Poisson-like property of spontaneous event trains and its relationship to scale-free dynamics

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Target Audience: Neuroscientists interested in spontaneous brain activity, scale-free dynamics.

Introduction: Scale-free brain dynamics, characterized by a linear relationship between *log power spectrum log(P(f))* and *log frequency log(f)*, has been widely observed in neurophysiological imaging/recordings, e.g. ECoG[1-3], EEG[4], MEG[4], fMRI[5-6], etc.; nevertheless, understanding of these arrhythmic brain activities is quite limited. Very recently, a preliminary study successfully simulated time series with a scale-free property by convolving Poisson-like spike trains with an impulse function representing dendritic response (two exponential functions)[3], suggesting that scale-free dynamics of ECoG signals may result from Poisson-like neuronal spike trains propagating through scale-free brain networks. It may thus be interesting to query whether a similar mechanism exists in other imaging modalities, say fMRI. Motivated by recent advances in point process analysis of fMRI time series[7-8], we suspect that *spontaneous event trains* (SETs, which refers to time points when the BOLD signal exhibits relatively large contrasts, and have been demonstrated to drive the overall network patterns at rest) and *event response functions* (ERFs, which have been shown to resemble canonical hemodynamic response functions (HRFs), of the form of exponential/gamma functions[8]) may serve as BOLD equivalents for neuronal spike trains and dendritic response functions. Here we examine whether time series generated in line with previous ECoG study[3] can account for the scale-free dynamics of BOLD signals.

Fig. 1

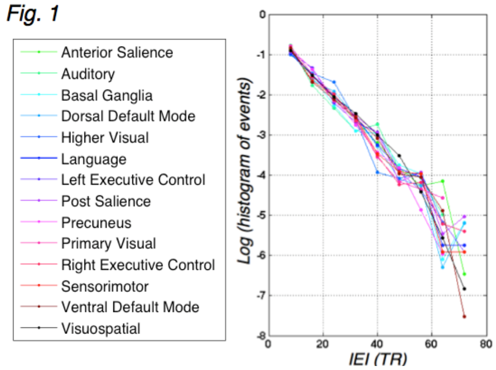
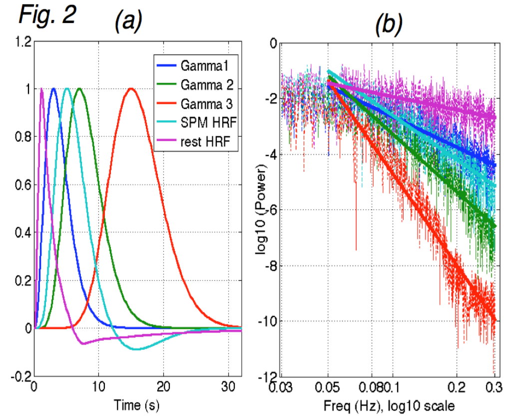


Fig. 2 (a) (b)



Analysis & Results: Two datasets: (1) Propofol-induced levels of consciousness: 17 subjects, each underwent four separate conscious state scans ('normal wakefulness*(NW)*', 'sedation*(SD)*', 'unconsciousness*(UC)*', 'recovery of consciousness*(RC)*', 197 fMRI volumes per state, TR = 2.46s)[9]; (2) rest vs. cognitive load: 17 subjects, each underwent a rest and a continuous 2 back working memory*(WM)* scan (both with 240 fMRI volumes, TR = 2s).

Preprocessing: included slice time correction, detrending, spatial smoothing (Gaussian FWHM = 4mm), nuisance regression (six head motion parameters, signals from the white matter and the CSF, subjects' behavioral data for the WM datasets[10]). Physiological noise was corrected using 'compcorr'[11] for datasets (1); 'retroicor'[12] and 'rvhrcor'[13] for datasets (2). Time series were low-pass filtered (<0.1 Hz) and normalized to the MNI template. Averaged signals within 90 rest ROIs (http://findlab.stanford.edu/functional_ROIs.html, encompassing 14 resting state networks) were extracted for each subject.

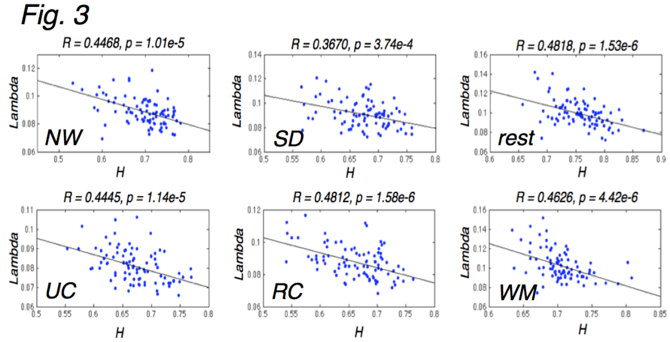
Poisson-like property of the SETs: Spontaneous events were defined as those time points with signal intensities > 1 s.d.. To examine whether the timing of SET resembles a Poisson process, i.e. random process, histograms of inter-spontaneous-event intervals (ISEI, compatible with scan duration) were plotted. The distribution of ISEIs associated with all the 14 networks and 6 mental states could be perfectly fitted by an exponential function: $log(P(ISEI)) \propto -\lambda\ ISEI$ (Fig. 1, results across all the subjects and all the ROIs within each resting state network were combined to provide adequate samples for estimation; only the result of 'rest' is shown, maximum $p < 4.2e\text{-}4$), suggesting Poisson-process-like properties in the SETs (the trend persisted when the threshold for spontaneous events varied from 0.8 to 1.5).

Scale-free time series generated by the convolution of SETs and ERFs (Scale-free Signal $_{\text{SET-ERF}}$): A Poisson-like property (random process) suggests a flat power spectrum of the SET, and therefore the spectrum of the output is completely determined by that of the ERF. In general cases where ERFs could be well fitted by exponential/gamma functions, the power spectrum of the ERF will by nature exhibit *scale-free-like* characteristics when the frequency *f* exceeds a certain threshold: (1) as shown in Eqn.1, combinations of exponential functions always lead to scale-free time series with power exponent $\beta = 2$ (the ubiquitous exponent in nature); (2) the proof of gamma functions is essentially similar, but with t^n (the item multiplied with e^{-at}) permitting more versatile β values. Fig. 2 intuitively demonstrates how the spectrum of ERFs (Fig2(a) three gamma functions and two HRFs[14]) can affect the power law parameters (Fig2(b), ERFs convolved with a homogeneous Poisson-process with $\lambda = 0.15/s$).

$$\log(P(f)) = \log(|F(e^{-at})|^2) = \log\left(\frac{1}{|a^2+4\pi^2 f^2|}\right) \propto -\log\left(\left|1+\frac{4\pi^2}{a^2}f^2\right|\right) \propto -2\log(f) \quad \text{when} \quad \left(\frac{2\pi}{a}f \gg 1\right) \quad \text{Eqn. 1}$$

Contribution from {Scale-free Signal $_{\text{SET-ERF}}$} to the overall scale-free dynamics of BOLD signals: Further analysis reveals significant negative correlation between the rate parameter λ of the Poisson-like SET (the fitted parameter in Fig. 1 that scales linearly with the power of {Scale-free Signal $_{\text{SET-ERF}}$}) and Hurst exponent of the raw BOLD time series (which is a linear function of the power law exponent β) (Fig. 3, see description of the datasets above). Here, each dot represents one ROI of 90 ROIs in total, and results across all the subjects were combined for the estimation of λ in each ROI. These results suggest that (1) the overall scale-free dynamics of BOLD time series is partly driven by {Scale-free Signal $_{\text{SET-ERF}}$}, and more fundamentally the local hemodynamic process; (2) {Scale-free Signal $_{\text{SET-ERF}}$} may possess a flatter power spectrum across frequencies compared to the unexplained residuals (which explains the negative correlation).

Fig. 3



Conclusion: Here, we have demonstrated that (1) BOLD activities driven by the SETs may explain (at least partially) the scale-free property reported by previous fMRI literature; (2) Scale-free dynamics of fMRI time series may carry non-neural information, e.g. local hemodynamic fluctuations, suggesting caution in studies attempting to employ metrics such as Hurst exponent as biomarkers for neuroimaging investigations, e.g. in cases such as when a caffeine stimulus or sedation alters baseline hemodynamics.

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References: [1] He et al., Neuron, 2010; [2] Miller et al., PLoS, 2009; [3] Freeman et al., Cogn. Neurodyn. 2009; [4] Dehghani et al., J. Comput. Neurosci.2010; [5] He et al., J. Neurosci. 2011; [6] Bullmore et al., HBM, 2001; [7] Liu et al., PNAS. 2013; [8] Tagliazucchi et al., Front Physiol 2012; [9] Boveroux et al., Anesthesiology 2010; [10] Chen et al., ISMRM 2013; [11] Behzadi et al., NeuroImage 2007; [12] Glover et al., MRM 2000; [13] Chang et al., NeuroImage 2009; [14] Chen et al., OHBM 2014.