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Abstract

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Good practices in EEG-MRI: The utility of \textit{retrospective} synchronization and PCA for the removal of MRI gradient artefacts.

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\textbf{Abstract}

The \textit{electroencephalogram} (EEG) recorded during \textit{magnetic resonance imaging} (MRI) inside the scanner is obstructed by the MRI gradient artefact (MGA) originating from the electromagnetic interference of the MRI with the sensitive measurement of electrical scalp potentials. Post-processing algorithms based on average artefact subtraction (AAS) have proven to be efficient in removing the MGA. However, the residual MGA after AAS still limits the quality and usable bandwidth of the EEG data despite further reduction through re-sampling, principal component analysis (PCA), and regressive filtering.

We recently demonstrated that the residual MGA can largely be avoided by means of hardware synchronisation. Here we present a new software synchronisation method, which substitutes hardware synchronisation and facilitates the removal of motion artefacts by PCA. The effectiveness of the retrospective synchronisation algorithm (Resync) is demonstrated by comparison to the aforementioned techniques. For this purpose we also developed a method for simulating the MGA and we propose new concepts for quantifying and comparing the performance of post-processing algorithms for EEG-MRI data. Results indicate that the benefits of (retrospective) synchronisation and PCA depend largely on the relative contribution of timing errors and motion artefacts to the residual MGA as well as the frequency range of interest.

\textbf{1.1 Keywords}

EEG, fMRI, gradient artefact, synchronisation, PCA, simulation

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1.2 Abbreviations
AAS average artefact subtraction
ACS auto-correlation sequence
DFT discrete Fourier transform
EEG electroencephalogram
FASTR fMRI Artefact Slice Template Removal
FIR finite impulse response (filter)
fMRI functional MRI
FFT fast Fourier transform
Fs EEG sampling rate
GE-EPI gradient-echo echo-planar imaging
IAR Imaging Artefact Reduction
MGA MRI gradient artefact
MRI magnetic resonance imaging
PC principal component (vector)
PCA principal component analysis
RMGA residual MGA (after AAS)
RTE relative timing error
SNR signal-to-noise ratio
STC Slice Timing Correction
TR (volume) repetition time (MRI)
Ts EEG sampling interval
Introduction

In recent years the combination of electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) in one fully simultaneous measurement has established itself as a new technique for the non-invasive investigation of human brain function in vivo. The prospects of combining the exquisite temporal resolution of EEG with the superior spatial resolution of MRI have motivated the development of solutions to the significant technical challenges inherent to the EEG-MRI technique. These originate mostly from the fact that the MRI scanner creates electromagnetic fields, which strongly interfere with the sensitive measurement of electrical scalp potentials by EEG. The most prominent MRI gradient artefact (MGA), which is present only during MRI scanning, typically exceeds the physiological EEG signal by about two orders of magnitude (Figure 1). Among the most popular solutions to this problem are those that require little or no specialised hardware or MRI pulse sequences as they rely exclusively on post-processing to recover a usable EEG signal from the heavily confounded raw data. The MRI sequence and thus the MGA are repetitive and highly reproducible from one image acquisition to the next, therefore the most successful post-processing algorithms are primarily based on average artefact subtraction (AAS) in the time domain [1]. We recently demonstrated that AAS works particularly well when the clocks of both systems, EEG and MRI, are synchronized using external hardware [2]. In the absence of such synchronization a substantial residual MGA commonly remains after AAS, because the MGA is not sampled consistently unless the repetition time TR of the MRI pulse sequence matches exactly a multiple of the EEG sampling interval.

Post-processing techniques based on AAS differ chiefly in the way they treat this residual MGA. Various combinations of interpolation, principal component analysis (PCA) and digital filtering have been proposed [1, 3, 4]. But a standard optimal processing scheme has not yet emerged. In fact, comparative studies in the field are scarce: Ritter and colleagues compare publicly available implementations of the IAR [1] and the FASTR [4] algorithm and quantify their performance based on an interleaved recording of confounded and baseline EEG in vivo [5]. By contrast Grouiller et al. (2007) model the EEG+MGA signal to test the same algorithms in a more controlled setting [6]. Both studies focus on a few compound algorithms and their net effect on a specific type of data. However, no firm conclusions are drawn with respect to generalising the results for different types of data and adapting algorithms for optimal performance. In other words, an open question remains: How does the optimal post-processing strategy depend on properties of the mixed EEG and MGA signal? The present study elaborates this question beyond previous work a) by considering the high bandwidth of the MGA (before sampling), which calls for simulations with high temporal resolution as well as a data analysis with high spectral resolution, and b) by assessing the potential of different post-processing strategies including possible improvements thereof rather than fixed algorithms.

By examining some of the most widely used post-processing strategies this study focuses on fundamental aspects of EEG-MRI experiments in a common setting. More specialised solutions to the MGA-problem, involving for instance spatial filters [7], external reference signals [8, 9], or specialised pulse sequences [10], are beyond the scope of this paper but may be regarded as complementary to the issues discussed here. Specifically, possible problems with experimental instability e.g. due to subject motion cannot be treated conclusively using the methods studied here, as more research into appropriate physical models is required [11].
Methods

1.3 The MRI Gradient Artefact (MGA)

The EEG signal recorded during an MRI scan represents a linear combination of the physiological EEG and several electromagnetic induction artefacts, most notably the MGA and the less significant BCG. This follows from the superposition principle in electrodynamics and is true for all practical purposes, i.e. as long as the amplifier’s dynamic range and digitisation errors are irrelevant. The MGA signal commonly originates from a dynamic i.e. repetitive/time-resolved BOLD fMRI sequence, more precisely the associated magnetic gradient fields disturbing the EEG. The resulting artefact recorded by EEG is likewise repetitive and extremely reproducible as long as the geometry of the experiment does not change. It follows that the most common and effective strategy for its removal by post-processing is average artefact subtraction (AAS) [1]. This means segmenting the EEG signal into epochs of one TR, each comprising one consecutive recording of the MGA, and then subtracting a weighted average artefact waveform from each epoch. If the recorded MGA in each epoch is as reproducible as the MRI sequence itself, the mean MGA waveform will match the MGA in each epoch exactly except for (random) noise that originates from averaging \( n \) epochs of EEG data. In this optimal scenario the SNR of the EEG signal recovered after AAS increases with \( n \) the number of averaged epochs and reaches the original \( \text{SNR}_0 \) asymptotically according to Equation 1 (see plot).

\[
\text{SNR} (\text{synchronised})
\]

1.3.1 The Residual MGA (RMGA) after AAS

The accuracy of the AAS method depends entirely on the consistency i.e. reproducibility of the repeated MGA as recorded by EEG. Under realistic conditions this reproducibility may be compromised (temporarily) by changes in the EEG recording geometry (e.g. by subject or cable motion), apart from that the most common and relevant source of MGA variation is inconsistent sampling due to a systematic shift in EEG sampling times relative to the MGA. In other words: The MGA is sampled repeatedly but not at the same instances unless TR, the repetition time of the MRI sequence matches exactly a multiple of the EEG sampling interval (Ts). An inconsistent phase relationship between the sampling pattern of the EEG and the MGA is almost inevitable unless the clocks driving the EEG and the MRI systems are synchronized. The undesirable consequence is an oscillation of the MGA amplitude around its mean and a substantial residual MGA (RMGA) after AAS.

The effect of a mismatch of size \( dt \) between TR and the nearest multiple of the EEG sampling interval Ts is easily understood by considering the steep temporal derivatives in a Taylor expansion of the MGA and their effect on the corrected EEG signal after AAS (Equation 2). In this case not only the recovered SNR, but also the magnitude of the residual MGA increases with the number (\( k \)) of consecutive epochs averaged. A local (i.e. moving) weighted average artefact template based on a limited number of artefact epochs is commonly employed to balance this trade-off [12]. Note that the odd terms in the Taylor expansion (Equation 2) cancel out when the moving average is computed symmetrically over preceding and following epochs, which is feasible for retrospective processing. To a first approximation the optimal number of summands \( m \) now depends on the second derivative of the gradient artefact scaled by the square of the time delay \( dt \) and \( m \) to the power of three. These factors quickly outweigh the contribution of \( \text{SNR}_0 \) and push the optimal balance towards small \( m \). Results presented later will show that an optimum for \( m \) could in principle be found experimentally by comparing moving averages of various lengths (Figure 2). However, in the following we will argue in favour of more effective strategies than the optimised moving average.
1.4 Avoiding the RMGA by (Re-)Synchronisation

According to the above theory, the residual MGA (after AAS) can be avoided if measures are taken to ensure that the TR of the MRI sequence matches an exact multiple of the EEG sampling interval. This has been demonstrated in experimental practice using a hardware phase locking device to synchronise the EEG with the scanner clock [2, 10]. Based on the same principle we now present a computational method that can be similarly effective and does not require any additional hardware or specialised MRI sequences.

Both the hardware-based and the software-based synchronisation methods operate by adjusting the EEG sampling rate such as to meet the synchronisation condition, namely that TR matches exactly an integer number of EEG samples. Physically this is done by driving the EEG clock. Computationally this can be achieved by interpolation of the EEG signal. The key question is how to determine the correct interpolation factor. A second important technical issue is finding an accurate and efficient method for interpolating an EEG signal of about 1e6 samples per channel with an arbitrary interpolation factor, which is generally not an integer but a real number very close to one. The solutions we propose constitute the Resync algorithm.

1.4.1 De-synchronisation Factor and Relative Timing Error (RTE)

Any EEG-fMRI recording is characterised by an effective MRI repetition time (TR) and the effective EEG sampling rate (Fs). TR and Fs are fixed parameters of the experiment, yet not always precisely known or controlled by the experimenter. More relevant with respect to the question of synchronisation and the RMGA is the absolute timing error \( dt \) (Equation 2), which may be expressed in terms of TR and Fs:

\[
dt = TR - \frac{\text{Round}(TR*Fs)}{Fs} \approx 0
\]

The desired synchronisation condition \( dt= 0 \) is met if the factor \( D := \frac{\text{Round}(TR*Fs)}{(TR*Fs)} \approx 1 \) equals unity. When different from one, the quantity D actually represents the interpolation factor i.e. the change in EEG sampling rate (Fs) required to meet the synchronisation condition. From a computational point of view this is the quantity of interest, which we will term the de-synchronisation factor \( D \). It accounts for the discrepancy between EEG and MRI clock speed in the common scenario, where TR and Fs meet the synchronisation condition formally but not in fact, simply because the two clocks diverge slightly. The de-synchronisation factor is inevitably very close to unity since \( dt<Ts<<TR \).

Both in terms of computational floating point precision and in the interest of legibility it makes sense to refer only to the decimal fraction \( R=D-1 \), which we term the relative timing error (RTE).

1.4.2 The Resync algorithm

The Resync algorithm is designed for the common scenario in which TR and Fs can neither be controlled nor measured precisely. Therefore the de-synchronisation factor \( D \) is not computed from TR and Fs, but rather estimated from the EEG data itself. The MGA in any EEG-MRI recording has an auto-correlation sequence that naturally peaks at regular lag intervals of one TR. Consistently high peak amplitudes close to 1 are indicative of a synchronised recording, whereas a non-zero RTE manifests itself in oscillations of the peak amplitude (Figure 3; [2]). Consequently, the peaks of the auto-correlation sequence may serve as an optimisation criterion, which can be maximised by interpolating the MGA signal. Interpolation and the computation of the auto-correlation sequence (ACS) can be done efficiently even for large sets of data using the Fast Fourier Transform (FFT) and associated theorems, specifically the time shift and time scaling theorems as well as the Wiener–Khinchin theorem. In other words, cross-correlations are computed as cross-spectral products, time-shifting a signal is performed by adding a linearly progressive phase to its discrete Fourier transform (DFT) and interpolation is achieved by changing the frequency grid upon back-transformation into the time domain (by inverse DFT)(Equation 3). The actual maximisation of auto-correlation peaks with respect to the interpolation factor \( D \) is left to a nonlinear optimisation algorithm.
available in Matlab (simplex method). To reduce the demand on memory and computational load an average of D is estimated on data segments conveniently chosen to equal a multiple of the nominal i.e. desired TR in length. Figure 3 shows typical auto-correlation sequences (ACS) for simulated and recorded data before and after application of the Resync algorithm. (It takes 30-40 seconds to estimate the RTE and 6-7 seconds to interpolate these data of about 800’000 samples (one channel) running Matlab 2008b under 64-bit Linux on a Dual Core AMD Operon CPU at 2.6GHz.)

**Equation 3 The Resync algorithm**

1.5 Removing the RMGA by PCA and other post-processing methods

We shall validate the Resync method and demonstrate its effectiveness by comparing it to established methods from the literature [1, 3, 4]. All of the algorithms considered are based on AAS, which means that they differ primarily in the treatment of the RMGA. For this purpose they employ various combinations of AAS, re-sampling, PCA and adaptive regressive filtering. Rather than testing any specific implementations of published algorithms as a whole, we will dissect and discuss the most relevant strategies. This approach better reveals pros and cons and leads to more general conclusions.

1.5.1 Slice Timing Correction (STC)

Interpolation on a local scale is part of several post-processing algorithms in the literature [1, 3, 4]: The time shifting of individual artefact epochs represents an approximate local solution to the synchronisation problem. For the sake of comparison with the Resync method we implemented an STC approach based on FFT interpolation applied to short data segments each comprising one MGA epoch (TR). The cross-correlation between the first and each subsequent MGA epoch is maximised by discretely time shifting the latter with a precision exceeding the sampling interval by a factor of 16-64.

1.5.2 Principal Component Analysis (PCA)

PCA has been used successfully to separate and remove RMGA from the underlying EEG signal [3, 4]. PCA can be regarded as a natural extension of AAS since PCA operates directly on its remainder – a single channel EEG signal segmented into epochs of duration TR, each comprising one consecutive occurrence of the MGA. Such a stack of digitized MGA epochs is treated as a time series of vectors in a high-dimensional linear space. This time series of vectors oscillates about a mean vector, which represents the MGA and is removed by AAS. Fluctuations about the mean represent the RMGA as well as the actual EEG signal. In the light of Equation 2 it is not surprising that the components of these vectors co-vary strongly in the presence of RMGA. This covariance forms the basis of signal separation by PCA, which effectively extracts the components of highest variance from a linear mixture of co-varying signals.

1.5.2.1 PC selection criteria

Dimensionality reduction techniques like PCA and ICA are useful for signal separation only if one signal of interest, the RMGA in our case, is projected into a linear subspace separate from the rest of the EEG signal, and preferably of limited dimensionality. In other words, desired and undesired signal components should become linearly independent in the transformed signal space. Assuming this to be the case the problem of identifying the basis vectors of this linear subspace still remains to be solved. In practice this means selecting a limited number of PCs that support (exclusively) the RMGA signal, and reducing or eliminating their contribution to the transformed signal matrix. The inherent risk or challenge lies in identifying all relevant contributions to the MGA signal, while at the same time avoiding the inadvertent removal of any desired signal components. We deliberately avoid the term **optimal basis set** [4] because PCs are in fact not optimized with respect to MGA signal separation, rather they capture the dimensions of largest variation, which will often but not always exclusively coincide with the MGA. Although PCs related to the MGA are
often evident upon visual inspection, manual selection is neither efficient nor is it reliable and reproducible enough to be recommended for processing EEG-MRI data of many channels. Two quantitative selection criteria have been proposed in the literature:

1. Niazy and colleagues [4] recognise the fact that a strong RMGA mostly manifests itself in a limited number of PCs of exceptionally high variance in comparison to the rest. Consequently, they eliminate the leading 2–5 PCs, depending on a number of thresholds to determine if their variance is sufficiently different from the rest. This strategy is computationally efficient since only the first 5–10 PCs and corresponding variance contributions need to be computed by SVD.

2. Negishi et al. [3] follow a more principled statistical approach by assuming that both MGA and EEG contribute to each PC signal like two independent Gaussian processes (at least on a short time scale). Following this rationale, they adjust the local (i.e. moving-average) mean and variance of each PC signal to match a baseline condition recorded before scan onset.

As we will demonstrate these criteria are geared toward de-synchronised EEG-MRI data, and may yield suboptimal results when confronted with different input. For this reason the PC selection criteria considered in this study comprise modified versions of the above methods, as well as two alternative criteria that we developed and found to be more robust.

A. **Variance Difference criterion**: Eliminate PCs of highest variance if significantly different from the rest (as proposed by Niazy et al.[4]).

B. **Cross-Correlation criterion**: Eliminate PCs for which the maximal cross-correlation between the mean MGA and the PC vector exceeds a threshold of 0.3.

C. **Variance Normalisation criterion**: Scale PC signals to match the pre-scan variance. The original method by Negishi et al. [3] computationally combines the normalisation of local variance with moving AAS and stipulates processing a full basis set of PCs. By contrast, our implementation of the method considers only the 10 strongest PCs and replaces local (i.e. moving-average) with global variance normalisation. The moving average filter is treated separately in our analysis. These simplifications are appropriate, since the variance of a stationary (simulated) signal essentially does not change over time. Moreover, weak PCs do not contribute much to the MGA and are essentially subject to the moving average filter.

D. **Wiener Filter criterion**: Assimilate PC signal spectra to the corresponding baseline spectra by eliminating peaks. An auto-regressive estimator is employed to obtain a smooth estimate of the average baseline and the scan-time (MGA) spectra for each PC signal. The ratio of these two spectra remains close to unity for PCs that are not related to the RMGA. Conversely, peaks in this ratio exceeding 19 (the 95\textsuperscript{th} percentile of the $F_{2,2}$-distribution) were used to identify the PCs and the spectral bands that support the RMGA signal. These spectral components were eliminated by applying an FFT filter.

In practice PCA always follows global AAS, since the global mean is subtracted off all MGA epochs from one segmented EEG channel in order to compute the covariance matrix, which is subsequently decomposed into its eigenvectors by singular value decomposition (SVD). These principal components (PCs) form an orthonormal basis, which by design maximises the variance in its leading dimensions. It is possible and generally sufficient to compute only the first 10-20 PCs to account for 99% of the total signal variance in one EEG channel. The display of PCs in Figure 4 et seq. always includes the mean MGA before AAS (black)
for comparison. The RMGA is removed by scaling or filtering rows of the transformed signal matrix $S_{pr}$ (Equation 4) according to the above criteria, before back-transformation into the original signal space. Some of the above criteria require a baseline PC signal for their computation: For each channel the baseline EEG signal recorded before MRI scan onset is segmented arbitrarily into epochs of the same length as the MGA. The resulting baseline signal matrix is then projected onto the same set of PCs after subtraction of the mean.

**Equation 4 PCA**

\[
M = P_{tr} * S_{pr} + R_{tr}
\]

$t = \text{time / samples}$

$r = \# \text{of TR epochs}$

$p = \# \text{of PCs}$

A matrix of segmented EEG data $M$ is decomposed into a basis of principal component vectors $P$ and a matrix of transformed PC-signals $S$ plus a non-zero remainder $R$, unless $P$ has full rank.

1.5.3 Regressive Filters

Some authors have suggested adaptive noise cancellation (ANC) i.e. regressive filters to further reduce residual MGA after STC, AAS and PCA [1, 4]. Simulated data offer the opportunity to assess the benefits of regressive filters in a best-case scenario. To do so, we took advantage of the System Identification Toolbox in Matlab [13]. Regressive filters were computed by the least-squares method using the previously removed MGA as a reference input signal and the pre-processed EEG signal (with any residual MGA) as output. To reduce the considerable computational load, data were down-sampled from 5kHz to 1kHz sampling rate prior to filter estimation. The input-output signal was split into segments to serve as estimation and validation data. Filters of length 1 – 200 equivalent to 5*TR were estimated to compare the percentile of signal variance explained in the validation data. There was no need to consider more complicated adaptive filters because the simulated EEG is a stationary signal.

1.6 Comparing post-processing performance

Testing and comparing algorithms based on their practical performance is straightforward unless the results depend on the chosen input data. In our case the choice of representative test data is complicated by the fact that different post-processing strategies were not necessarily designed and optimised for the
same type of EEG-MRI data. In this situation the simulation method presented below serves two purposes: A) to investigate EEG-MRI recording parameters that determine algorithm performance, and B) to achieve more reliable quantification results based on a controlled baseline.

1.6.1 Simulation of the MGA
In order to simulate the effects of the RTE and RMGA one needs a model that reproduces the full bandwidth of the MGA signal before it is sampled. For our purposes it is not necessary to model any particular EEG-MRI experiment, but we need to reproduce a realistic frequency spectrum and – most importantly – the relationship between the RTE and the (R)MGA in order to assess the behaviour of the algorithms under investigation.

The scanner software was used to export the gradient signals of a standard single-shot GE-EPI sequence (gradient-echo echo-planar-imaging) commonly used for (EEG-)fMRI experiments on our 3T MRI system (Achieva 3T, Philips Healthcare, Best, Netherlands). One slice acquisition is sufficient to define the whole MRI sequence, repetitive as it is. This model signal has a temporal resolution of 6.4 µs and represents the full bandwidth of the MGA before it has been recorded or even transmitted (~80kHz ≈ 1/6.4µs/2). The gradient system does not actually reproduce every fine detail of this input signal. High frequencies of the MGA are also strongly attenuated by analogue filters in the EEG system. For our purposes the exact spectrum of the model signal is not important as long as the signal is well defined and its bandwidth realistically far exceeds the Nyquist frequency of the EEG (2500Hz). The three components (XYZ) of the gradient signal are summed to form an arbitrary linear combination. The signal is first filtered at a normalised frequency of 0.5 to limit the highest frequencies, then differentiated numerically to mimic Faraday’s law, by which the voltage induced in an EEG circuit would be proportional to the change in magnetic flux. Analogue EEG filters are imitated by two FIR filters of order 100 with cut-off frequencies at 1500Hz and 250Hz. Before down-sampling, an additional FFT filter is used to make sure that all signal power above the EEG Nyquist limit of 2500Hz has been eliminated. The latter two filters were optionally omitted to investigate the effects of aliasing artefacts. Making use of linear interpolation the high-resolution MGA template of 40ms length (one slice acquisition) is sampled repeatedly along a continuously shifting grid of equidistant EEG sampling points so as to obtain a simulated MGA signal of about 40 seconds length. In doing so the employed EEG sampling rate of 5kHz is de-tuned by a de-synchronisation factor in order to mimic the effect of an RTE on the order of 1e-9 to 1e-4. We will see that the de-synchronisation factor and the aliasing filters play a decisive role with respect to the effects described below. Other simulation parameters are rather inconsequential and can be chosen quite arbitrarily.

Subject motion during an experimental run causes changes in the MGA waveform. The size and temporal dynamics of motion effects are variable and a comprehensive treatment is beyond the scope of this paper. However, given the commonness of motion events the potential of any EEG-MRI post-processing method to tolerate or even compensate for such features is of considerable interest. For this reason, our simulations optionally incorporate an abrupt change in MGA waveform halfway through the experiment by randomly changing the weighting of the XYZ-gradient signals, which make up the MGA.

1.6.1.1 The EEG reference signal
The MGA signal is finally normalised to have zero mean and unit variance and added to an equally unbiased (artificial) EEG reference signal. To be in realistic proportion the latter is scaled to have 1% of the MGA variance, thus leaving two orders of magnitude difference between the two. The question whether or not this baseline signal may influence processing results was addressed by considering a number of alternatives:
1) **Zero**: Unrealistic and computationally problematic resulting in spectra with extremely high dynamic range, rank deficient covariance matrices and divergent residual error estimates dominated by numeric errors.

2) **White Noise**: Computationally convenient, but unrealistic for lack of any covariance structure.

3) **Artificial Coloured Noise**: Comb-filtered white noise plus variable frequency sinusoids. Interesting only to the extent that it mimics a realistic EEG baseline.

4) **EEG baseline signal** measured in vivo prior to scan onset: Realistic and useful, not necessarily a stationary signal suitable for averaging spectra.

5) **Simulated EEG baseline signal**: Using an auto-regressive filter estimated from EEG baseline data to reshape white noise into the same spectral composition – realistic and convenient for generating a stationary signal of arbitrary length. This was used for the simulations presented below.

1.6.2 **Qualitative comparison by PCA**

So far we have elaborated on the use of PCA for isolating and preferentially removing the MGA from a confounded EEG signal. However, in the context of this study we advocate the use of PCA primarily for the purpose of characterising the RMGA in EEG-MRI data. Even when the signal separation achievable by PCA is not adequate for artefact removal, inspection of the leading PCs and their contribution to the overall variance yields qualitative and semi-quantitative insight into the presence and magnitude of any RMGA and the effect of post-processing methods thereupon (Figure 6).

1.6.3 **Quantitative comparison by spectral analysis**

The question how to quantify appropriately and compare sensibly the performance of post-processing algorithms is complicated by a few facts: Firstly, a true reference (baseline) signal required for accurate quantification is available only for simulated data. For data recorded in vivo or in vitro one must rely on a baseline signal recorded before scan onset to estimate the baseline spectrum. For non-stationary signals like the EEG recorded in vivo this is a significant source of bias. Secondly, the effectiveness of different algorithms depends on the input signal (MGA), for which they were designed. These two issues are addressed by the use of simulated data. Finally, the benefit of post-processing depends on the extent to which the removed MGA actually overlaps with the EEG signal of interest: The simplest quantification of post-processing performance might consider no more than the effected change in total signal variance. However, this metric would be preferentially biased toward techniques that indiscriminately remove more signal, possibly even when it is not part of the MGA and/or located outside the EEG signal range. The latter issue leads us to adopt the following scheme for spectral analysis (Figure 2):

- Spectra of the processed signal \([A(f)]\) as well as the (pre-scan) baseline \([B(f)]\) (Figure 2A)
- Spectrum of the processed signal normalised by the baseline \([A(f)/B(f)]\) (Figure 2B).
- Integrated normalised residual error spectrum \(C(F) = \sum_{f=1}^{\delta} |A(f)/B(f) - 1|\) (Figure 2C)
- Stacked bar graph of normalised residual error integrated over a number of spectral bands.

In practice we compute the power spectra of the processed EEG signals (as well as the corresponding baseline) either by the Welch method (using a Hanning window) or by Thompson’s multi-taper method [14]. In any case the effective spectral resolution is chosen such that the line spectrum of the MGA is well resolved.
The MGA-reduced EEG spectrum is then normalised by the baseline spectrum computed in an identical fashion. After subtracting the expectation value of one the cumulative sum of this normalised error spectrum helps to visualise the total error incurred as a function of signal bandwidth. Note that in this context any signal unrelated to the MGA is considered a (potentially) useful part of the baseline. Finally, the normalised error spectrum is broken down into contributions from six relevant spectral bands, which can be displayed and compared side-by-side in the compact form of a stacked bar graph (Figure 5). For reference this comparison includes an estimate of the minimum error theoretically achievable by applying AAS to the baseline signal.

The cumulative spectra are dominated by the contributions from the MGA line spectrum. To elucidate any differential effect that post-processing might have on the uncontaminated part of the EEG spectrum one may perform the spectral analysis separately for frequencies that fall on harmonics of 1/TR and those that fall exactly in between (Figure 2AB). For this interleaved spectral analysis we use a multi-taper spectral estimator with a bandwidth adjusted to cover one quarter of the separation between spectral lines, thus leaving a transition band of equal size for good separation from the neighbouring lines.

Figure 2 Spectral analysis

All signal processing and data analysis was implemented using the software package Matlab (The MathWorks Inc., Natick, MA, USA). The problems and solutions presented are very generic and therefore expected to be essentially independent of the experimental platform we used to collect the EEG-MRI data.

1.7 EEG-fMRI experiments
The EEG-fMRI data presented in this study were acquired using the MR-compatible EEG system BrainAmp (BrainProducts GmbH, Munich, Germany), which features a sampling rate of 5kHz, hardware filters at 250Hz and a phase-locking device for (optional) synchronization with the clock of the MRI system. For experiments in vivo the 65 sintered Ag–AgCl ring electrodes incorporating 5kΩ resistors were mounted in an MR-optimized electrode cap (EASYCAP GmbH, Herrsching-Breitbrunn, Germany), which covered all positions of the 10–20 system, as well as most electrodes of the 10–10 system, plus two ECG electrodes. Fz served as recording reference and AFz as ground. Some experiments were performed in vitro, which means that the electrodes were immersed in a beaker of tap water inside the scanner.

Recordings were performed inside a Philips Achieva scanner at 3 Tesla field strength (Philips Healthcare, Best, Netherlands) with 40 mT/m and 200 mT/m/ms gradients using the standard quadrature head coil in transmit and receive mode. The MRI sequences used are typical for BOLD fMRI experiments i.e. multi-slice single-shot GE-EPI scans with an echo time (TE) of 20-40ms and a (volume) TR of 1-3sec. A total scan duration of 3 minutes results in 4500 slice acquisitions at 25 slices/volume and TR=1 sec. About one minute of baseline EEG without MGA was recorded prior to scan onset i.e. the equivalent of 1500 MGA epochs.

Results

1.8 MRI gradient artefact (MGA)
To illustrate the basic properties of the MGA, Figure 1A&C show two typical waveforms recorded in vitro. The corresponding power spectra of the MGA (Figure 1B&D) are mostly determined by the MRI parameters TR(volume) and TR(slice), which define the fundamental periodicities of a dynamic fMRI sequence. The convolution of two sets of harmonics predictably leads to the complicated line spectrum seen in Figure 1B. However, a judicious choice of TR(volume) as a multiple of TR(slice) will result in a much simpler line
spectrum with only one fundamental frequency: All signal power of the MGA becomes concentrated in harmonics of $1/\text{TR(slice)}$ when there is no interruption of the fMRI sequence by a time delay or additional pulses between consecutive volume acquisitions. This mechanism offers a simple way to limit the “contaminated” MGA spectrum to fewer narrow bands.

The following treatise considers MRI sequences with only one fundamental period (40ms), which will be referred to as TR. Effectively, this implies TR(slice) but could just as well refer to TR(volume) if that were the length of MGA epochs chosen for segmentation. This is done for simplicity and without loss of generality, because the amplitude of the RMGA depends almost exclusively on the EEG recording and the extent to which it is phase-locked or synchronised with the MRI sequence. The MRI sequence by itself only determines the frequency content of the MGA and hence the RMGA, which is of less concern here.

1.9 Residual MGA (RMGA) and relative timing error (RTE)

The influence of the relative timing error (RTE) and the effect of re-synchronisation on the RMGA are exemplified in Figure 3, which compares 6 representative sets of data, three recorded in vivo (top panels) and 3 simulations with corresponding parameters (bottom panels). The two graphs in each panel show the standard deviation (STD) of the RMGA as well as the normalised auto-correlation sequence (ACS) of the MGA sampled at lag-intervals of one TR. The magnitude of the RTE increases from panel to panel left to right. For the in-vivo data this results from recording A) with matching TR and clock synchronisation hardware, B) with matching TR but without clock synchronisation, and finally C) with a deliberate mismatch in TR, where hardware synchronisation becomes irrelevant. The RTE estimated as part of the Resync procedure is printed at the top of each panel and reflects this change from ~1e-9 to 1e-7 and 1e-3 (Δtime/time) for the in-vivo data. Notably, for the simulated data the exact parameter values of 0.0, 2e-7 and 2e-4 are estimated very accurately by the Resync algorithm. Estimation accuracy increases with signal length: About 100 MGA epochs are required to reach 0.1% precision.

The effects of re-synchronisation (light $\rightarrow$ dark lines) are naturally most visible for the severely de-synchronised data (panels C&F). As the cohort of MGA epochs becomes more coherent through re-synchronisation the variance of the RMGA (C1) decreases strongly. At the same time the peaks of the normalised auto-correlation sequence (C2) are maximised. These features are consistent with a reduction in RTE as observed in the same data prior to re-synchronisation (light lines). For the synchronised data (panels A&D) the effects of re-synchronisation are negligible. Unsystematic fluctuations in the ACS (A2) are most likely due to subject motion and the BCG in vivo. A slight deviation from zero (~1e-9) that seems apparent in the RTE estimated from synchronised data recorded in vivo (A) is most likely due to the precision limit of the estimate. The ACS in Figure 3B exhibits both the spurious fluctuations seen in (A) as well as the systematic trend in (E). Notably, the latter becomes dominant with increasing RTE (C+F).

Figure 3 illustrates the three qualitatively different types of MGA, which we consider for our comparison of post-processing methods, namely synchronised, weakly de-synchronised and strongly de-synchronised. This corresponds to essentially no RMGA, a little RMGA and a lot of RMGA dominating the EEG signal after AAS.

1.10 Simulated and recorded data

Figure 3 confirms that simulated data and data recorded in-vivo are similarly affected by the Resync procedure. PCA applied to the same sets of data (Figure 4A-C) yields a more qualitative but revealing comparison: PCs obviously related to the MGA (red) become more numerous and account for more variance as the RTE increases. These findings are equally typical for simulations as for in-vivo data. One
might add that the results of spectral analysis following various post-processing procedures also show no fundamental difference between in-vivo data and simulations (data not shown). That is, apart from the deviations in the recorded baseline (Figure 2A), which motivate the use of simulations in the first place. With regard to the later discussion, it is important to note that MGA-related PCs do not necessarily all rank first in terms of their variance contribution and that other significant PCs code for EEG signal: e.g. the sinusoidal components at roughly 10Hz (Figure 4A-C, green) capture alpha waves in these data collected from occipital EEG channels. The ranking of PCA components effectively depends on the presence and significance of the RTE and other sources of RMGA.

1.11 Re-synchronisation

The effectiveness of the Resync technique is further demonstrated by comparing a number of different post-processing strategies in terms of the residual normalised error power integrated over 6 spectral bands (Figure 5). These strategies (see figure legend) have been applied to representative sets of de-synchronised, re-synchronised and synchronised data (three panels left to right), both from simulations and recordings in vivo (top / bottom panels). The first bar in each panel (AAS0) represents the (theoretically) achievable optimum estimated by applying AAS to the corresponding baseline signal.

In simulations this optimum is reached by AAS of synchronised data (Figure 5C) as well as re-synchronised data, on condition that the EEG sampling rate is sufficiently high. Accordingly, the discrepancies between AAS0 and AAS observed in the present example (Figure 5B) mostly at high frequencies are levelled out by increasing the sampling rate from 5 to 10kHz (not shown). This suggests that interpolation errors play a decisive role. Before re-synchronisation (Figure 5A+D) post-processing methods based on PCA excel in terms of achieving the lowest residual error particularly at high frequencies. But after re-synchronisation AAS by itself (see arrow) yields the lowest error and PCA remains ineffective at least in simulations (Figure 5B, Figure 6A+B).

For data recorded in vivo typically none of the post-processing methods reach the signal level of AAS0 irrespective of hard- or software synchronisation (Figure 5E+F). This is almost certainly the consequence of RMGA contributions unrelated to the RTE. In the presence of a moderate RTE (~1e-6) other sources of RMGA like subject motion become more relevant and the benefits of synchronisation more and more restricted to higher frequencies (Figure 5D-F). Note that the data underlying Figure 5F is not the same as in Figure 5D+E, because the experimental setup does not allow recording with and without hardware synchronisation at the same time. In this situation one may compare the ranking of methods within each panel, but a quantitative comparison between panels is problematic, considering the variability of in-vivo data. Nevertheless, one may observe comparable results for hard- and software synchronisation, given two equally (un-)stable EEG-MRI recordings.

1.12 EEG sampling rate & aliasing filters

Simulations of the MGA offer an opportunity to investigate the influence of sampling rate and aliasing filters on the results of EEG-MRI post-processing. Confirming previous results [2], synchronised data, devoid of any RMGA to begin with, is found to be robust against changes in sampling rate as well as anti-aliasing filters, judging by the absence of affected PCs (data not shown). Figure 6 focuses on de-synchronised data with a simulated RTE of 2e-4 (same as Figure 3F and Figure 4F). The 2x2 table Figure 6A-D compares data...
resulting from two different filter settings (strong/weak = top/bottom) both before and after re-synchronisation (right / left): Less stringent aliasing filters with a wider pass band and less stop-band attenuation result in more MGA-related PCs (compare Figure 6B+D). Moreover, the signal contributions due to weak filters defy elimination through re-synchronisation of the data (Figure 6C). A change in sampling rate also effects an opposite change in the number of MGA-related PCs (data not shown); however, these remain amenable to re-synchronisation as long as good control of aliasing is maintained. Thus, even without re-synchronisation a high sampling rate by itself ameliorates the problem of RMGA in two ways: 1) through a reduction of aliasing artefacts, and 2) by limiting the absolute timing error (dt, Equation 2), which is bounded from above by half a sampling interval.

**Figure 6** Anti-aliasing filters + sampling rate

### 1.13 Alternatives & supplements to (re-)synchronisation

#### 1.13.1 Principal component analysis (PCA)

The preceding results argue for synchronisation (by hardware or software) in combination with global AAS as the strategy of choice for EEG-MRI post-processing. Nevertheless, PCA may yield comparable or even superior results under certain conditions. Specifically, when there is RMGA originating from sources other than the RTE, PCA may supplement or substitute (re-)synchronisation. The following results shed light on the potential and caveats of the PCA approach and in particular the merits of various PCA criteria.

The preceding comparison of relative error power (Figure 5) already indicates that post-processing by PCA tends to be more beneficial at higher frequencies than in the low frequency range. The opposite is true for the moving AAS shown for comparison. The differences between the PCA criteria compared in this study are exemplified in Figure 7. In this example all criteria were applied to a typical PCA decomposition of in-vivo data with a (large) RTE of ~2e-4. Among the strongest 10 PCs numbers 1, 2, 5, 7, 8 and 10 seem visibly related to the MGA. Evidently, other PCs carrying EEG signal are interspersed. And some components like #6 are visibly mixed. It is interesting to examine the characteristic behaviour of different PCA criteria in this challenging scenario:

- **A. The difference-in-variance criterion** (based on Niazy et al. 2005) identifies only leading i.e. strong MGA components (Figure 7A, red), but tends to ignore weaker ones (Figure 7A, green). It is therefore rather conservative and well suited for cases in which MGA and EEG are cleanly separated by PCA.

- **B. The cross-correlation criterion** is more flexible in that respect. It identifies even weak MGA components with high probability (Figure 7A, red + green), potentially at the risk of capturing mixed components as well.

- **C. Variance Normalisation** (loosely based on Negishi et al. 2004) is seen to attenuate MGA related components to baseline levels while maintaining their non-white temporal structure, however. The method tends to yield decent results in terms of total error variance (Figure 5). However, it is likely to attenuate physiological EEG signals like alpha waves under certain conditions.

- **D. The Wiener filter criterion** is more specific in removing variance related to the oscillating RMGA, thus equalising not just the variance but the spectrum between the baseline and scan time PC signals (Figure 7E). In spite of certain transition effects or ringing that often result from such frequency-domain filters, the Wiener filter criterion was generally found to yield the best results in terms of total error power (Figure 5).
1.13.2 PCA and motion artefacts
In spite of the aforementioned caveats the application of PCA as a supplement to re-synchronisation may be indicated in situations, where some or all of the RMGA signal originates from sources other than the RTE. As an example the data in Figure 8A simulates an abrupt change in the MGA signal waveform halfway through the experiment. As one might expect, PCA captures such a persistent signal change in merely one or two components, which are easily removed. However, the number of PCs implicated quickly multiplies in the presence of RTE (Figure 8B). In this situation re-synchronisation is found to be beneficial in disentangling the mixed components facilitating but not superseding their subsequent removal by PCA (Figure 8C).

1.13.3 Regressive filters
Regressive filters of 1 – 200 samples length (up to 5 TR) were estimated for simulated data with and without (re-)synchronisation as well as other types of post-processing (AAS, PCA). For data with substantial RMGA regressive filters explain some but by far not all of that residual variance. This agrees with previous results [4]. Interestingly, the estimated filter coefficients at lag times corresponding to multiples of TR tend to be the only significant ones. For data previously processed by AAS and PCA regressive filters show no benefit. On the contrary, the residual error for the validation data tends to increase with filter length, as the filter approximates the EEG signal in the estimation data. In the light of these preliminary results it does not seem worthwhile to pursue regressive filters further. The data are not shown.
Discussion

1.14 EEG-MRI post-processing: New methodology

1.14.1 Relative Timing Error and Re-Synchronisation

The analysis of theoretical and practical properties of the MGA identifies the RTE as one principal cause of RMGA and a key to avoiding it. Precise synchronisation (i.e. phase-locking the EEG acquisition to the MRI sequence) practically eliminates both the RTE and the associated RMGA. Based on this insight, we propose a new synchronisation method for the purpose of avoiding the RMGA after AAS. The Resync algorithm consists of two procedures: (1) Estimating the RTE by jointly maximising the peaks of the auto-correlation function of the MGA. (2) Equidistant and continuous interpolation over the entire EEG signal (one channel at the time). In both stages the Resync algorithm avoids up-sampling by performing all operations – continuous time shifting, cross-correlation and interpolation – in the spectral domain, which is efficient by the use of FFT and precise to the limits afforded by data SNR and numeric precision. All of the above distinguish Resync from previous interpolation approaches, which use limited fixed-rate up-sampling of short data sections. These methods commonly suffer from limited accuracy and may introduce artefacts as a result of inconsistent processing of data segments. Unlike Resync they generally necessitate further processing for instance by PCA even under optimal conditions (i.e. simulated data). The fact that the Resync method can be applied retrospectively and does not require specialised hardware also sets it apart from the previously suggested hardware synchronisation method [2].

The results (Figure 3 et seq.) demonstrate the effectiveness of the Resync method and suggest that it can substitute hardware synchronisation in most practical scenarios, because advantages of the latter only come to bear in EEG experiments with an exceptionally large RTE in combination with a low sampling rate coupled with long averaging periods (mAAS) and in the absence of more significant motion artefacts. For common experiments in vivo with a moderate RTE and some inevitable RMGA due to motion, BCG and respiration the advantages of hardware over software synchronisation are largely restricted to frequencies far above 100Hz and of little relevance in practice (Figure 5E+F). Naturally, hardware synchronisation remains the method of choice, if available. But a significant advantage over retrospective (software) synchronisation is expected only in the aforementioned (extreme) situations, therefore entirely dependent on the individual recording and hard to quantify in a general fashion.

Likewise one may suspect that subject fixation might be the only fundamental solution to the problem of motion artefacts, if not the related respiratory and BCG artefacts. Regardless of (re-)synchronisation the mAAS and PCA methods included in this study can be rather effective for in-vivo experiments, but they do not represent a patent solution in our experience: Since the RMGA is dependent on electrode position an optimal post-processing strategy based on mAAS and PCA is not guaranteed to generalise across EEG channels, much less separate experiments. Moreover, an optimal post-processing strategy is likely to depend on the frequency band of interest, which may call for band-specific processing as recently suggested by Ritter and colleagues [20]. In this situation we advocate an optimisation approach based on quantification of the RMGA as a function of post-processing by re-synchronisation, (m)AAS and PCA.

1.14.2 Simulation and Quantification

A method for simulating the MGA was developed as part of a new concept proposed for quantifying and comparing the performance of various post-processing algorithms. The quantification is based on spectral analysis. This resembles some previous approaches, but in contrast to those we emphasise the necessity to spectrally resolve the sharp line spectrum of the MGA (Figure 1) and to distinguish it from the
uncontaminated EEG spectrum. This makes the method more specifically sensitive to the RMGA and allows better assessment of EEG signal preservation. Apart from spectral analysis we demonstrate and advocate the use of PCA for a sensitive qualitative assessment of the RMGA. Our simulations take the high bandwidth of the MGA signal before EEG sampling into account. This is necessary to observe the crucial effects of the RTE and aliasing artefacts.

The described framework of simulation and quantification methods was used to validate the Resync method in combination with and in comparison to established techniques based on AAS, re-sampling, PCA and digital filters. In doing so we also addressed the important question, to what extent the performance of different post-processing algorithms depends on certain properties of the input data. This is a concern that has been raised, but could not be treated experimentally in previous studies [5, 6]. The ability to vary and explore parameters for different recording scenarios is a key advantage of using simulated data in addition to data recorded in vivo and in vitro. A second motivation is the availability of an exact and controlled baseline for quantification purposes, which cannot be obtained from recorded data. Note that all signal not related to the MGA is considered part of the EEG signal baseline in the context of this study.

1.15 EEG-MRI recordings: relevant parameters and resulting types of data

This investigation has its primary focus on optimising post-processing strategies for EEG-MRI experiments. However, the results reveal that recording parameters actually have the largest influence on post-processing results. As a rule, any effect that modulates the MGA signal (to be removed later) must be avoided during an experiment. This is particularly true for changes in experimental geometry such as subject or cable motion or even changes in electrode conductance. However, the present study is more concerned with parameters that are less likely to be beyond experimental control, specifically the RTE, aliasing and TR/TR(slice). Of course, the problem of RMGA originating from experimental instability in a more general sense remains to be solved and will require methods that are beyond the scope of this paper [11, 15]. Nevertheless, the observed interactions between different effects suggest that RMGA from different sources can and should be treated sequentially (Figure 8). The relative proportion of RMGA due to the RTE and other artefacts actually determines the effectiveness and relevance of retrospective as well as synchronisation in comparison to other measures for a given EEG-MRI experiment, data set or even EEG channel.

1.15.1 Recording: TR(volume)/TR(slice)

Adjusting TR/TR(slice) such that TR(slice) becomes the fundamental period of the MGA may in practice be the simplest measure to improve EEG data quality, if the scanner software provides suitable parameter options. This strategy may not be practical for EEG-fMRI experiments that require a time delay for stimulus presentation between volume acquisitions or close temporal proximity between slice acquisitions. However, circumstances permitting, one should not forsake the advantages of a shorter effective TR:

- an EEG spectrum less disturbed by fewer, more widely spaced spectral lines of the MGA (Figure 1)
- more redundancy for averaging the MGA resulting in better SNR after AAS (Equation 1)
- (more reliable estimation of the RTE by Resync)
- and, when PCA is applied:
  - a smaller computationally more tractable covariance matrix and PCs of lower dimensionality
  - fewer MGA-related PCs, which are...
  - ... unlikely to capture auto-correlated EEG signal at frequencies below 1/TR

Instead of making the MRI sequence more regular some authors propose segmenting the MGA signal at irregular intervals to obtain a shorter, but more redundant artefact template of length TR(slice) instead of
TR(volume)[1, 3, 4, 16]. It must be taken into account, however, that these irregularly spaced templates of MGA(slice) are not 100% equivalent and any empty gap between volume acquisitions is also likely to be confounded with after effects of the MGA. These residuals can easily outweigh any SNR gained by averaging a larger number of samples, especially considering the flattening curve in Equation 1. Therefore, slice-averaging methods require further processing by ANC, PCA or a second averaging step with a volume template all the same. However, according to theory (Equation 1) two averaging steps do not improve but degrade SNR, which is dominated by the noise contribution from the averaged EEG signal and therefore limited by the lesser number of samples.

1.15.2 Recording: Aliasing
The EEG and the MGA signals differ vastly in bandwidth and dynamic range (both roughly by a factor of 100). The necessity to record and then separate both signals by AAS makes the experiment highly susceptible to residual aliasing artefacts. Aliasing is a generic problem that must inevitably be solved by electronic filters before analogue-to-digital conversion. A high sampling rate relaxes the requirement for strong filters. Also, strong filters are easier to implement digitally in practice. In the light of these two propositions, our simulations suggest that a high sampling rate at the recording stage in combination with strong digital filters is advantageous, and would sensibly be followed by down-sampling to a moderate sampling rate required for further processing.

The same conclusion is supported by the fact that the amplitude of the RMGA scales with the product of the absolute timing error (dt) and derivatives of the MGA signal (Equation 2). These derivatives are limited by signal bandwidth and power at high frequencies. The timing error dt, on the other hand, is bounded from above by half the EEG sampling interval (Ts/2). In other words, an increase in sampling rate and a decrease in MGA bandwidth will serve to minimise the RMGA amplitude.

The above aspects may be taken into consideration when designing new EEG-MRI experiments. Although the requirement for MR-compatibility constrains the choice of usable hardware, a large dynamic range (>40dB), high sampling rate (>80kHz) and real-time digital filters are fairly generic requirements for a digital signal processing device likely to be commercially available.

As a sideline one might mention that dynamic range too can be gained by trading off electronic and digital signal processing. Oeltermann and colleagues demonstrate how electronic pre-compensation can reduce the MGA amplitude to a point where intra-cortical recordings of single cell activity in the monkey cortex can be resolved after signal processing by AAS and PCA [17]. Finally, it has been demonstrated that MRI pulse sequences can be designed in an intricate way such that gradient artefacts occur only in between but not during EEG sample acquisitions. By avoiding the MGA this so-called Stepping Stone technique [10] also requires less dynamic range and achieves better EEG resolution. But the requirement for specialised pulse sequences and their precise synchronisation with the EEG represents a significant limitation of this technique.

1.15.3 Recording: RTE
A principal source of RMGA is the RTE due to lack of synchronisation between the EEG and the MRI acquisitions. This point has been reiterated here and elsewhere. As demonstrated earlier [2, 10], synchronisation requires a phase-lock between the clocks of the EEG and the MRI system as well as precise control over TR, which must match a multiple of the EEG sampling interval. Both can be elusive in experimental practice, depending on the availability of specialised hard- and software. This justifies the present exploration of alternative methods for avoiding the RTE and thereby the RMGA. Perfect hardware synchronisation promises not only optimal SNR by AAS alone, but also robustness against residual aliasing artefacts. The latter point is not shared by any of the alternative methods discussed here. Nonetheless,
they offer a technically less demanding and therefore attractive alternative to hardware synchronisation. Moreover, methods like PCA may supplement hardware synchronisation in the presence of RMGA from sources unrelated to the RTE.

Three categories of EEG-MRI data
The experience with hardware synchronisation initially prompted us to make the important distinction between EEG-MRI recordings with and without synchronisation. Better theoretical insight and new methodology now allow us to quantify the accuracy of synchronisation by estimating the RTE. For the purpose of this comparative study we categorise EEG-MRI data broadly into three groups, based on the RTE (zero, low, high) and associated properties listed in Table 1. These categories correspond to the experimental observation of 1) recordings with hardware synchronisation and matching TR, 2) recordings without hardware synchronisation but with TR still matching a multiple of Ts at least nominally, and 3) recordings without matching TR, in which case clock synchronisation becomes irrelevant. Apart from recording modalities the above classification is based on the auto-correlation sequence (ACS) of the MGA, which serves as a numeric test of synchronisation (Figure 3). Synchronised data exhibits an ACS uniformly close to unity, whereas strongly de-synchronised data is easily discerned by an ACS that oscillates between -1 and 1 (Figure 3). At an intermediate stage the ACS will oscillate with a period that is large compared to the duration of the experiment. Effectively the ACS is seen to decline slowly (Figure 3E). One full cycle of the ACS corresponds to an absolute timing error of one sampling interval (Ts) acquired over the course of the whole experiment (T) and therefore an RTE on the order of \( \frac{Ts}{T} = 10^{-4} \) s / \( 10^{2} \) s = \( 10^{-6} \).

More relevant than the oscillation period of the RMGA is, of course, its amplitude relative to the EEG signal. The initial theory (Equation 2) could be elaborated to relate the recoverable SNR to the bandwidth and power of the recorded MGA signal as well as the RTE or alternatively the EEG sampling interval, which poses an upper limit to the absolute timing error (dt). However, the purpose of this study is not to derive an analytical solution based on parameters that are hard to determine in practice, but rather to propose a practical approach to optimising experimental parameters, specifically in a situation, where a moderate RTE may not be the limiting factor for SNR in vivo.

| Table 1 Types of EEG-MRI data categorised by RTE: |
|---|---|---|
| **essentially synchronised** | **weakly de-synchronised** | **strongly de-synchronised** |
| RTE ~ 0 < 10e-8 | RTE < Ts / T ~ 10^5 = 10^5 s/10^2 s | RTE ~ 10e-4 >> Ts / T |
| ACS steady ~ 1 | 1 > ACS slopes > ~0.9 | 1 > ACS oscillates > -1 |
| Recorded with matching TR and (hardware) clock synchronisation. | Recorded with matching TR, but without clock synchronisation. | Recorded with a mismatch in TR (clock synchronisation irrelevant). |
| PCA shows no MGA-related components among the strong, leading ones. | PCA shows ~1-3 (leading) MGA-components. | PCA shows ~1-3 strong MGA-components and potentially many weaker ones as well. |

1.16 Re-Synchronisation
When simulated and recorded test data is subjected to the Resync algorithm, one essentially observes that it becomes comparable to data recorded with hardware synchronisation, according to the characteristic properties listed in Table 1. The comparison of auto-correlations (Figure 3), RMGA variance (Figure 3), PCA (Figure 6) and cumulative spectral power (Figure 5) attest to the fact that the Resync method can effectively eliminate the RTE and the RMGA, yielding results comparable to hardware synchronisation both for simulated data and experiments in vivo. As a consequence AAS applied to (re-)synchronised data achieves a reduction of the MGA that is optimal in the sense that further post-processing (by PCA e.g.)
remains ineffective and unnecessary unless there are sources of RMGA other than the RTE. This is advantageous not only from a computational, but above all from a statistical point of view, because the results of AAS are predictable, statistically accountable and without bias toward any particular type of signal. In this regard AAS is superior to other procedures like PCA or ANC.

1.17 Principal Component Analysis

PCA in the way it is set up here is a powerful method for capturing and removing RMGA based on its auto-covariance over a period of one TR. As a model-free, generic method PCA is flexible enough to extract RMGA components including but not limited to those contingent upon the RTE. This means that resynchronisation can replace PCA, unless there is RMGA due to alternative sources like subject motion (Figure 8), in which case PCA may actually supplement Resync. In this flexibility also lies a major caveat, since desired and undesired signal components of high auto-covariance may be captured and removed equally well (Figure 4). To prevent unanticipated consequences PCA should best be avoided and replaced by Resync if possible. Nevertheless, we advocate inspection of the leading 10-20 PCs for a qualitative assessment of the RMGA in EEG-MRI data. Of course, visual inspection is neither an efficient nor a reliable and reproducible approach to processing EEG data sets of many channels. We therefore emphasise the importance of finding quantitative criteria for automatically identifying relevant PCs. Since the post-processing performance of methods based on PCA completely depends on the selection procedure, a number of different approaches were included in this comparison of post-processing techniques. The two criteria found in the literature are clearly geared toward de-synchronised data, and likely to yield sub-optimal results in other circumstances. For this reason we propose alternative criteria, which were found to be more robust in many instances.

1.17.1.1 Variance-Difference criterion (VD)

Niazy et al. proposed a computationally efficient criterion, which compares only the total variance contribution of the strongest 1–5 PCs i.e. the eigenvalues of the RMGA covariance matrix. In our experience eliminating the leading PCs if they are of exceptionally high variance compared to the rest is indeed an effective strategy in an ideal but not unlikely scenario where the RMGA is concentrated in few but strong PCs. Our experiments and simulations show that such data results from EEG-MRI recordings without synchronisation but with good control of aliasing artefacts. However, the Niazy criterion becomes problematic in the presence of weak RMGA components, i.e. ones that are comparable in variance to the EEG signal. As a result partially synchronised data or residual aliasing artefacts may render the Niazy criterion inadequate for identifying relevant PCs, which may not rank among the first i.e. strongest.

1.17.1.2 Cross-correlation criterion (XC)

Under such more challenging conditions the equally heuristic cross-correlation criterion we propose exhibits better sensitivity in identifying RMGA related PCs irrespective of their variance relative to other components or the baseline. Motivated originally by the visual similarity between the mean MGA and related PCs, the success of this pattern matching approach can be explained by the fact that RMGA, which results from time shifting or amplitude scaling of the MGA inevitably inherits a similar spectral composition. In fact PCs related to the RTE are expected to represent derivatives of the MGA according to Equation 2. This explains the linear, quadratic and cubic curves often observed in the time courses of MGA-related PC signals (Figure 7B).

1.17.1.3 Variance Normalisation criterion (VN)

Unlike the aforementioned criteria the local variance normalisation method by Negishi et al. (2004) draws upon a baseline measurement to rescale PC signals accordingly [3]. Though well-founded in theory we find that this method yields varied results in practice. One reason is the assumed Gaussian distribution, which is
in fact an unlikely model for PC signals constituting the MGA. In particular the temporal structure and the
peaked power spectra of such signals attest to the contrary (Figure 7). By rescaling instead of eliminating
such signal components their non-white temporal structure and a significant artefact at harmonics of 1/TR
is actually retained. In the original method of Negishi et al. this drawback is partly offset by the combination
with moving AAS, which amounts to a notching filter at frequencies that are multiples of 1/TR. A more
problematic variable source of error is the baseline measurement, which would have to be representative
and without bias to avoid erroneous scaling of physiological signal components. This is not a safe
assumption for a non-stationary physiological signal like the EEG. The problem is aggravated by the
proposed processing of all PCs i.e. a full basis set, which is computationally expensive moreover. In
summary, the variance normalisation method fails to fully capitalise on the capability of PCA to separate
signal components related to the RMGA and the EEG.

1.17.1.4 Wiener Filter criterion (WF)
In spite of being a potential source of bias the use of a baseline record to formulate criteria is not an
unattractive idea. To address the above criticism an improved method needs to take the temporal structure
of PC signals into account. A patent solution presents itself in the Wiener Filter designed to equalise the
power spectra of two signals. The variant we propose here involves smooth spectral estimators as well as a
binary transfer function, which either passes or blocks signal completely. The underlying rationale is an
assumed separation between EEG-dominated and MGA-dominated parts of the PC spectra. Note that
operating on PC spectra is not the same as manipulating the EEG signal spectrum directly, as has been
suggested by Hoffmann et al. (2000) [18]. In spite of certain transition effects or ringing that often result
from such frequency-domain filters, the Wiener criterion excelled frequently in our comparisons of residual
error power (Figure 5).

1.18 Slice Timing Correction (STC)
The Resync algorithm was designed as an extension to and replacement of previous STC methods to
achieve increased accuracy by means of continuous rather than discrete-time time optimisation and
regularisation based on a global interpolation model i.e. the notion of the RTE. Although one can argue and
even demonstrate that a high interpolation makes traditional STC almost equivalent to Resync under ideal
conditions (i.e. little or no EEG signal to interfere with the MGA), this discussion would be largely academic.
Consistent with the literature we find that independently time shifting individual MGA epochs results in
residual MGA, which requires supplementary processing e.g. by PCA [1, 3, 4]. PCA on the other hand can
actually replace STC in our experience. And Resync in turn replaces both PCA and STC. Moreover, piecewise
signal processing that is not necessarily consistent between MGA epochs can even be expected to induce a
processing artefact at precisely 1/TR e.g. due to discontinuous transitions or systematic errors like the
residual bias in AAS e.g.

1.19 Moving Average Artefact Subtraction (mAAS)
AAS forms the basis of all post-processing algorithms considered here. The theory and experimental
practice presented focus on the most common variant, namely AAS with a symmetrical (weighted) moving
average [12]. Theoretical justification for this approach is found in Equation 2, where the RMGA is seen to
depend on the averaging length (m) and exclusively odd-order derivatives of the MGA. In the absence of
RMGA the SNR recovered after AAS increases with averaging length so that a global average becomes the
optimum in theory (Equation 1). In experimental practice the optimal suppression of the averaged EEG
signal must be traded off against and is quickly outweighed by the RMGA due to the RTE and experimental
instabilities. We have shown that the former is minimised by hardware or software (re-)synchronisation to
the point of becoming negligible in relation to other sources of RMGA. In the presence of RMGA the
optimal averaging length could in principle be sought experimentally using the quantification methods
presented here (Figure 2). Alternatively, one might determine a minimal (sufficient) averaging length by considering the available (initial) and required (final) SNR of the (artefact free) EEG signal (Equation 1). A short averaging length serves to limit RMGA irrespective of its source and will not necessarily sacrifice much SNR for lack of averaging, specifically when operating in a low-baseline-SNR regime, where the graph of Equation 1 is flat.

Moving AAS is mathematically equivalent to a *notching filter*. Longer filters achieve narrower stop-bands with stronger attenuation as seen in Figure 2A resulting in less spectral leakage to affect other frequencies. The trade-off between these factors can also be modified by a weighting scheme as suggested by Becker et al. [12], which amounts to *windowing* or *apodisation* of the filter function. However, filter theory asserts that only a filter length equal to the period of (RTE-induced) MGA modulation can actually match the artefact line shape. By the same token, it is clear that no uniform averaging scheme can cope with non-stationary sources of RMGA e.g. subject motion. To address this problem selective (non-uniform) averaging has recently been proposed, based on motion correction parameters extracted from the fMRI time series [15, 19]. This strategy seems most suitable for isolated motion events disrupting an otherwise stable recording of the MGA. Furthermore, weighting schemes based on the covariance of MGA epochs have been proposed [19, 20]. This sort of heuristic bears formal resemblance to PCA decomposition and fitting in a least-squares sense, thereby also inheriting the risk of removing physiological EEG signal. Ironically, the risk increases under stable recording conditions that enhance the relative influence of minor signal components. Freyer et al. [20] address this problem by constructing MGA templates only from epochs recorded in the absence of stimulation, presumably not containing any signal of interest. As expected the exponential weighting scheme employed still exhibits the aforementioned trade-off between MGA reduction and suppression of the averaged EEG acting as noise. In any case moving or selective AAS will entail temporal variations in SNR and artefact suppression.

Notwithstanding possible benefits to be gained by drawing on additional information, in our opinion there is not much incentive to further explore the (weighted) moving AAS: In practice the combination of (re-)synchronisation and global AAS seems to offer greater benefits (Figure 5) and the supplement of PCA is found to be rather effective in removing significant RMGA arising from subject motion or other non-stationary sources (Figure 8).

### 1.20 Regressive Filters

The same is true in our opinion for regressive filters, which have been included in the post-processing algorithms of previous studies [1, 4]. None of these studies actually explore filtering parameters nor do they provide quantitative evidence proving their effectiveness. Simulated data provide an opportunity to do so. However, we were unable to establish any unambiguous benefit even under ideal conditions. In particular regressive filters did not improve post-processing results obtained by fully exploiting AAS and PCA. On the contrary, they would effectively attenuate an artefact-reduced EEG signal, given the previously removed MGA as input, presumably because of residual correlations. We did not pursue the regressive filtering approach in any more detail, since it does not seem advantageous in our specific context. This is not to say that the method cannot serve a purpose for removing residual MGA or more likely other artefacts like the BCG given a different, more representative disturbance signal as input.

### 1.21 Digital Filters

The recovered SNR for any EEG signal ultimately depends on the overlap between the EEG and the MGA spectra as well as on the selective filtering properties of the post-processing algorithms. Most post-processing algorithms for EEG-MRI data rely heavily on digital low-pass filters limiting signal bandwidth to 40-80Hz. The reason is not only the concentration of EEG signal at frequencies below 40Hz in contrast to
the MGA, which has a bandwidth of many kHz, but also because post-processing techniques tend to be less effective at higher frequencies. By restricting signal bandwidth to the frequency range of interest SNR is inevitably increased. (Not surprisingly, the SNR of test signals below 40Hz was found to benefit more from low-pass filtering than from hardware synchronisation in a recent study by Gebhardt et al. (2008) [21].)

Conclusions: Good practices in EEG-MRI
In light of the preceding discussion an optimal strategy for EEG-fMRI experiments should focus primarily on **minimising the RTE by means of the synchronisation** and interpolation techniques discussed here. This effectively avoids a primary source of RMGA and facilitates the removal of other RMGA components by PCA. If available, **hardware synchronisation** remains the method of choice, not least because it is insensitive to (low) sampling rates and (associated) residual aliasing artefacts. In situations, where the required clock synchronisation through external hardware or precise control over the scanner software cannot be taken for granted, the **retrospective synchronisation method** presented here offers a practical substitution for hardware synchronisation. In our experiments prospective and retrospective synchronisation show equivalent results in simulations within reasonable limits depending on the sampling rate and signal bandwidth. In vivo the advantages of (retropective) synchronisation are mostly limited to lower frequencies (<~100Hz) depending, however, on the relative contributions of the RTE and other artefacts (motion, respiration, BCG) to the RMGA. Digital signal processing with high temporal resolution and good fixation of subject and EEG cables are recommended for the suppression of RMGA especially in the absence of hardware clock synchronisation.

The optimal post-processing strategy for EEG-MRI data depends on properties of the recording. Having estimated and if necessary corrected for any RTE by means of the Resync algorithm, AAS alone will usually yield results that require no further post-processing in simulations. In vivo the presence of other disturbances like motion artefacts may or may not justify the supplemental application of **moving AAS** and PCA to improve SNR, depending entirely, however, on the overlap of the MGA spectrum with the EEG bandwidth of interest. In the presence of temporal instabilities, **moving AAS** may improve SNR by limiting the affected signal albeit at the expense of manipulating the EEG spectrum with a broad notching filter. In any case a judicious choice of TR(slice) as a divider of TR(volume) effectively mitigates the problem of MGA removal by limiting its power to narrower and more widely spaced spectral lines.

PCA is well suited to assess and potentially remove RMGA from arbitrary sources. However, the inadvertent removal of (physiological) EEG signal must be kept in mind as a serious caveat, especially since PCA efficiently decomposes sinusoidal signals like brain waves. A judicious choice and critical review of PCA selection criteria is imperative. We have shown criteria proposed in the literature to be geared toward de-synchronised data and have suggested improvements that are found to be more robust under general conditions. A representative recording of the EEG baseline (without MGA, before/after MRI scanning) is an important prerequisite for assessing the performance of post-processing methods, even though it constitutes a potential source of bias at the same time. Until a gold standard for EEG-MRI experiments becomes available it may be most practical to optimise post-processing parameters depending on the individual recording, also taking into account the EEG spectrum of interest. The framework of simulation and quantification methods presented here is extensible to new techniques and designed to serve this purpose.
Acknowledgements

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**Figure Captions**

**Figure 9 MRI gradient artefact (MGA)**

Two (pseudo-)EEG signals recorded in a water phantom (A+C) and the corresponding power spectra (B+D) exemplify the MGA in a single EEG channel for two typical fMRI sequences. Both sequences acquire a volume of 30 slices in TR= 1800ms, but only one sequence (A) incorporates a time delay between subsequent volume acquisitions. This results in a line spectrum (B) that is more dispersed in comparison to the other sequence (C), which has only one fundamental period (D), namely TR(slice)= TR/30= 60ms.
Figure 10 Spectral analysis
For comparison, a number of different post-processing algorithms (see legend below) are applied to the same set of experimental EEG data (1 out of 65 EEG channels). A) Power spectra of the processed data juxtaposed to the unprocessed data (MGA) and the pre-scan baseline (Bas) evidence the prominent MGA line spectrum at harmonics of 1/TR as well as the largely uncontaminated spectrum in between. B) The corresponding normalised (by baseline) spectra show the full bandwidth of the EEG/MGA signal (2500Hz) and are split in an interleaved fashion into frequencies on and off spectral lines of the MGA (top/bottom). C) The cumulative normalised error spectra reveal a divergence in normalised error power between methods mostly at frequencies above 80Hz. For better comparison the total normalised error power for each method is finally integrated over 6 spectral bands (vertical lines) to be displayed side by side as a stacked bar graph in Figure 13.

Figure 11 (Re-)Synchronisation affects RMGA and ACS
The two graphs in each panel (top/bottom) represent the standard deviation (STD) of the RMGA over one TR (40ms) as well as the normalised auto-correlation sequence (ACS) of the MGA sampled at lag intervals of TR. Light and dark lines refer to the same data before and after re-synchronisation. Each of the six panels represents a different set of data – three sets recorded in vivo on the top row and three simulations with corresponding parameters on the bottom row. The relative timing error (RTE) increases from panel to panel left to right. The effects of re-synchronisation are most noticeable for de-synchronised data (panels C+F): As the ACS increases the STD decreases. Note that the xy-scales in C and F have been adjusted to visualise strong oscillations.

Figure 12 Simulated vs. in-vivo data.
PCA is used to characterise the MGA in six sets of EEG data (one channel of each). As before (Figure 11) the three top panels represent data recorded in vivo and the bottom panels three sets of simulated data with corresponding parameters, specifically the RTE is similar and increases left to right. Each panel shows the mean MGA and the strongest 10 PCs. (All curves are normalised to unit variance.) Note that the sinusoidal components at roughly 10Hz (green) will capture alpha waves in these EEG signals taken from occipital channels.
Figure 13 Normalised error power before and after re-synchronisation
Different variants of post-processing (see legend below) are compared in terms of their normalised error power (|signal/baseline - 1|) integrated over six spectral bands (colour-code). For a typical set of simulated data global AAS yields the largest error power before re-synchronisation (panel A) but the smallest thereafter (panel B, arrow). In simulations the discrepancy between the (theoretical) optimum (AAS0) and the result of AAS (panel B) is reduced to zero by increasing the EEG sampling rate, thus yielding a result equivalent to synchronised data (panel C). (NB: AAS0 is not zero, because of AAS filtering.) For data recorded in viva (panels D-F) the above results typically hold only for low frequencies (<~90Hz) depending very much on the relative proportions of RMGA due to the RTE and other sources. This typical example of a moderate RTE= 2e-6 in the presence of substantial motion artefacts shows modest but comparable effects of hard- and software synchronisation mostly at high frequencies. In this situation additional PCA is found to be advantageous, but none of the methods achieve the (estimated) theoretical optimum AAS0.

Legend: AAS0= AAS-filtered baseline; AAS= average artefact subtraction (global); mAAS(#)= moving AAS (# of epochs averaged); PcX(#) = PCA+cross-correlation criterion; PcW(#) = PCA+Wiener Filter criterion; PcN(#) = PCA+variance normalisation criterion; PcD(#) = PCA+Difference in variance criterion; (#)= Number of PCs modified; Mga = original MGA without correction.

Figure 14 Anti-aliasing filters
After re-synchronisation (A) there is no sign of the MGA-related PCs (B) previously dominant among the strongest 10 PCs in this typical set of simulated data. However, weak anti-aliasing filters impair re-synchronisation resulting in a larger number of MGA-related PCs thereafter (C) as well as before (D).

Figure 15 PCA criteria
PCA of a typical EEG channel recorded in vivo and without synchronisation illustrating the differences between PC selection criteria: A) Leading component(s) eliminated by the variance-difference (VD) criterion (red). Components identified additionally by the cross-correlation (XC) criterion (green). The mean MGA before AAS (black) and other components (blue) are also considered for the variance normalisation (VN) and Wiener filter (WF) criteria. B) Part of corresponding PC signals (TR=40ms) before/after (dark/light) rescaling according the variance-normalisation criterion (VN), which considers the baseline signal before the scan onset at t=30sec. Note the piecewise linear, quadratic and cubic wave forms in PCs 1, 2 and 5 (quasi derivatives of the MGA). C) MGA variance before (black – left scale) and after application of the above criteria (right scale: red=VD, green=XC, cyan=VN, pink=WF). D) Variance fraction (VF, black), cross-correlation (XC, green, right scale) and F-statistic (FS, blue) for each of the leading 10 PCs. Dashed lines mark a threshold of 0.25 for the XC criterion (green) and 2.0 for the F-criterion (blue). E) Smoothed power spectra of PC signals: Blue = baseline, green = scan time, and pink = peaks eliminated according to the Wiener Filter criterion (WF).

1.22

Figure 16 PCA + Motion Artefact
A) An abrupt change in MGA waveform half way through the simulated experiment is reflected in merely two PCs (1+9, cyan). B) The number of affected components multiplies in de-synchronised conditions (compare Figure 12F without motion). C) Re-synchronisation recovers the “synchronised” components, but PCA is still required to remove the motion artefact.
Equations
Equation 5 SNR (synchronised)
The SNR of the EEG following subtraction of a moving average artefact depends on the averaging length n (in epochs of TR) as well as the SNR of the original EEG signal: \( \text{SNR}_0 = \sqrt{V/v} \) ratio of EEG signal variance and EEG noise variance (both assumed to be independent between epochs). The original EEG signal in each epoch gets scaled by \((n-1)/n\), but the final SNR is largely determined by adding EEG signal from \(2m\) adjacent epochs, which amounts to a noise variance of \((V+v)/2m\). Note that \( \text{SNR}_0 \) is reached asymptotically, but as little as 10 epochs are enough to reach 90\% of an \( \text{SNR}_0 < 1 \).

\[
\begin{align*}
\text{SNR}^2(n) &= \frac{\left(\frac{n-1}{n}\right)^2 V}{\left(\frac{n-1}{n}\right)^2 v + \frac{1}{n-1} (V + v)} \\
\iff \text{SNR}^2(n) &= \frac{\left(\frac{n-1}{n}\right)^3 \text{SNR}_0^2}{\left(\frac{n-1}{n}\right)^3 + 1 + \text{SNR}_0^2} \\
\iff \text{SNR}^2(n) &= \frac{\text{SNR}_0^2}{1 + \left(\frac{n-1}{n}\right)^3 (1 + \text{SNR}_0^2)}
\end{align*}
\]

Equation 6 SNR (de-synchronised)
Using the Taylor expansion: \( \ldots \) and the following identity:

\[
\text{SNR}^2(m) \approx \frac{\text{SNR}_0^2}{1 + \left(\frac{2m+1}{2m}\right)^3 (1 + \text{SNR}_0^2) + \frac{1}{V} \left[O\left(\frac{\text{m}^2}{d^3}\right)\right]^2}
\]

The clean EEG signal \( S_m \) after subtracting a moving average of \((2m+1)\) epochs can be expressed in terms of \( E_k \) and \( G_k \) the EEG and the MGA signal \( k = m \ldots 0 \) epochs before and after the centre epoch \((k=0)\). \( G_k \) is expressed in terms of a Taylor expansion of the MGA around \( G_0 \). In contrast to Equation 1 the expression for \( \text{SNR}(m) \) depends not only on the EEG signal and noise variance \((V & v)\) but also on the temporal mismatch \( dt \) representative of the RTE. The strong dependence on \( m^3 \) will drive the optimum towards smaller \( m \), depending on the size of \( (G''dt)^3 \).
Equation 7 The Resync algorithm

\[
X_{m,k} = \sum_{t=0}^{T-1} x_{mT+t} \exp(-i \frac{2\pi}{N} \Omega t)
\]

\[
w_m = \arg \max_{-\frac{N}{2} \leq n < \frac{N}{2}} \Re \left( \sum_{k=0}^{T-1} X_{m,k} \exp(i \frac{2\pi}{N} n k) \right)
\]

\[
D = 1 + \frac{1}{2\pi} \{w_{m+1} - w_m\}
\]

Interpolation by inverse DFT for \( t = 0..\text{Round}(ND)-1 \):

\[
y_t = \frac{2}{M} \Re \sum_{0 \leq n \leq \frac{M}{2} + 1} Y_n \exp \left( i \frac{2\pi}{M} n t \right)
\]

where \( M = \min(N, ND) \), \( X[n] = \text{DFT}(x[t]) \) and

\[
Y_n = \begin{cases} 
\frac{1}{2} X_0 & n = 0 \\
\frac{2}{M+1} X_n & 0 < n < \frac{M}{2} + 1 \\
\frac{1}{2} X_{M+1} & n = \frac{M}{2} + 1 \left( \text{if } \left\lfloor \frac{M}{2} \right\rfloor \text{ integer} \right)
\end{cases}
\]

The discrete EEG signal \( x[t] \) of length \( N \) is split into epochs \( x[m,T] = x[mT+t], t=0..T-1 \), each comprising one MGA of \( T \) samples length (= TR(slice)). Each epoch undergoes DFT \( X[m,k] \) and the linear phase offset \( w[m] \) between the first and each consecutive epoch \( m \) is estimated by maximisation of the cross-correlation at lag zero. The mean phase difference divided by \( 2\pi \) plus one yields the interpolation factor \( D \), and the desired re-synchronised signal \( y[t] \) of length \( \text{Round}(ND) \) is finally obtained by Fourier interpolation of the original EEG signal as a whole. (The formula given is complicated by the fact that \( N \) may be odd and \( ND \) a real number larger or smaller than \( N \).)
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Figure 1 MRI gradient artefact (MGA)
Two (pseudo-)EEG signals recorded in a water phantom (A+C) and the corresponding power spectra (B+D) exemplify the MGA in a single EEG channel for two typical fMRI sequences. Both sequences acquire a volume of 30 slices in TR= 1800ms, but only one sequence (A) incorporates a time delay between subsequent volume acquisitions. This results in a line spectrum (B) that is more dispersed in comparison to the other sequence (C), which has only one fundamental period (D), namely TR(slice)= TR/30= 60ms.
Figure 2: Spectral analysis
For comparison, a number of different post-processing algorithms (see legend below) are applied to the same set of experimental EEG data (1 out of 65 EEG channels). A) Power spectra of the processed data juxtaposed to the unprocessed data (MGA) and the pre-scan baseline (Bas) evidence the prominent MGA line spectrum at harmonics of 1/IR as well as the largely uncontaminated spectrum in between. B) The corresponding normalised (by baseline) spectra show the full bandwidth of the EEG/MGA signal (2500Hz) and are split in an interleaved fashion into frequencies on and off spectral lines of the MGA (top/bottom). C) The cumulative normalised error spectra reveal a divergence in normalised error power between methods mostly at frequencies above 80Hz. For better comparison the total normalised error power for each method is finally integrated over 6 spectral bands (vertical lines) to be displayed side by side as a stacked bar graph in Figure 5.

A) Power spectra

B) Power spectra normalised by baseline

Legend:
Bas = pre-scan baseline
Mga = original MGA without correction
AAS = global AAS
mAAS(#) = moving AAS (over # epochs)
PcX(#) = PCA+cross-correlation criterion
PcN(#) = PCA+variance normalisation criterion
PcD(#) = PCA-Difference in variance criterion
PcW(#) = PCA+Wiener Filter criterion
(##) = Number of PCs modified

C) Cumulative normalised error power
Figure 3 [(Re-)Synchronisation affects RMGA and ACS]
The two graphs in each panel (top/bottom) represent the standard deviation (STD) of the RMGA over one TR (40ms) as well as the normalised auto-correlation sequence (ACS) of the MGA sampled at lag intervals of TR. Light and dark lines refer to the same data before and after re-synchronisation. Each of the six panels represents a different set of data – three sets recorded in vivo on the top row and three simulations with corresponding parameters on the bottom row. The relative timing error (RTE) increases from panel to panel left to right. The effects of re-synchronisation are most noticeable for de-synchronised data (panels C+F): As the ACS increases the STD decreases. Note that the y-scale in C and F have been adjusted to visualise strong oscillations.

<table>
<thead>
<tr>
<th>RTE &lt; 1e-8</th>
<th>RTE &lt; 1e-6</th>
<th>RTE &gt; 1e-4</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Graph A" /></td>
<td><img src="image2" alt="Graph B" /></td>
<td><img src="image3" alt="Graph C" /></td>
</tr>
<tr>
<td><img src="image4" alt="Graph D" /></td>
<td><img src="image5" alt="Graph E" /></td>
<td><img src="image6" alt="Graph F" /></td>
</tr>
</tbody>
</table>

- **A)**: RTE(deltat) = 3.74e-09
- **B)**: RTE(deltat) = 2.26e-07
- **C)**: RTE(deltat) = 2.03e-4
- **D)**: RTB(deltat) = 3.81e-11
- **E)**: RTB(deltat) = 2e-07
- **F)**: RTB(deltat) = 2e-4

**Notes:**
- STD / a.u.
- ms
- sec
Figure 4 Simulated vs. in-vivo data.
PCA is used to characterise the MGA in six sets of EEG data (one channel of each). As before (Figure 3) the three top panels represent data recorded in vivo and the bottom panels three sets of simulated data with corresponding parameters, specifically the RTE is similar and increases left to right. Each panel shows the mean MGA and the strongest 10 PCs. (All curves are normalised to unit variance.) Note that the sinusoidal components at roughly 10Hz (green) will capture alpha waves in these EEG signals taken from occipital channels.
Figure 5 Normalised error power before and after re-synchronisation

Different variants of post-processing (see legend below) are compared in terms of their normalised error power \( \left( \frac{signal - baseline}{baseline} \right) \) integrated over six spectral bands (colour-code). For a typical set of simulated data global AAS yields the largest error power before re-synchronisation (panel A) but the smallest thereafter (panel B, arrow). In simulations the discrepancy between the (theoretical) optimum (AASO) and the result of AAS (panel B) is reduced to zero by increasing the EEG sampling rate, thus yielding a result equivalent to synchronised data (panel C). (NB: AASO is not zero, because of AAS filtering.) For data recorded in vivo (panels D-F) the above results typically hold only for low frequencies (<50Hz) depending very much on the relative proportions of RMGA due to the RTE and other sources. This typical example of a moderate RTE=2e-4 in the presence of substantial motion artefacts shows modest but comparable effects of hard- and software synchronisation mostly at high frequencies. In this situation additional PCA is found to be advantageous, but none of the methods achieve the (estimated) theoretical optimum AASO.

Legend: AASO = AAS-filtered baseline; AAS = average artefact subtraction (global); mAAS(#) = moving AAS (# of epochs averaged); Pcx(#) = PCA+cross-correlation criterion; PcW(#) = PCA+Wiener filter criterion; PcN(#) = PCA+variance normalisation criterion; Pcd(#) = PCA+Difference in variance criterion; (#) = Number of PCs modified; Mga = original MGA without correction.
Figure 6 Anti-aliasing filters
After re-synchronisation (A) there is no sign of the MGA-related PCs (B) previously dominant among the strongest 10 PCs in this typical set of simulated data. However, weak anti-aliasing filters impair re-synchronisation resulting in a larger number of MGA-related PCs thereafter (C) as well as before (D).

Figure 7 PCA criteria
PCA of a typical EEG channel recorded in vivo and without synchronisation illustrating the differences between PC selection criteria: A) Leading component(s) eliminated by the variance-difference (VD) criterion (red). Components identified additionally by the cross-correlation (XC) criterion (green). The mean MGA before AAS (black) and other components (blue) are also considered for the variance normalisation (VN) and Wiener filter (WF) criteria. B) Part of corresponding PC signals (TR=40ms) before/after (dark/light) rescaling according the variance-normalisation criterion (VN), which considers the baseline signal before the scan onset at t=30sec. Note the piecewise linear, quadratic and cubic wave forms in PCs 1, 2 and 5 (quasi derivatives of the MGA). C) MGA variance before (black – left scale) and after application of the above criteria (right scale: red=VD, green=XC, cyan=VN, pink=WF). D) Variance fraction (VF, black), cross-correlation (XC, green, right scale) and F-statistic (FS, blue) for each of the leading 10 PCs. Dashed lines mark a threshold of 0.25 for the XC criterion (green) and 2.0 for the F-criterion (blue). E) Smoothed power spectra of PC signals: Blue = baseline, green = scan time, and pink = peaks eliminated according to the Wiener Filter criterion (WF).
Figure 8 PCA + Motion Artefact

A) An abrupt change in MGA waveform half way through the simulated experiment is reflected in merely two PCs (1+9, cyan). B) The number of affected components multiplies in de-synchronised conditions (compare Figure 4F without motion). C) Re-synchronisation recovers the “synchronised” components, but PCA is still required to remove the motion artefact.
Equations

**Equation 1 SNR (synchronised)**

The SNR of the EEG following subtraction of a moving average artefact depends on the averaging length \( n \) (in epochs of TR) as well as the SNR of the original EEG signal: \( \text{SNR}_0 = \frac{\sqrt{V}}{\nu} \) ratio of EEG signal variance and EEG noise variance (both assumed to be independent between epochs). The original EEG signal in each epoch gets scaled by \((n-1)/n\), but the final SNR is largely determined by adding EEG signal from \( 2m \) adjacent epochs, which amounts to a noise variance of \((\nu + \nu)/2m\). Note that \( \text{SNR}_0 \) is reached asymptotically, but as litte as 10 epochs are enough to reach 90% of an \( \text{SNR}_0 < 1 \).

\[
\text{SNR}^2(n) = \frac{(\frac{n-1}{n})^2 V}{(\frac{n-1}{n})^2 v + \frac{1}{n-1} (V + v)}
\]

\[
\iffalse \text{SNR}^2(n) = \frac{(n-1)^2 \text{SNR}_0^2}{n^2} + 1 + \text{SNR}_0^2
\fi

\[
\iffalse \text{SNR}^2(n) = \frac{\text{SNR}_0^2}{1 + \frac{n^2}{(n-1)^2} (1 + \text{SNR}_0^2)}
\fi

\]

**Equation 2 SNR (de-synchronised)**

\[
S_m = E_0 + G_0 - \frac{1}{2m+1} \sum_{k=-m}^{m} (E_k + G_k) = E_0 - \frac{1}{2m+1} \sum_{k=-m}^{m} E_k - \frac{G_0}{2m+1} (2m+1) (m+1) (m+2) + O(\delta t^4)
\]

Using the Taylor expansion: \( G_k = G_0 + \frac{G_0}{2m+1} (k \delta t) + \frac{1}{2} \frac{G_0}{2m+1} (k \delta t)^2 + O(\delta t^3) \)

...and the following identity: \( \sum_{k=1}^{m} k^2 = \frac{m^3}{3} + m (m+1)(2m+1) \)

\[
\iffalse S_m = \frac{2m}{2m+1} E_0 + \sum_{k=1}^{m} (\frac{2m}{2m+1})^2 v + \frac{1}{2m} (V + v) + O(\delta t^2 m^3)
\fi

\[
\iffalse \text{SNR}^2(m) \approx \frac{\text{SNR}_0^2}{1 + \frac{(2m+1)^2}{(2m)^3} (1 + \text{SNR}_0^2)} + \frac{1}{8} \left[ O(\delta t^2 m^3) \right]^2
\fi

\]

The clean EEG signal \( S_m \) after subtracting a moving average of \( 2m+1 \) epochs can be expressed in terms of \( E_k \) and \( G_k \) the EEG and the MGA signal \( k = -m \ldots m \) epochs before and after the centre epoch \( k = 0 \). \( G_k \) is expressed in terms of a Taylor expansion of the MGA around \( G_0 \). In contrast to Equation 1 the expression for \( \text{SNR}(m) \) depends not only on the EEG signal and noise variance \((V \& \nu)\) but also on the temporal mismatch \( \delta t \) representative of the RTE. The strong dependence on \( m^3 \) will drive the optimum towards smaller \( m \), depending on the size of \( (G^2 \delta t^2) \).
Equation 3 The Resync algorithm

\[ X_{m,k} = \sum_{t=0}^{T-1} x_{m}^{T+t} \exp(-i \frac{2\pi}{T} kt) \]

\[ w_m = \arg\max_{-\pi < \omega < \pi} \Re \left( \sum_{k=0}^{T-1} X_{m,k}^{*} e^{i\omega X_{0,k}} \right) \]

\[ D = 1 + \frac{1}{2\pi} (w_{m+1} - w_m)_m \]

\[ y^* = \frac{1}{ND} \sum_{n=0}^{N-1} X_{m,n}^{*} \exp(i \frac{2\pi}{ND} nt) \]

The discrete EEG signal \( x[n] \) of length \( N \) is split into \( M \) epochs \( x[m,n] = x[n]_{T+1}, m=0, T-1 \), each comprising one MGA of \( T \) samples length (= TR(slice)). Each epoch undergoes DFT \( \{X[m,k]\} \) and the linear phase offset \( w[m] \) between the first and each consecutive epoch is estimated by maximisation of the cross-correlation at lag zero. The mean phase difference divided by \( 2\pi \) plus one yields the interpolation factor \( D \), and the desired re-synchronised signal \( y[n] \) of length \( T = 0 \ldots \text{Round}(ND) - 1 \) is finally obtained by Fourier interpolation of the original EEG signal as a whole \( \{X[n] = \text{DFT}(x[n])\} \).