An efficient stimulus design for detecting neuronal non-linarities with BOLD fMRI.

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Introduction

The m-sequence probe method (1-4) allows for efficient estimation of non-linear effects in fMRI (4). A binary m-sequence is a pseudo random sequence, whose bit values represent two stimulus conditions, one active and one rest state. Some properties of these sequences are: a) they can be easily generated with a shift register with appropriate feedback taps; b) their auto correlation is a delta function; c) the product of a sequence with a shifted version of itself results in the same sequence with a different shift. The second property makes m-sequences very useful for estimating the BOLD response curve, while the third property allows for determination of nonlinear characteristics of the response (1). Because the BOLD is slow, acts as a low-pass filter and is to a large extent linear (4), while the (mostly neuronal) nonlinear processes are fast, the standard m-sequence design does not have optimal sensitivity. This study presents a stimulus paradigm that has improved sensitivity compared to the standard m-sequence, while retaining other favorable m-sequence properties.

Theory

An m-sequence consists of 2^n sequential bins (Fig. 1a), each controlling the stimulus condition. The power spectrum is shown in Fig. 2 for a base period (bin size) of 1s. For stimulation of the fast nonlinear elements, the spectrum needs to have energy in the higher frequencies, i.e. for a large nonlinear neuronal response the binsize needs to be short, creating a high density of transitions in the stimulus. However, this would spread the power over a larger portion of the spectrum, leading to a low output of the BOLD signal because of its low-pass characteristics, suppressing rapidly changing signals. A possible solution is to reduce the bin size, but at the same time repeat every bit of the sequence a couple of times, as shown in Fig. 1b. This leads to the desired high number of transitions, while the averaging effect of the repeated bits concentrates the power in the frequency band of the BOLD. This can be seen in the power spectrum of the modified m-sequence, Fig 2. Every second, a gap is inserted to prevent retrograde interactions (from a_2 to a_1 etc.).

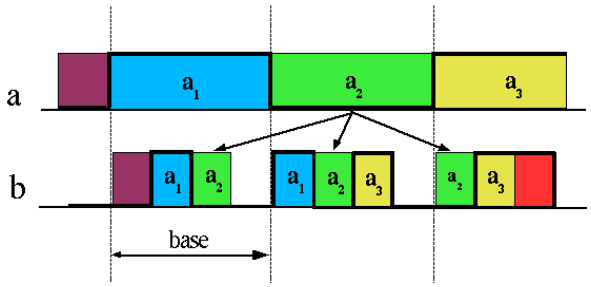

Figure 1. Part of a standard m-sequence design (a) and the modified sequence derived from it (b).

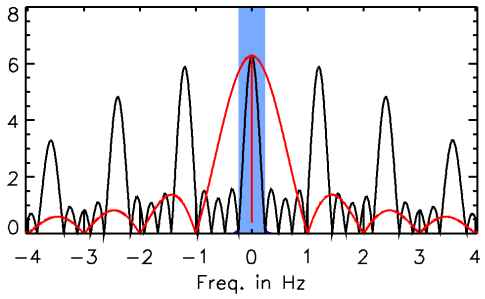

Figure 2. Power spectrum of standard (in red) and modified m-sequence (black). The blue band is approximately the BOLD sensitivity band.

Methods

The design was tested on six volunteers, scanned after giving informed consent under IRB approved protocol on a GE 3T scanner with a 16 channel Nova head coil and home build digitizer. Scan parameters: rate 2 SENSE-EPI, TR 1s, TE 40ms, 192x144 pixels over 220x165mm fov, 8 slices, thickness/gap= 1.5/0.5mm, 600 repetitions. A 255 bin m-sequence was used, extended to 300 bins and followed by it inverse. Each second contained 5 bits of 130ms, plus 350ms gap. The stimulus was circular checkerboard projected on a screen in the bore, with condition 1 being a single contrast reversal and condition 0 and the gaps a uniform grey field. The data was analyzed by correlating each pixel time course with the m-sequence in two sections of 255, from the first and second half of the scan.

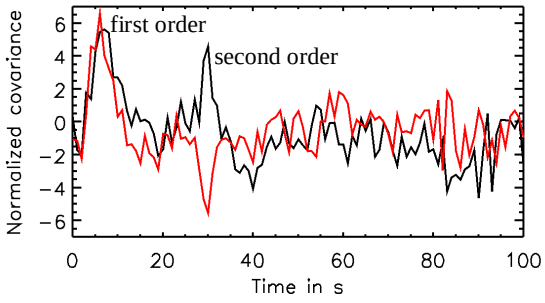

Figure 3. Example of correlation of single voxel data with the m-sequence .

Results & Discussion

All volunteers showed robust first order activation. The second order averaged 18% (range 0-45%) of the first order as measured in the active pixels in early visual areas. An example of the resulting correlation in a single pixel is plotted in Fig. 3, showing the first sequence (black) and the inverse repeat (red). The curves are normalized to the temporal SD in the correlogram. The main applications of this method are expected to be in the study of sensory systems.

References

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