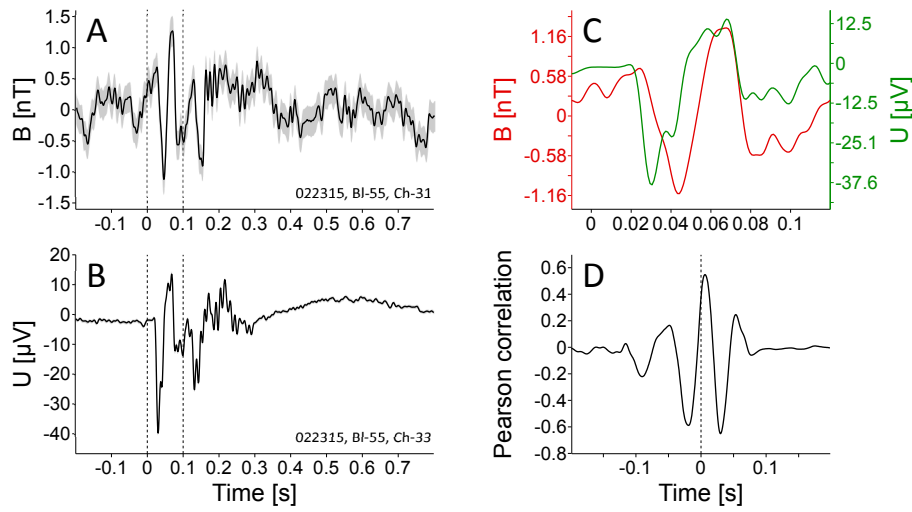


Caruso et al., Fig. 3

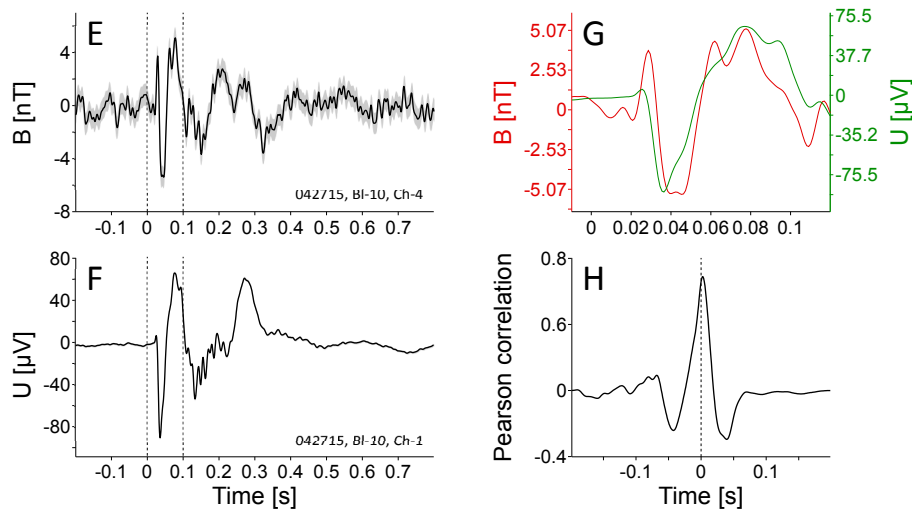


Caruso et al., Fig. 4

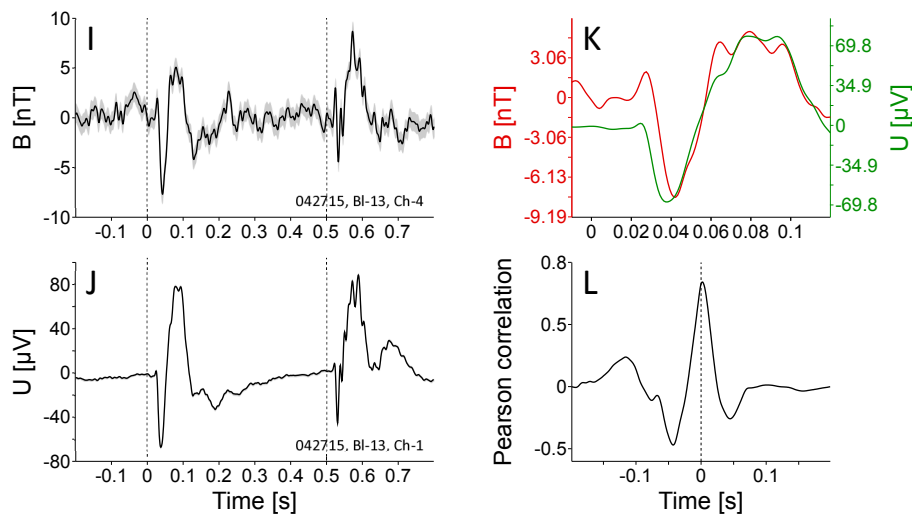
### Cat 1

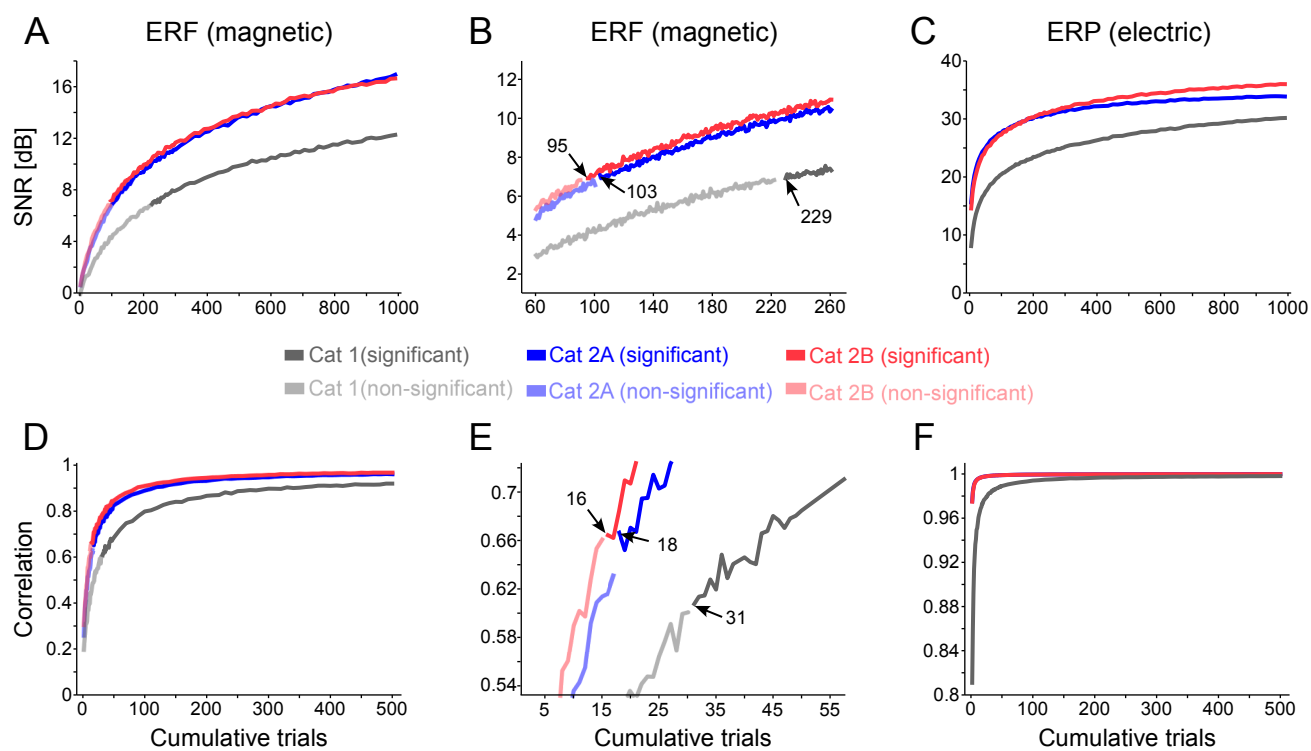


### Cat 2A

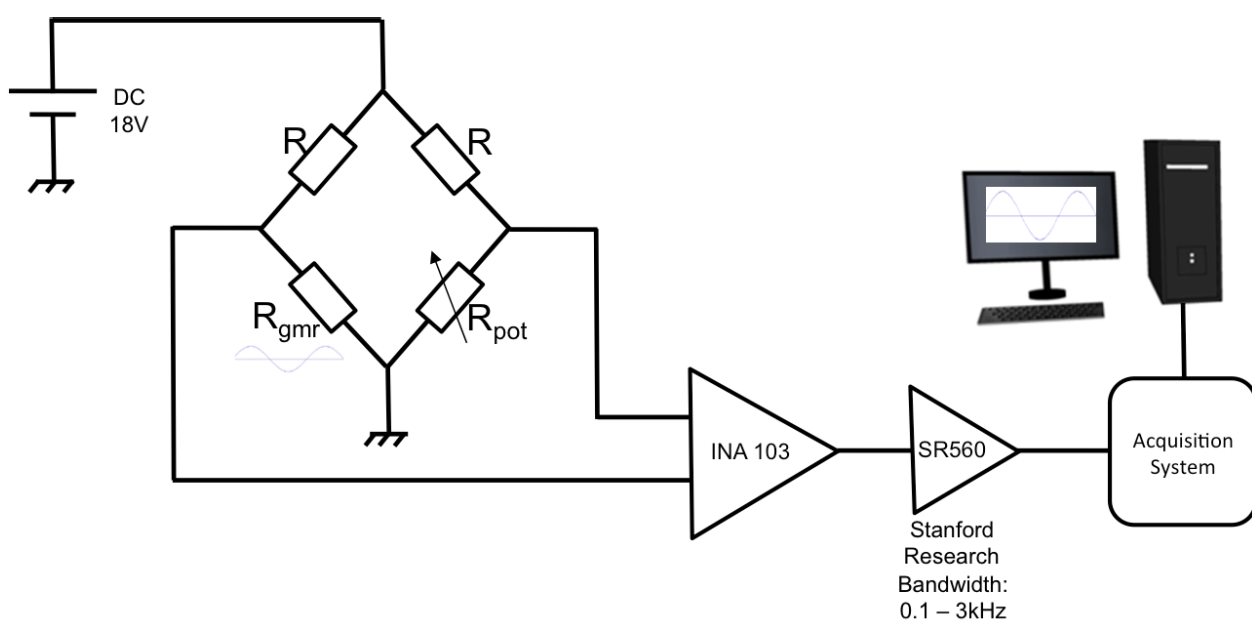


### Cat 2B



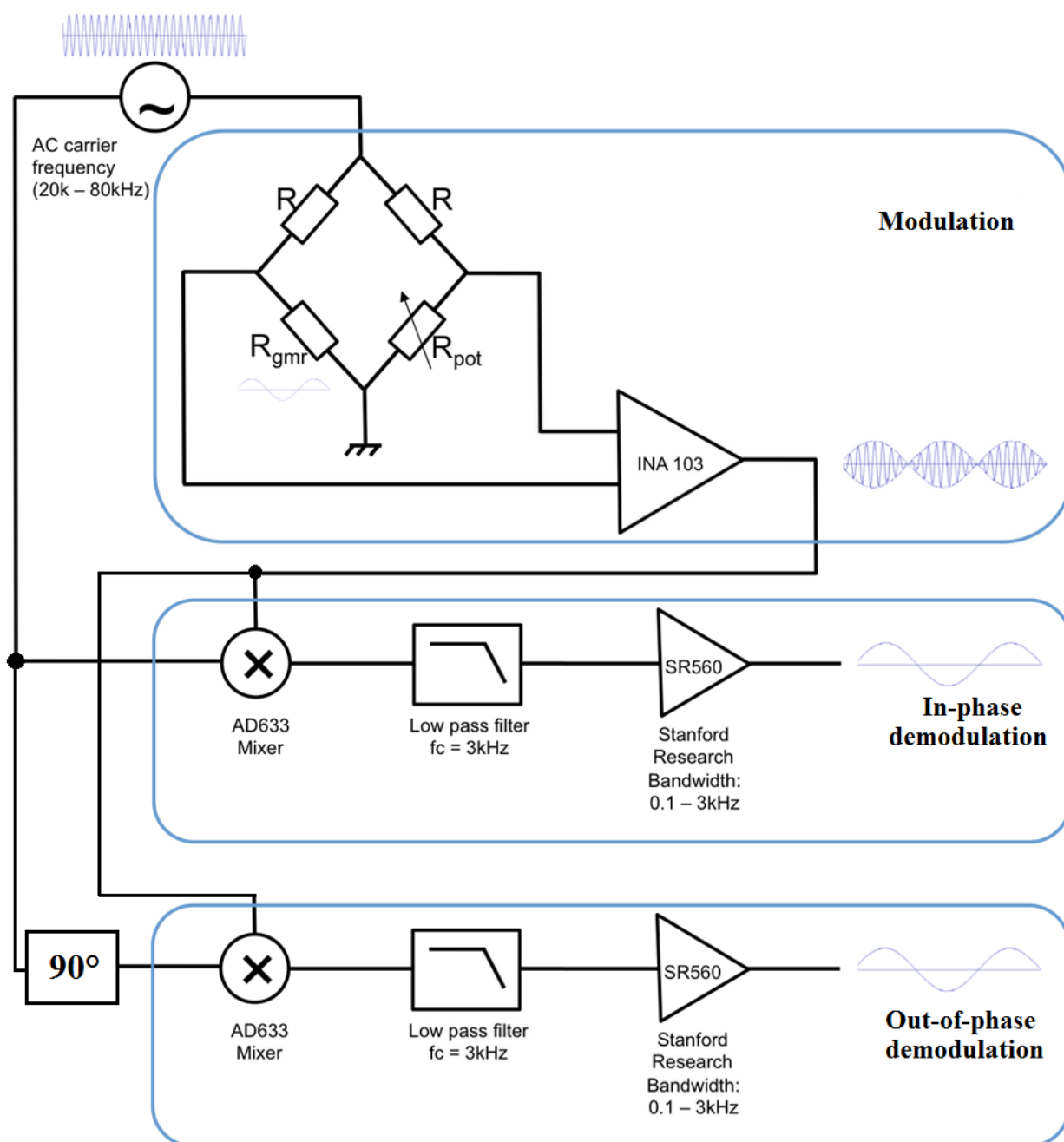


Caruso et al., Fig. 6

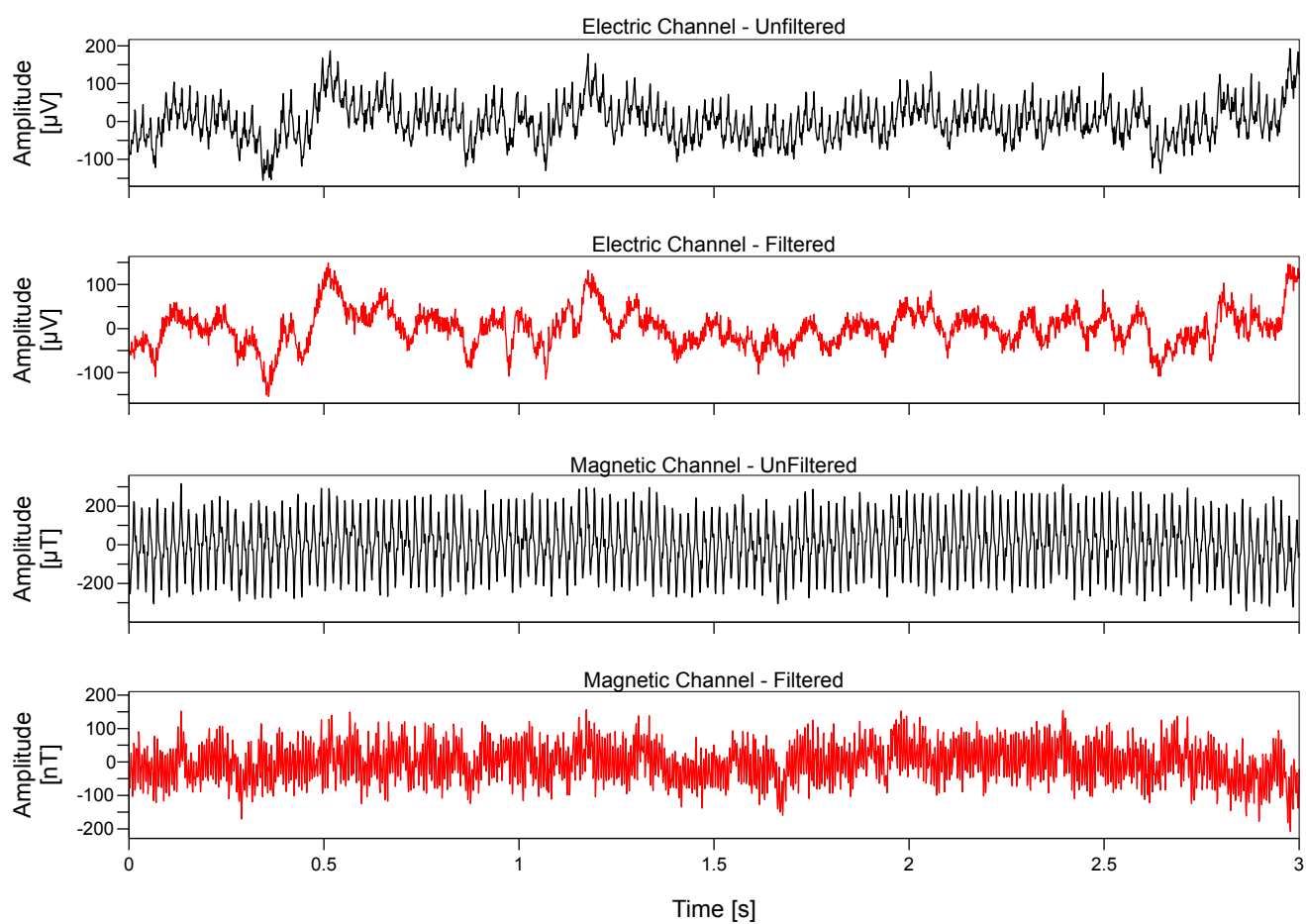


Caruso et al., Fig. S1

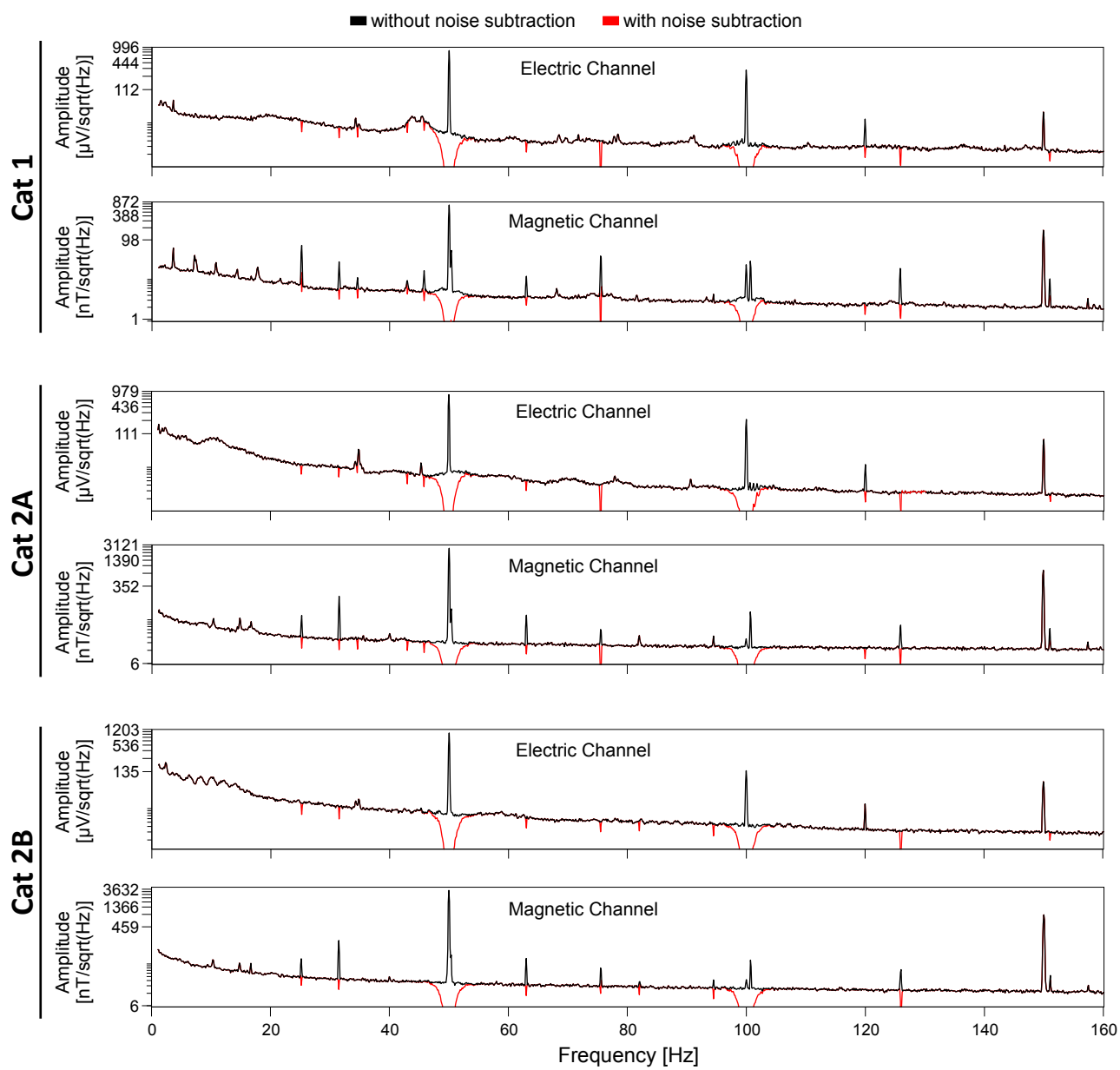




Caruso et al., Fig. S2



Caruso et al., Fig. S3



	GMR	Contacts	Passivation	Deep RIE
Photoresist		Shibley 1813		HDMS + AZ4562
Developer		MF319		AZ400K+H <sub>2</sub> O (1 :4)
Spin coating		5s at 500 rpm and 60s at 5000 rpm		30s at 2000 rpm
Exposure		25s at 10W/cm <sup>2</sup>		60s
Development time		60s		240s
Bake 1 (before UV exposure)		3 min at 110°C		60 min at 90°C
Bake 2 (after UV exposure)		3 min at 110°C		