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# EEG microstates relate to fMRI resting-state networks through scale-free dynamics

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Over the past decade, researchers using human functional magnetic resonance imaging (fMRI) have started to investigate spontaneous brain activity during "resting state", leading to an intriguing research topic. Such studies allow probing into the intrinsic organization of the brain in large-scale functional networks [Mesulam1998, Bullmore2009], which are remarkably similar to those revealed by tasks probing their function and which show a close link with underlying anatomical connections [Vincent2007]. In the fMRI literature, resting-state fluctuations of the BOLD signal were first revealed by looking into functional connectivity (i.e., temporal correlation of timecourses) between a chosen seed region and every other voxel in the brain. In particular, Biswal et al. observed early on connectivity within the functional motor network during rest [Biswal1995]. Since then, exploratory methods such as independent component analysis (ICA) have contributed to establishing a large number of reproducible large-scale functional networks in resting-state fMRI [Damoiseaux2006]. Their slow temporal dynamics are very striking; i.e., coherent BOLD fluctuations are generally found in the very slow frequencies (<0.1 Hz), which is hardly compatible with the rapid dynamics necessary for normal brain function [Bressler1995, Bressler2006].

The resting-state networks as measured by fMRI are relying on the hemodynamic response as a proxy for neuronal activation; however, their electrophysiological counterpart remains a matter of debate. Using EEG, one can follow the temporal evolution of the scalp electrical potential, where the EEG measurements can be represented as a matrix with time in one dimension and space in the other one, the former being a local and the latter a global measure of momentary brain activity. Conventional analyses of resting EEG consider the presence of spontaneous EEG rhythms at selected electrodes, which has been acknowledged literally since the very beginning [Berger1929]. Several attempts have tried to show a direct link between EEG frequency bands and fMRI resting state networks, albeit with mixed results [Laufs2003, Tyvaert2008]. A complete correlation signature of different EEG bands with ICA-defined fMRI resting-state network has been established, which revealed no clear direct link between different EEG frequency bands and fMRI-resting state networks [Mantini2007].

Topographic EEG analyses consider the temporal evolution of the topography of the scalp electric field, which is a global spatial measure of momentary brain activity with high temporal resolution. These topographies remain quasi-stable during ~80-120ms and are termed “EEG microstates” [Lehmann1987]; surprisingly, only four predominant topographies occur during resting state and all of them can be reliably identified in healthy individuals across the entire life span [Koenig2002].

Recently, we recorded EEG in the MR scanner and convolved the rapid occurrence signals of each of the predominant microstates during spontaneous EEG with the canonical hemodynamic response function; this step basically reduces the dynamics to the 10s timescale. We then fed the convolved and demeaned timecourses into a conventional general linear model (GLM) to analyze the simultaneous fMRI recordings, revealing four large-scale resting-state networks; i.e., the visual, auditory, self-referential, and dorsal attention networks [Britz2010]. We thus showed for the first time a direct link between a global electrophysiological and the hemodynamic measure of brain activity at rest. In Figure 1, we show the scalp topographies of the four EEG microstates with the associated fMRI resting-state networks obtained by the GLM analysis. We have also determined the ICA resting-state networks and paired four of them to the EEG-induced GLM maps using wavelet-based statistical resampling [Patel2006].

To uncover the underlying mechanism of how timescales of EEG and fMRI so different can be linked, we hypothesized and confirmed scale-free behavior of EEG microstate dynamics. Using wavelet-based fractal analysis, we found a clear signature of monofractality over 6 dyadic scales covering the 256ms-10s range [VanDeVille2010], which confirms that the temporal dynamics of resting-state activity is two orders of magnitude faster than fMRI measures alone suggest. Moreover, the degree of long-range dependency was maintained when shuffling the local microstate labels but became indistinguishable from white noise when equalizing microstate durations, which indicates that the temporal dynamics are their key characteristic. In sum, the four rapidly varying EEG microstates seem to represent the neurophysiological correlates of four known resting-state networks and their scale-free dynamics allow them to be measured at the slow fMRI timescale. In Figure 2, we illustrate this finding with a 4-seconds segment of the EEG microstate sequence and a 4-minutes segment of the fMRI regressor after convolution of the microstate occurrence signal. We also show the Hurst exponent that is the single parameter of a monofractal process and representative of long-range dependency.

These findings provide further evidence that the brain is functionally organized in a scale-free way. Other manifestations of fractal behavior have been observed at many instances [Buzsaki2006, Freeman2007], including for signals measured at single EEG electrodes [Lutzenberger1992], using MEG recordings [Linkenkaer2001] or invasive electrocorticography [He2010], or fMRI timeseries [Maxim2005, Ciuciu2008]. More recent work on dynamical aspects of MEG and fMRI recordings have focused on the coexistence of stationary and non-stationary processes [dePasquale2010] and on the power-law scaling behavior of synchronization metrics [Kitzbichler2009].

## Figures

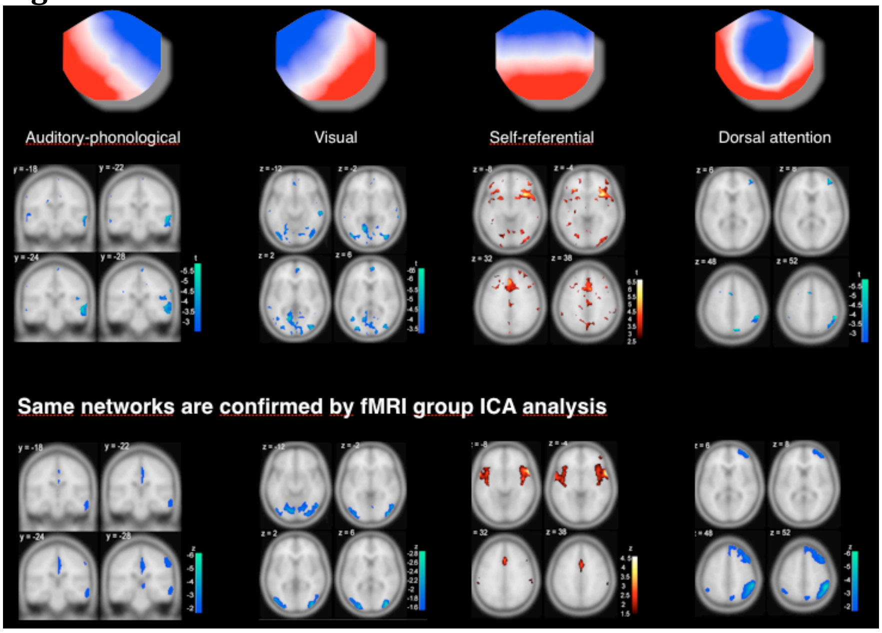


*Figure 1.* The occurrence signals of the four predominant EEG microstates can be linked to large-scale fMRI resting-state networks that are confirmed by fMRI-only group independent component analysis (ICA). Adapted from [Britz2010].

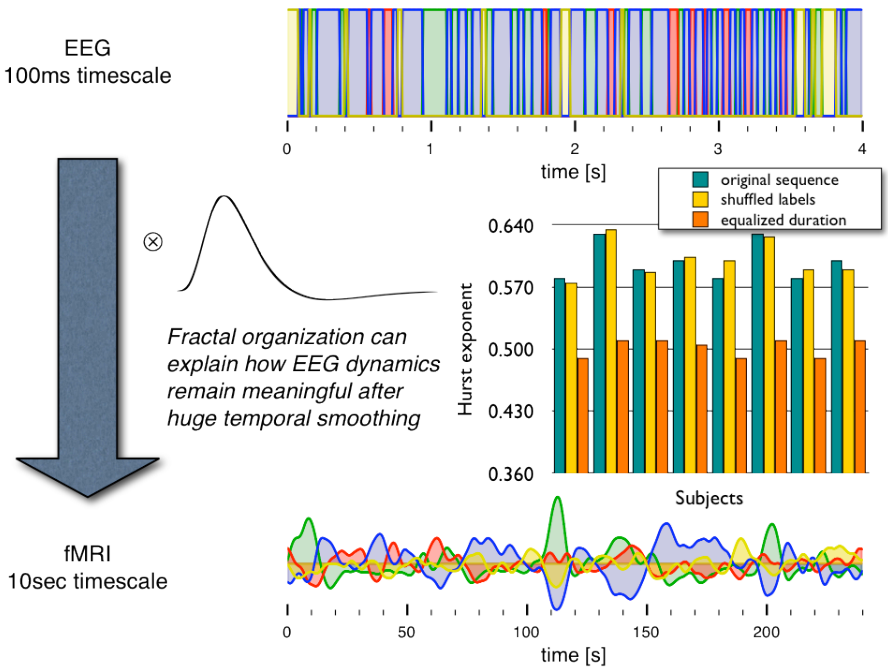


*Figure 2.* The meaningful correlation of the EEG microstate signals after convolution with the hemodynamic response function can be explained by scale-free organization of the switching between the different microstates. Specifically, we found monofractal behavior that can be characterized by a single parameter (i.e., the Hurst exponent), which is significantly different from its value for white noise (H=0.5) and thus reflects the long-range dependency of the fractal organization. This parameter remains unchanged after shuffling the microstate labels but reverts to its value for white noise (H=0.5) after equalizing the duration of all microstates [VanDeVille2010].

## References


[Berger1929] Berger, H. (1929) Über das Elektrencephalogramm des Menschen. Arch. Psychiatr. Nervenkr. 87:527-570.

[Biswal1995] Biswal, et al. (1995) Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. Magn Reson Med 34:537-541.

[Bressler1995] Bressler SL (1995) Large-scale cortical networks and cognition. Brain Res Rev 20:288–304.

[Bressler2006] Bressler SL, Tognoli E (2006) Operational principles of neurocognitive networks. Int J Psychophysiol 60:139–148.

[Britz2010] Britz J, Van De Ville D, Michel CM (2010) BOLD correlates of EEG topography reveal rapid resting-state network dynamics. Neuroimage 52:1162–1170.

[Bullmore2009] Bullmore E, Sporns, O (2009) Complex brain networks: graph theoretical analysis of structural and functional systems. Nat Rev Neurosci 10:186-198.

[Buzsaki2006] Buzsaki G (2006) Rhythms of the Brain. Oxford: Oxford University Press.

[Ciuciu2008] Ciuciu et al. (2008) Log Wavelet Leaders Cumulant Based Multifractal Analysis of EVI fMRI Time Series: Evidence of Scaling in Ongoing and Evoked Brain Activity. IEEE Journal of Selected Topics in Signal Processing 2:929–943.

[Damoiseaux2006] Damoiseaux JS, et al. (2006) Consistent resting-state networks across healthy subjects. Proc Natl Acad Sci USA 103:13848–13853.

[dePasquale2010] de Pasquale F, et al. (2010) Temporal dynamics of spontaneous MEG activity in brain networks. Proc Natl Acad Sci USA 107:6040–6045.

[Freeman2007] Freeman WJ, Breakspear M (2007) Scale-free neocortical dynamics. Scholarpedia 2:1357.

[He2010] He et al. (2010) The temporal structures and functional significance of scale-free brain activity. Neuron 66:353-369.

[Kitzbichler2009] Kitzbichler MG, Smith ML, Christensen SR, Bullmore E (2009) Broadband criticality of human brain network synchronization. PLoS Comput Biol 5:e1000314.

[Koenig2002] Koenig, T., Prichep, L., Lehmann, D., Sosa, P.V., Braeker, E., Kleinlogel, H., Isenhart, R., John, E.R. (2002) Millisecond by Millisecond, Year by Year: Normative EEG Microstates and Developmental Stages. Neuroimage 16:41-48.

[Laufs2003] Laufs, et al. (2003) Electroencephalographic signatures of attentional and cognitive default modes in spontaneous brain activity fluctuations at rest. Proc Natl Acad Sci USA 100:11053-11058.

[Lehmann1980] Lehmann D (1980) Functional States of the Brain: Their Determinants, eds Koukkou M, Lehmann D, Angst J (Elsevier, Amsterdam), pp 189–202.

[Lehmann1987] Lehmann D, Ozaki H, Pal I (1987) EEG alpha map series: Brain micro-states by space- oriented adaptive segmentation. Electroencephalogr Clin Neurophysiol 67:271–288.

[Linkenkaer2001] Linkenkaer-Hansen, et al. (2001) Long-range temporal correlations and scaling behavior in human brain oscillations. J Neurosci 21:1370-1377.

[Lutzenberger1992] Lutzenberger W, Elbert T, Birbaumer N, Ray WJ, Schupp H (1992) The scalp distribution of the fractal dimension of the EEG and its variation with mental tasks. Brain Topogr 5:27–34.

[Mantini2007] Mantini D, Perrucci MG, Del Gratta C, Romani GL, Corbetta M (2007) Electrophysiological signatures of resting state networks in the human brain. Proc Natl Acad Sci USA 104: 13170–13175.

[Maxim2005] Maxim et al. (2005) Fractional Gaussian noise, functional MRI and Alzheimer's disease. NeuroImage 25:141-158.

[Mesulam1998] Mesulam MM (1998) From sensation to cognition. Brain 121:1013–1052.

[Patel2006] Patel RS, Van De Ville D, DuBois Bowman F (2006) Determining significant connectivity by 4D spatiotemporal wavelet packet resampling of functional neuroimaging data. Neuroimage 31:1142–1155.

[Raichle2001] Raichle et al. (2001) A default mode of brain function. Proc Natl Acad Sci USA 98:676-682.

[Tyvaert2008] Tyvaert, L., LeVan, P., Grova, C., Dubeau, F., Gotman, J. (2008) Effects of fluctuating physiological rhythms during prolonged EEG-fMRI studies. Clin. Neurophysiol. 119:2762-2774.

[VanDeVille2010] Van De Ville D, Britz J, Michel CM (2010) EEG microstate sequences in healthy humans at rest reveal scale-free dynamics. Proc Natl Acad Sci USA 107:18179-18184.

[Vincent2007] Vincent, J.L., Patel, G.H., Fox, M.D., Snyder, A.Z., Baker, J.T., Van Essen, D.C., Zempel, J.M., Snyder, L.H., Corbetta, M., Raichle, M.E. (2007) Intrinsic functional architecture in the anaesthetized monkey brain. Nature 447:83-86.