### Temporal correlation in fMRI examined by the scaled windowed variance

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## INTRODUCTION

The raw fMRI signal needs to be statistically analyzed by methods such as the parametric Student's t-test or the non-parametric Kolmogorov-Smirnov (KS) test to yield measures of various modalities such as blood flow, volume, oxygenation, etc. The fundamental assumption underlying this analysis is that successive events in the raw signal are independent (white noise) [1] hence of a Gaussian distribution. However colored noise if present in the dynamic fMRI data can cause high false positive rate, e.g., in KS-test [2]. Such positive correlations have been reported in human fMRI data [1, 2] which are characterized by a spectrum with increasing power toward the low frequencies referred to as the I/f pattern. This pattern can be numerically characterized by a fractal parameter, the Hurst exponent, H. Fractal fluctuations of blood cell flux in the brain cortex have been reported in animal models [3, 4], which further substantiate the need for determining if fMRI signals are of white or colored noise patterns.

#### **METHODS**

Animal preparation: Twelve artificially ventilated Sprague-Dawley rats were anesthetized by  $\alpha$ -chloralose (40 mg/kg/hr) and *D*-tubocurarine chloride (0.5 mg/kg/hr), i.p. An arterial line was used for monitoring blood pressure and taking samples for blood pH, pO<sub>2</sub>, pCO<sub>2</sub> throughout the experiment. <u>MRI measurements</u>: All fMRI experiments were conducted on a 4.0T or 9.4T spectrometer (Bruker, Billerica, MA) using a <sup>1</sup>H resonator/surface-coil radio-frequency probe [5]. Gradient-echo EPI data were acquired with T<sub>R</sub>=0.2s. The images were collected in matrix 32x32 (4.0T) and 64x64 (9.4T) spatial resolutions; the slice thickness was 2 mm, the volume of one voxel is ~0.6 µL (4.0T) and ~0.15 µL (9.4T). The slice position was selected at the level of bregma. Data were collected *in vivo* and *post mortem*. <u>Fractal analysis</u>: Scaled windowed variance (SWV) method [6] was applied to every voxel-based time series to calculate the fractal parameter, *H* and the nearest neighbor correlation coefficient, r<sub>1</sub> [7]. The length of the time series, 4096 scans (4.0T) and 8192 scans (9.4T), was adequate for a reliable estimation of the Hurst exponent [8]. Our analysis was based on the stationary/nonstationary noise/motion model of the 1/f signal pattern [4], because SWV method is applicable only to motion type signal [6]. Hence, prior fractal analysis the motion/noise feature of the signals was determined by the Signal Summation Conversion method (SSC) [4, 8]. When the signal was found noise type signal by SSC, it was cumulatively summed to obtain a motion type signal suitable for the SWV analysis [4].

## **RESULTS and DISCUSSION**

Noise in fMRI data is composite with a measurement component (white noise) and a component attributed to some fluctuations in a physiological parameter (can be white or colored noise). Only the 9.4T magnetic field produced an acceptable signal to noise ratio, in other words fMRI data from the 4.0T magnet was dominated by white noise of  $H=0.53\pm0.014$ . All 9.4T fMRI time series showed fractional Gaussian noise with H>0.5, different from white noise. The Hurst exponent of fractional Gaussian noise within its lower and upper bounds of 0 and 1 characterizes the correlation structure itself: with H=0.5 the signal is white noise (i.e., random events with no temporal correlation), H<0.5 indicates anticorrelation with a negative nearest neighbor correlation coefficient (r<sub>1</sub>), H>0.5 correlation with positive r<sub>1</sub> (or memory in the signal) [8]. Representative Hurst



exponent maps obtained *in vivo* and *post mortem* at 9.4T are shown in Fig. 1. Cortical and subcortical gray matter regions exhibit much higher  $H(0.73\pm0.05)$  that white matter regions  $(0.57\pm0.01)$  (Fig. 2, black and white bars). The former corresponds to strong, the latter to a weak nearest neighbor correlation,  $r_1$ =0.38 and  $r_1$ =0.10, respectively [7]. Death results in significant (p<0.05) decrease in fractal structure obtained in the gray and white regions of the brain (H=0.61±0.03 and H=0.56±0.03, respectively) and in a breakdown of the fractal or colored noise correlation structures in the gray matters ( $r_1$ =0.17) only.

# CONCLUSION

High magnetic field fMRI mapping is suitable to reveal fractal patterns in spontaneous fluctuations across the brain. The fact that these fluctuations in gray and white matter alike are of higher values of H in vivo than post mortem suggests that they attribute to normal behavior of the vasculature. These findings should have implications in fMRI data processing; in that successive events of the fMRI signal are correlated hence statistical mapping should be used with prior treatment of data, such as creating surrogate time series, which destroys the correlation structure in a signal without the modification of the values [9].

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Fig. 2. Average Hurst exponents calculated on 4.0T fMRI signals (gray bar), on 9.4T fMRI signals in gray (black bar) and in white matter (white bar)