Authors’ Instructions for the Preparation  
of Camera-Ready Contributions  
to Cognitive Neurodynamics Proceedings

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1 Introduction

The goal of scientific theory is to reduce complex description into a simpler ones. The interpretation of “simple” is, however, not context free and depends on the scientist’s experience and the current state of knowledge. For example, the problem of control a mechanical system can successfully be approached analytically, for example, solving the Newton-Euler equations or numerically, via optimization methods, notably, back-propagation, provided by the numerous machine learning computational libraries.

While optimization methods to solve classification problems might now be considered trivial, the characterization of the signal vis a vis the noise is far from being a solved issue. It is the implementation of statistical methods rather than the statistical theories what have suffer a profound transformation in the last 40 years.

Bootstrap methods, for example Monte Carlo simulations, were conceived before the required machinery for running extensive combinatorial computations existed. Bootstrap methods has boosted new ways to statistical inference. The surrogate data testing is a form of bootstrapping that is used here to study the time series of fMRI.

Here we characterize the time series of n cadaveric brains. A dead brain might seem a remarkably uninteresting system to study if we assume under the assumption that the BOLD signal must be entirely noisy. Here we prove that the contrary is true.

1.1 Checking the PDF File

It is important to differentiate between noise in thermodynamics which is a fundamental uncertainty about the world that can not be eliminated and noise in the statistical sense which is anything that our model does not explain ($\sigma$).

Physiological noise in the fMRI literature refers to fluctuations with a physiological underpinning that are uninteresting for our study. These include, among others, haemodynamic fluctuations caused by cardiac and respiratory cycles \cite{birn2006separating}, tissue motion \cite{soellinger20093d} but also neuronal activity that is not directly related to the task in task-based experiments. Thus, to some extent physiological noise is what the experimenter cannot fully predict nor control and is this failure to control what carries the negative connotation associated with the term noise \cite{wald2016impacting}.

In a cadaveric brain, physiological noise components such as cardiac and respiratory artifacts are necessarily absent in the fMRI time-series and only thermal noise should be expected.

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2 Methodology

MRI data were acquired on a 3T scanner (GE Healthcare, Milwaukee, WI) at the Fundación Reina Sofia, Centre for Research in Neurodegenarative Diseases, Madrid, Spain. Both T1 and T2\* images were collected postmortem x hours after death occurred.

The raw T1 images underwent skull-striping to remove non-brain tissue and background (BET algorithm). A linear registration was performed between the skull stripped image and the standard Montreal Neurological Institute (MNI) structural template.

The resting-state functional images (rsfMRI) were acquired with the following parameters: TR = 2500 ms, flip angle = 81°, in-plane resolution = 64 × 64, 32 slices, FOV = 240 mm × 240 mm, thickness/gap = 2.6/0.5 mm and 120 volumes (5 min). The first four volumes were discarded to allow for magnetization to reach equilibrium.

Functional images were minimally preprocessed to study the time series as free as possible of model bias or spurious correlations that could be introduced in standard preprocessing such as spatial smoothing. The bodies were in rigor mortis condition and no motion correction was necessary. We verified this point with the motion correction algorithm MCFLIRT, returning negligible values of absolute mean displacements: 0.33mm (bcpa0578), 0.05mm (bcpa0650) and 0.155mm (bcpa0537). Slice timing correction (interleaved) was performed. all volumes were linearly co-registered onto the corresponding T1 image and the T2\* onto T1 transform was combined with the T1 to MNI linear registration to map the rsfMRI onto the Montreal Neurological Institute (MNI) template (resampling voxel size = 2 mm × 2 mm × 2 mm). No spatial smoothing (FWHM=0) was performed and the high pass filter cut off was set to allow frequencies above 0.008Hz. After preprocessing, linear trend was removed (Jenkinson M, Beckmann CF, Behrens TEJ, Woolrich MW, Smith SM. FSL. Neuroimage. 2012;62: 782–90. pmid:21979382).

We are interested in determining or at least make a reasonable guess about the underlying dynamical process of the observed data, in this case postmortem fMRI. While the final motivation of this work is to disentangle the different influences, we set a more realistic goal which aims at characterizing the signal, in particular we address the question:

Is the signal random or has some temporal structure? and

How many degrees of freedom (correlation dimension) does it have?

One would expect that a dead body will have a stationary signal which is tantamount to saying that is in statistical equilibrium. In a more fundamental level, a dead body will be closer to thermal equilibrium than an alive one, that is to say, the probability distribution over the states of a dead body has larger entropy than an alive one. This can be tested empirically calculating the distance between the theoretical equilibrium’s distribution as given by the Boltzmann´s equation and the observed distribution, the distance should be greater for an alive body than for a dead one \cite{bialek2012statistical}.

2.1 Surrogate Data method

In order to arrive to a satisfactory answer to the two above questions we need two things, one is a null hypothesis against which data are tested and two, a number that acts as discriminating statistic that quantifies the goodness of fit of the hypothesized model. The distribution of the statistic is finally compared with the observed data, if the statistic is different for the observed data than could be expected under the null hypothesis we reject the null hypothesis. Thus, to study whether there is any dynamics at all in postmortem fMRI we hypothesized that the signal is independent and identically distributed Gaussian noise (null model).

The surrogate data method estimates the distribution of the statistic using Monte Carlo simulations, where an ensemble of realizations are generated from the observed data. The surrogate data method is certainly better than trying to derive analytically the distribution, which is not only unknown but inferred from a signal with a strong noise component (postmortem fMRI) and that, to our knowledge, has not been sufficiently investigated.

The resting state fMRI contain 120 time points or 5 minutes duration. Let denote the observed time series and let the surrogate data generated under the null hypothesis. The surrogate data are generated using Monte Carlo simulation preserving some properties of the observed time series, for example, the first statistics or the power spectrum density of the observed time series, but are otherwise random. For each surrogate data ensemble, , where n is the number of realizations, we calculate the discriminating statistic and from the resulting ensemble of statistics we estimate the distribution. A significance test is directly calculated as the difference between the observed data time series and the mean of the statistic from the surrogate data. For example, for n realizations we would reject the null hypothesis if the observed time series mean is in the n-th percentile, that is, a p-value . Table 1 describes the null hypothesis and the discriminant statistics used.

2.2 Null hypotheses

Linearly autocorrelated Gaussian noise. An alternative explanation for the observed data have been generated by a stationary Gaussian process, for example, an autoregressive moving average (ARMA) process. An ARMA process will show characteristic linear correlations that reflect the ARMA structure formalized as:

|  |  |
| --- | --- |
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We iterate the ARMA model of equation () to generate an ensemble of n=100 realization of the model. We calculate the distribution of the correlation dimension statistic and we compare it with the original time series. The null hypotheses is that the time structure of the observed data is fully described by the autocorrelation function, this is equivalent to say that the power spectrum is preserved (Wiener Khinchin theorem). We fit the coefficients of Equation () to the observed data and we iterate using a pseudio random generator for the error term. Alternatively , we can generate the surrogate data by randomizing the phases of the Fourier transform. Specificaaly, we take the Ft of the original time series, randomize the phases, and then invert the transform.   
The correlation dimension C() of a set of data points measures the number points that are separated a distance no more than . The correlation dimension is a type of fractal dimension in chaos theory. It is used to between deterministic low-dimensional chaos and truly random noise. This measure has the advantage that is easily calculated and scales. Formally, (Scheinkman and Lebron)

|  |  |
| --- | --- |
| The correlation dimension can be used to describe the geometry chaotic attractors. It is calculated as a correlation sum C(r) which is the fraction of points in the phase space whose distance is smaller than r. If the relation between C(r) and r can be described as a power la, C(r) \sim r^D then D is the correlation dimension of the system. The maximum D for a d-dimensional system is d. This value is obtained for systems that expand uniformly in each dimension with time and the minimum is 0 (the system visits only one point in phase space). The algorithm (Grassberger-Procaccia) calculates C(r) for a range of different r and then fits a straight line into the plot of log(C(r)) versus log(r). We run the algorithm for one-dimensional (scalar) time series, therefore before calculating C(r), a delay embedding of the time series is performed to yield emb\_dim dimensional vectors. Choosing a higher value for emb\_dim allows to reconstruct higher dimensional dynamics (I have note that after 4 the correlation dimension drops to 0). The algorithm returns the correlation dimension as slope of the fitted line C(r) versus log(C(r)) | (**2**) |

iid Gaussian noise. A time series can be seen as a regression problem. A regression tries to predict the value of the variable from a set of regressors ,

|  |  |
| --- | --- |
|  | (**1**) |

Thus, a time series can be represented a regression problem in which the features are lagged values of the independent variable

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| --- | --- |
|  | (**2**) |
| Importantly, this model of the time series is only appropriate when the time series is iid Gaussian (being e Gaussian) noise. Pure noise is spatially and temporally uncorrelated and therefore we do not need to care if the time series presents autocorrelation or is non stationary.  We calculate the correlation between the original time series and the ensemble of n=100 realizations of the shuffle time series, for lags between 1 and 5. Thus, we destroy the time structure of the time series and we calculate the correlation for different time lags. In case the original time series has time structure, the correlation should be maximum for lag=1 with a monotonic decreasing for larger lags. | |

**Table 1.** Null hypotheses and surrogate data statistics used. The null hypotheses specify that certain properties of the original data are preserved (amplitude and power spectrum), the surrogate data are thus generated to mimic these features and is otherwise random.

|  |  |  |
| --- | --- | --- |
| Null model | Surrogate data | Statistic |
| The observed data is iid Gaussian noise | The original time series data are shuffled, the temporal structure is destroyed preserving the amplitude of the distribution | Correlation |
| The observed data is linearly autocorrelated Gaussian noise | ARMA model parameters estimated from the original time series | Dimension correlation |
|  |  |  |



**Fig. 1.** One kernel at *xs* (*dotted kernel*) or two kernels at *xi* and *xj* (*left and right*) lead to the same summed estimate at *xs*. This shows a figure consisting of different types of lines. Elements of the figure described in the caption should be set in italics, in parentheses, as shown in this sample caption.

3 Results

The second hypotheses is more stringent than the first one. The first hypotheses tests whether the original time series can be fully reproduced as white noise, while the second hypotheses is more stringent, it not only predicates on the white noise nature of the data it also specifies whether the data could have been obtained by any linear filter of white noise.

The null hypothesis iif Gaussian noise is tested by shuffling the original time series with different lags. The original time series data is extracted from voxel X in the DMN (or the entire brain). The original time series structure is destroyed by shuffling with different time lags. The resulting surrogate data consists on an ensemble of n time series for each lag, , where n is the number of realizations (n=100) and l is the time lag (l =5).

The dynamic time warping (FastDTW Salvador, Chan) fimds the optimal alignment between time series and can be used to find time series similarity for classification. DTW finds the optimal alignment or path between two time series by warping the time axis. The DTW is a distance measure between time series and has been applied to multiple domains including speech recognition, robotics, manufacturing and recently in neuroimaging (rsfMRI) (doi: 10.3389/fnins.2017.00075). DTW was introduced (Kruskall, The Symmetric Time Warping Problem: From Continuous to Discrete.) to rectify the problems encountered with comparing time series using the Euclidean distance eg. Two ts that are identical but phase locked will be very distant, this is anti intuitive. The DTW problem can be easily stated as giving two time series X,Y of length |X| and |Y| find the warp path W such that

W = w1…wk, max(|X|, |Y|) \leq < |X| + |Y|, where k is the length of the path and the k-th element of the path is k-th= (i,j), where I, j are indexes in the time series X and Y repspectively. The warp path starts at the beginning of each time series, that is, (1,1) and finish at the end (|X|, |Y|) so every index is visited by the warp path

4 Discussion

Human beings are always trying to picking up patterns to make sense of the external world. This modus operandi, given the surrounding complexity, is primordial for survival but it can be also lead to deception, for example identifying non-existent patterns that happen to suit our personal needs.

The first null hypothesis is that the observed data consists of independent draws from a fixed probability distribution,, the surrogate tiem series are easily obtained by randomly shuffling the observed data. If we find significantly different serial correlations in the data and in the shuffles we can reject the null hypothesis. The second hypothesis generates surrogate data constrained, in particular, the constrained realizations require that the surrogate data share the same Fourier amplitudes with the original data.

We have found serial correlations in a time series, that is, the first null hypotheis of independence cab be rejected. The next step is to ask of what nature these correlations are.

we create permutations withour replacement

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References

1. Baldonado, M., Chang, C.-C.K., Gravano, L., Paepcke, A.: The Stanford Digital Library Metadata Architecture. Int. J. Digit. Libr. 1 (1997) 108–121

2. Bruce, K.B., Cardelli, L., Pierce, B.C.: Comparing Object Encodings. In: Abadi, M., Ito, T. (eds.): Theoretical Aspects of Computer Software. Lecture Notes in Computer Science, Vol. 1281. Springer-Verlag, Berlin Heidelberg New York (1997) 415–438

3. van Leeuwen, J. (ed.): Computer Science Today. Recent Trends and Developments. Lecture Notes in Computer Science, Vol. 1000. Springer-Verlag, Berlin Heidelberg New York (1995)

4. Michalewicz, Z.: Genetic Algorithms + Data Structures = Evolution Programs. 3rd edn. Springer-Verlag, Berlin Heidelberg New York (1996)

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