A Strategy to Reduce Bias of Entropy Estimates in fMRI Signal

Albert C. Yang, Shih-Jen Tsai, Ching-Po Lin, and Chung-Kang Peng

***Abstract*—We present a minimizing error approach to reduce the bias of sample entropy (SampEn) and multiscale entropy (MSE) in resting-state functional magnetic resonance imaging (fMRI) data. The strategy explored a range of parameters that minimized the relative error of SampEn of fMRI signal in cerebrospinal fluids (CSF) where minimal physiologic information was present, and applied these parameters to calculate SampEn of fMRI signal in gray matter regions. We examined the effect of various parameters on the results of SampEn and MSE analyses of a large aging adult cohort (354 healthy subjects aged 21–89 years). The results showed that a tradeoff between pattern length *m* and tolerance factor *r* was necessary to maintain the accuracy of SampEn estimates. Overall, the parameters m = 1 and r = 0.20–0.45 provided reliable MSE estimates in short resting-state fMRI signal. For a single scale SampEn analysis, a wide range of parameters was available with data lengths of at least 97 time points. This study provides a minimization error strategy for future entropy analysis of fMRI signal to account for bias of entropy estimates.**

I. Introduction

Complexity analysis of resting-state fMRI signal using entropy methods has attracted considerable attention. SampEn [1] or MSE [2] has been applied to study the temporal dynamics of fMRI signal. However, results of entropy analyses of resting-state fMRI signal also come with the inconsistency of parameter selection for entropy calculation. Generally, the selection of these parameters in fMRI studies have been based on maximizing the between-group difference in entropy estimates [3, 4], prior SampEn reports on other signal [5], or the conceptual notion that a sufficient pattern length was required to capture underlying dynamics [6].

II. Methods

SampEn is defined by the negative natural logarithm of the conditional probability that a data set of length N, having repeated itself within a tolerance of r (similarity factor) for m points (pattern length), will also repeat itself for m + 1 points without allowing self matches [1]. MSE was introduced to assess SampEn of coarse-grained time series across a set of scale factors [2]. We developed a general strategy to explore a range of parameters that minimized the relative error of SampEn of fMRI signal in CSFs; where minimal physiologic information was present. The obtained parameters were then applied to study the SampEn of fMRI signal in gray matter. This minimization strategy considers the distinct fMRI signal properties between CSFs and gray matter and is presumed to be consistent across studies; thus, problems in prior approaches that maximize the between-group difference of entropy estimates in gray matter regions are avoided.

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A. C. Yang and C. K. Peng are with the Division of Interdisciplinary Medicine and Biotechnology, Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, Massachusetts, USA (617-667-4553; fax: 617-667-4894; e-mail: cyang1@bidmc.harvard.edu).

S. J. Tsai was with Department of Psychiatry, Taipei Veterans General Hospital/Division of Psychiatry, School of Medicine, National Yang-Ming University Taipei, Taiwan (e-mail: sjtsai@vghtpe.gov.tw).

C. P. Lin is with the Institute of Brain Science, National Yang-Ming University, Taipei, Taiwan (e-mail: chingpolin@gmail.com).

III. Results

Fig. 1 shows the color map of the relative error of SampEn calculation in CSF fMRI signal. The lower SampEn relative error indicates a higher consistency (i.e., lower variation) of SampEn among the CSF voxels. We set the criteria for the selection of m and r to have a relative error lower than 0.1. The optimal m and r in this range was m = 1, r = 0.30 (relative error = 0.087). When m ≥ 2, the minimum error rate was beyond 0.1. The parameters m = 1 and r = 0.20–0.45 provided reliable MSE estimates in short resting-state fMRI signal. For a single scale SampEn analysis, a wide range of parameters was available with data lengths of at least 97 time points.

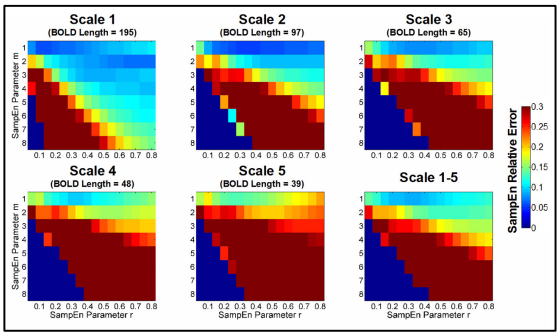

Figure 1. Color map of the relative error of SampEn of CSF fMRI data for appropriate selection of m and r.

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