

Complexity Analysis on Functional-Near Infrared Spectroscopy Time Series: a Preliminary Study on Mental Arithmetic

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Abstract—It is well known that physiological systems show complex and nonlinear behaviours. In spite of that, functional near-infrared spectroscopy (fNIRS) is usually analyzed in the time and frequency domains with the assumption that metabolic activity is generated from a linear system. To leverage the full information provided by fNIRS signals, in this study we investigate topological entropy in fNIRS series collected from 10 healthy subjects during mental arithmetic task. While sample entropy and fuzzy entropy were used to estimate time series irregularity, distribution entropy was used to estimate time series complexity. Our findings show that entropy estimates may provide complementary characterization of fNIRS dynamics with respect to reference time domain measurements. This finding paves the way to further investigate functional activation in fNIRS in different case studies using nonlinear and complexity system theory.

I. INTRODUCTION

The promise of capturing metabolic activity related to neural activity non-invasively and in ecologically valid settings has been an interesting field of research with the advent of functional near-infrared spectroscopy (fNIRS) [1]. Similarly to functional magnetic resonance imaging (fMRI), fNIRS measures blood oxygen level dependent signal [2]. Standard methods of extracting features in fNIRS signals assume an underlying linear physiological system producing the hemodynamic response [3]. In spite of their wide use, these analyses are limited in their scope to fully consider the complexity and nonlinearity of physiological systems [4]–[6].

Entropy analysis is commonly used to analyze physiological time series' irregularity and complexity. Sample entropy (SampEn) [7] and fuzzy entropy (FuzzyEn) [8] are examples of algorithms that converge to the Kolmogorov-Sinai metric to analyze regularity. SampEn is an amelioration of the approximate entropy algorithm, where SampEn forgoes comparing states to themselves in the entropy calculation while also being less dependent on data length. Fuzzy entropy extends approximate and sample entropy by using a fuzzy membership function to calculate class membership of a state vector. Distribution entropy (DistEn) is yet another extension that particularly analyzes the spatial complexity of

the attractor while also reducing the use of fixed parameters [9].

Though entropy analysis has been heavily researched for studying electrophysiological signals [10], its application in fNIRS is still nascent. Permutation entropy [11] was used in several studies and was able to determine variations in complexity reflected by mental stress, for example where it succeeded in revealing greater complexity in fNIRS signals for an attention deficit hyperactivity disorder population vs a control population [12], [13]. Sample entropy was used to discern an Alzheimer's population from a control population [14], [15]. Beyond fNIRS studies, entropy had been applied on metabolic activity in fMRI, such as multiscale entropy for the analysis of resting state fMRI [16], and analysis of reduction of complexity in brain dynamics due to age [17]. In spite of the illustrated success of entropy in the aforementioned studies, to our knowledge its use has not been particularly highlighted in comparison to traditional analysis such as the first-order moment changes between activity and baseline. Aiming to understand if complementary associative areas are observed in fNIRS-related entropy estimates, further research is needed to fully characterize nonlinearities and complexity in fNIRS series [18], [19].

To this extent, in this preliminary study we investigate entropy features to quantify the irregularity and complexity of fNIRS series. Particularly, we investigate the performance of entropy analysis applied to fNIRS acquired during established mental arithmetic tasks with well known neural and metabolic correlates. We compared mental arithmetic with baseline activity using publicly available data provided by Shin et al. [20].

II. MATERIALS AND METHODS

A. Experiment Design

fNIRS signals used in this study were taken from a publicly-available dataset, whose details are reported in [20]. Briefly, twenty-nine healthy subjects (aged 28.5 ± 3.7) were involved in the experiment, split by 15 females and 14 males. Figure 1 illustrates the block design of the experimental protocol. In this preliminary study, data from 10 subjects were considered for further analyses (5 female and 5 male subjects). There were three trials of each of mental arithmetic activity and baseline activity per subject. A total of 36 fNIRS source detector pairs were acquired with a 10Hz sampling rate by matching 16 detectors with 14 sources as illustrated in figure 1.

The experimental protocol began with a 60s of resting state, after which the subjects were presented an instruction

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(an “-” for baseline, an arithmetic operation for mental arithmetic, or “←” and “→” for motor imagery) on the screen telling them which task was to be performed. Afterwards, the subject performed the task for 10s, with a subsequent 15s of resting state before the next task. After 20 repetitions of these instructions and tasks, a 60s rest was performed.

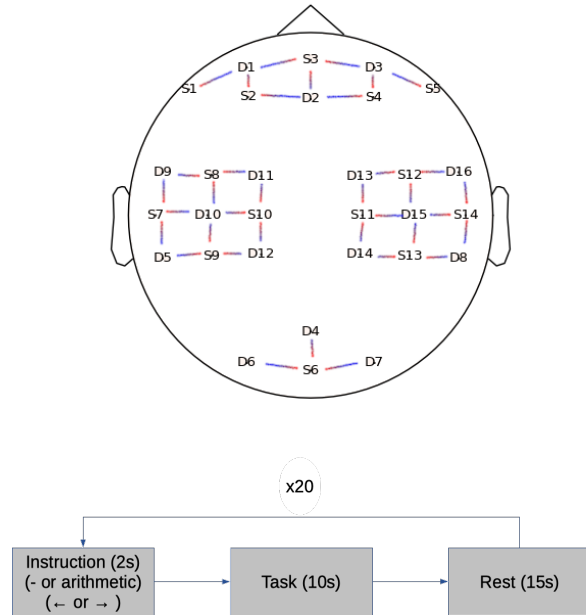


Fig. 1. Top graphic displays the position of the NIRS sources and detectors, source labels prepended by an “S” and detector labels prepended by a “D”. The lines between source detectors illustrate their matching. The bottom graphic illustrates the protocol block design for each trial.

B. fNIRS signals

The fNIRS setup comprised of 36 channels. The two wavelengths used were 760nm and 850nm. The modified Beer-Lambert law was used to convert optical density time series collected from 760nm and 850nm to deoxyhemoglobin (Hb) and oxyhemoglobin (HbO). Total hemoglobin was derived from adding the two hemoglobin signals after preprocessing described in the next section.

C. Preprocessing

Figure 2 diagrams the preprocessing steps. For the modified Beer-Lambert law used to convert the optical density signals to Hb and HbO, the first 60s were considered as baseline, corresponding to a resting state. Then, a low-pass Butterworth filter of order 6 with cutoff at 0.6 Hz was applied to highlight the hemodynamic response, and a passband Butterworth filter with cutoff frequencies at 0.8 Hz and 2Hz was used to include the pulsatile cardiac component of the fNIRS signal [21]. The rationale behind including the pulsatile component was to analyze the complexity that may arise also from such a behavior. After the frequency filters, a wavelet filtering approach was used to further reduce

noise in the oxy- and deoxyhemoglobin signals [22]. Briefly, a discrete wavelet transform using a Daubechies 5 mother wavelet decomposed the signal into 9 levels and subsequently thresholded detail coefficients with low probability assuming coefficients are zero mean normally distributed. Thereafter, the signals were separated into epochs. Each channel at each activity block was referenced to the mean of the previous 5s. Total hemoglobin was thereafter derived from the addition of both Hb and HbO. Having been preprocessed as described here, the data was then further processed to extract features of interest.

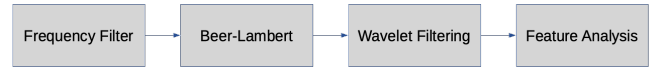


Fig. 2. Analysis pipeline used for each fNIRS signal in the dataset

D. Entropy Analysis

In order to apply Takens theorem to reconstruct the attractor of each fNIRS signal, we first searched the optimal values of time delay and embedding dimension referred to each time series. The first zero of the autocorrelation was used as the time delay, and false nearest neighbours approach was applied to determine the optimal embedding dimension [23].

After the attractor reconstruction, SampEn algorithm was applied. We used the value of $R = 0.2 \times \sigma_x$, as the threshold to determine which class a distance between two states belonged to (neighbours or not), where σ_x is the standard deviation of the fNIRS time series [24]. In the computation of FuzzyEn, an exponential decay function was used as the membership function to weigh the distances between the phase space points, reusing the same parameter R as sample entropy and a fuzzy power $n = 2$ to scale how fast the exponential function decays [8]. Concerning DistEn, Scott’s method was used to determine the bin size for the empirical probability density function as represented by a histogram [25]. From the histogram, shannon entropy can be calculated to get the reported DistEn value.

Beer-Lambert law derives both a time series for HbO and Hb. From adding these two time series, a third time series, total hemoglobin (THb) can be computed. Thus, an attractor can be reconstructed from each of these three time series. Furthermore, an attractor can be reconstructed jointly from Hb and HbO (“Concat”). All of these attractor reconstructions have been explored to evaluate entropy as a metric for assessing changes in brain activity.

E. Statistical Analysis

For each fNIRS channel, Friedman non-parametric statistical tests were performed in order to determine whether repetitions of activities in each trial were significantly different. Afterwards, a Wilcoxon test was applied for each channel using a median calculation over trials to compare significant areas of activation between the two tasks (i.e.

baseline and mental arithmetic). A post-hoc analysis was performed considering a Bonferroni correction for multiple comparison over activities, with an alpha of 0.05 being considered significant. Furthermore, a qualitative visual inspection was used to understand overlaps and complements between various estimates association areas.

III. RESULTS

A. Statistical results on task repetitions

Concerning the results of Friedman statistical test in the analysis of repetitions, it can be seen from Table I that we may accept the null hypothesis that all repetitions have the same effect for mean estimate, DistEn, and SampEn. However, with FuzzyEn, in the case of total, concatenated and HbO, we found that repetitions may be associated with different random variables. FuzzyEn metrics are thus not retained for further analysis between tasks.

TABLE I

RESULTS OF FRIEDMAN TEST CONCERNING STATISTICAL ANALYSIS ON TASK REPETITIONS.

Metric	Mental Arithmetic	Baseline
HbO	0.1735	0.1147
Hb	0.0870	0.0841
Total Hb	0.0331	0.2449
$SampEn_{HbO}$	0.0610	0.1414
$SampEn_{Hb}$	0.0891	0.2844
$SampEn_{Total}$	0.2013	0.2528
$SampEn_{concat}$	0.0408	0.1147
* $FuzzyEn_{HbO}$	0.0934	0.0023
$FuzzyEn_{Hb}$	0.0145	0.0106
* $FuzzyEn_{Total}$	0.0708	0.0051
* $FuzzyEn_{concat}$	0.0219	0.0078
$DistEn_{HbO}$	0.6658	0.1735
$DistEn_{Hb}$	0.1272	0.0115
$DistEn_{Total}$	0.0871	0.0874
$DistEn_{concat}$	0.0408	0.0408

The symbol * denotes when $\alpha = 0.01$ we must reject the null hypothesis of the Friedman test (i.e., there were significant variations between repetitions with $p < \alpha$).

B. Statistical analysis between baseline and mental arithmetic task

We used Wilcoxon non-parametric statistical tests to discern mental arithmetic task from baseline, and Figure 3 shows the results from such a statistical analysis obtained using the mean estimates, SampEn, and DistEn estimated from HbO, Hb, THb, and Concat time series. It can be noted that brain areas associated with significant p-values are shown along with the increase/decrease of the specific metrics.

When looking at significant regions of activity, DistEn provides a greater region of activation than sample entropy, while providing complementary regions to mean estimates. For example, in HbO, DistEn highlights a region in the posterior cortex for activity that is not included in the mean estimates. Furthermore, the frontal cortex in Hb provides frontal cortex activity in DistEn where mean estimates do not. On the other hand, SampEn both in Hb and HbO fails to attain areas of significance. Looking at THb and Concat,

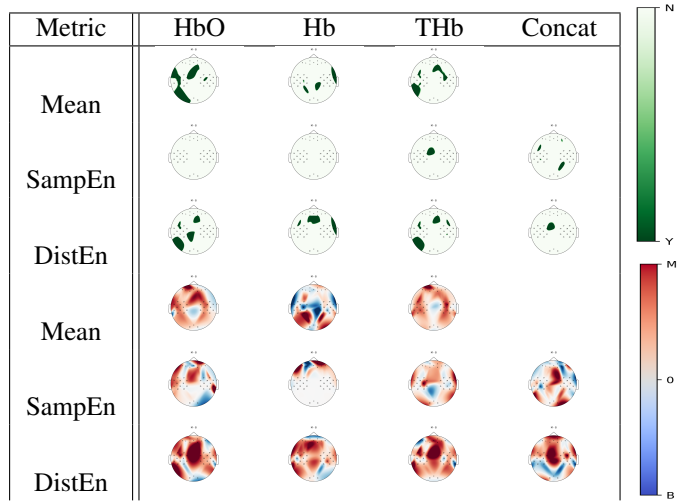


Fig. 3. Significant activations between mental arithmetic activity and baseline activity are shown in the p-value plots using a green colormap, where Y denotes significant areas with $\alpha = 0.05$ and N denotes insignificant. In the red to blue colormap arbitrary unit (A.U) differences between baseline and mental arithmetic are mapped, with M red implying higher values for mental arithmetic than baseline and B implying the reverse

SampEn provides complementary areas to DistEn and mean estimates.

IV. DISCUSSION

In this study, we analyzed irregularity and complexity features of brain activity dynamics for each possible configuration of the fNIRS signals: Hb, HbO, THb, Concat. The fNIRS signals were taken from a publicly available dataset, described in [20]. We considered ten subjects and compared their metabolic brain activity during mental arithmetic tasks and a baseline session. We applied three different entropy algorithms, i.e., SampEn, DistEn, and FuzzyEn, alongside the mean estimates of the four time series. From SampEn and DistEn estimates as well as the traditional mean estimate for activity, no significant differences were found among repetitions of an activity. This allowed us to perform post-hoc analysis to analyze whether mental arithmetic activity was statistically different from baseline activity using a summary statistic, i.e. the median, of all trials for the subject.

Concerning linear metrics, we were able to find areas in the cortex that corresponded to what we expected from previous fNIRS literature, particularly the prefrontal cortex, parietal and temporal regions [26]. When we applied Wilcoxon statistical tests to entropy estimates, it appeared that DistEn was able to find areas that complement the areas that mean estimates were able to uncover, while SampEn was only able to do so when applied to THb and Concat attractors. The complementary areas found from the complexity estimates are interesting due to the increase of information it provides, possibly uncovering significant activity in experiment protocols which in the past could not say anything conclusive, or perhaps even in cases of brain machine interfaces where a richness in features can improve performance.

DistEn may have been more capable of uncovering more activation areas than SampEn from its ability to reveal complexity alongside regularity of a signal in the phase space, allowing the DistEn algorithm to better analyze feedback loops; an analysis that SampEn can not perform without a multiscale extension.

Finding complementary areas by entropy estimates is of interest as mental arithmetic studies are designed such that they can incite a large enough activation that show a saturating superposition effect, an effect that is easily captured by looking at absolute values of blood oxygen levels. Further research is still needed to understand and model the underlying physiology driving these nonlinear and complex effects to explain the results. At a speculative level, one explanation can hinge on the cardiac components underlying in the fNIRS signal. In fact, the pulsatile component of the signal may have contributed to the fNIRS complexity changes with respect to a baseline pulsatile activity, thus the fNIRS complexity might be linked to a change of vasoreactivity dynamics.

Previous evidence highlight that long-term stimuli follow a more linear behavior than short-term stimuli [18]. From this knowledge, one may expect that instead of looking at long term stimulation activity as this study does, using short term stimuli, entropy would be more capable than linear methods at finding activities, i.e. unraveling activation areas unseen by traditional methods.

V. CONCLUSIONS

From this preliminary study, we conclude that entropy estimates may provide information regarding activity in mental arithmetic protocols different than metrics defined in the time domain. Furthermore, DistEn proved to be more powerful in uncovering activity than SampEn. Entropy was able to not only demonstrate a subset of mean estimates, but also complementary set of activation areas. Nonetheless, the underlying physiology needs to be understood further in order to explain precisely why these complementary areas arise. Future studies can also investigate nonlinearities present in protocols with short duration stimuli where nonlinear responses is better understood.

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