Analysing Continuous-Time Neural Signals

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As technology advanced during the course of time, researchers developed more accurate methods to investigate the mind. Instead of behavioral data, which mainly reflected activity in higher levels of abstraction, neural can reflect lower levels at higher spatial and temporal resolutions. Now, the brain philosophers, psychologists and neuroscientists can come together and examine their theorems under the name of system neuroscience.

In this assignment, we are trying to get our hands dirty while exploring some neural data. The data we are speaking of here is continuous-time, meaning that it has a continuous structure by nature and is sampled by a fixed rate. The discrete-time neural signals (a.k.a action potentials) carry an inherent discontinuity; At a given time, a neuron has either fired or not. Such data modalities are covered in your final assignment. Meanwhile, let us begin neural data analysis gathered by methods of EEG, LFP and fMRI.
Keywords: neural data, neuronal data, signal processing, cognitive science, neuroscience, phase locking, causality, connectivity, fmri, lfp, eeg, rsa, rdm, granager, rsvp, mgs, ants, skull stripping, brain imaging

1. Data Modality: Electroencephalogram

Recall the Representational Dissimilarity Matrices from the second assignment. As stated before, RDM is a common method to compare several modalities in system neuroscience. In this question we employ Representational Similarity Analysis in the context of neural signals. Moreover, we will apply common pre-processing techniques to the raw EEG data and analyse the results.

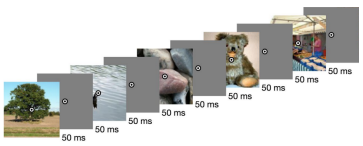

Figure 1: Rapid serial visual presentation design of data. Each image presented for 50ms, followed by a 50 ms blank screen. Bullseye overlaid at the centre of each image to help participant maintain fixation.

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Related EEG data (`eeg.set`) recorded from a normal-vision participants. Stimuli-set contains 12 image of 1854 concepts which are shown to participant in random order in a Rapid Serial Visual Presentation (Refer to Appendix). The sequences were presented at 10Hz, with a 50% duty cycle as shown in Figure 3. Data downsampled to 250 Hz due to reduce computational complexity.

1.1. Pre-Processing Steps

Import EEG data file in EEGLAB, a MATLAB extension of signal processing environment for electrophysiological signals. preprocess data based on related workshop (the last three steps are not needed.)

1. Filter the data with high-pass (0.1 Hz) and low-pass (100 Hz) Hamming windowed FIR filter.
2. Re-referenced to the average reference (online referencing was Cz channel).
3. Remove line noise with notch filter.
4. Create epochs and baseline normalise for each stimulus onset ranging from -100 to 1000 ms ("E 1" is a stimulus onset event).

Questions

(a) Describe the effect of the high-pass filter and notch filter on the data. Also, mention the reason why these phenomena happened.
(b) Explain the logic of noise removal steps (referencing and baseline normalization).
(c) Sanity check your data with Event-Related Potentials (ERPs) over channels (Report bad electrode if there is any).

1.2. Representational Dissimilarity Matrices (RDMs)

The representational dissimilarity matrix is a hub that relates different representations (behavioral experimentation, brain-activity experimentation, and computational modeling). For each pair of experimental conditions, activity patterns of separate representation compared by spatial correlation and the dissimilarity ($1-corr$) computed with it. By calculating all the dissimilarities for all possible pairs of conditions, matrix will become complete. Activation pattern is typically a spatial response in FMRI or time range in M/EEG data, where we are interested to study the effect of that. Moreover, RSA model is another analysis which computes mean correlations value of similar conditions across different activation patterns [1].

1. Find epochs of "face", "chair" and "dog" in EEG data based on object column in `events.csv`.

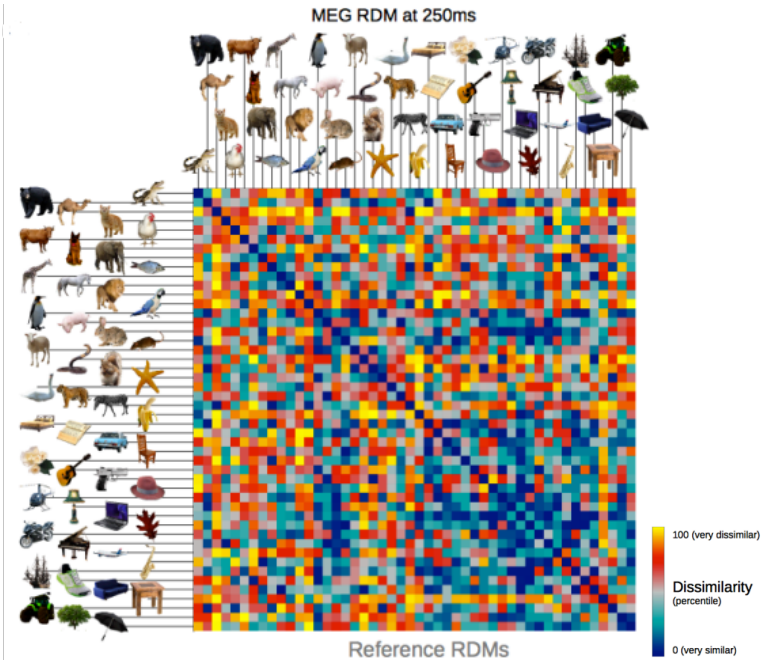


Figure 2: RDMs of different visual stimuli trial in MEG data compared to their names (reference). One cell in the matrix represents the dissimilarity between the MEG activation patterns for one pair of object exemplars. In this figure activation pattern is in 250 ms.

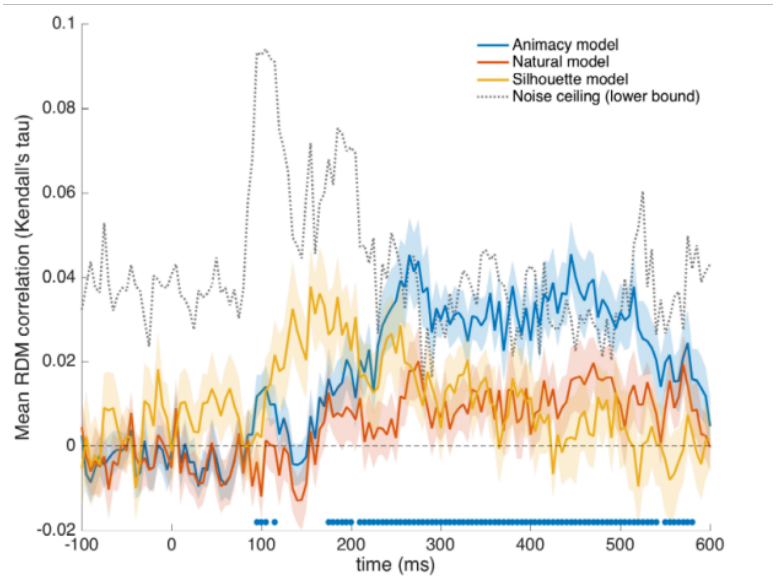


Figure 3: RSA model evaluation. At each time point, the RDMs for each subject are correlated with the three RDMs model (Animacy, Natural, Silhouette).

2. Create RDMs on these three conditions. To this end, use Spearman rank correlation coefficient at mean value of 175-225 ms.
3. plot RSA model of mentioned RDM.

Questions

(a) Is 200 ms (center of above range) a good activation pattern for differentiating these three categories? If not, name your preferred activation pattern. Is this time point scientifically explainable?

(b) Bonus Use some statistics to show the strength of the average correlations and how well the model fits the data.

2. Data Modality: Local Field Potentials [1]

In this question, you are asked to perform several types of connectivity analysis on a dataset comprised of several sessions in which LFP (low-frequency potential) activities of a trained Macaque monkey is recorded when performing a memory-guided-saccade (MGS) task Refer to appendix for more information). As illustrated in Figure 4, two electrodes were planted inside subject's brain: one inside "V4", a brain region in visual cortex, and another inside "FEF", a crucial area for visual attention and working memory inside prefrontal cortex.

1: Although I am a Python enthusiast myself, I STRONGLY recommend you to use MATLAB for answering this question.

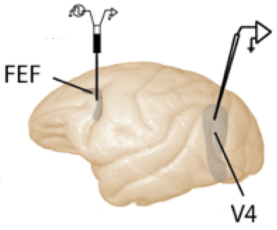


Figure 4: An illustration of V4 and FEF inside Macaque monkey's brain. During the MGS task, the LFP activities of these two areas were being recorded.

2.1. Phase-Locking Value (PLV) Analysis

Phase Locking Value (PLV) is a statistic that can be used to investigate task-induced changes in long range synchronization of neural activity. PLV statistic is a time course, meaning that for every time point in data, a measure of connectivity can be calculated. Therefore, this quantity can be employed to observe transient changes in connectivity/synchrony without defining a time window of analysis. As depicted in Figure 5, to compute PLV quantity for a pair of time-series, there are a few steps to be performed in a consecutive order:

1. Filtering each time-series to a specific frequency-band of interest.
2. Extracting the phase time course for both time-series. Hilbert transform is an excellent option.
3. Calculating the average exponentiated phase difference over trials (n) at each time point using the following equation:

$$PLV(t) = \frac{1}{N} \times \sum_{n=1}^{N} \exp\left(\Phi_{1,n}(t) - \Phi_{2,n}(t)\right)$$

4. Normalizing the result to baseline. In this problem, you may consider PLV values computed over the fixation period in the MGS task as the baseline.

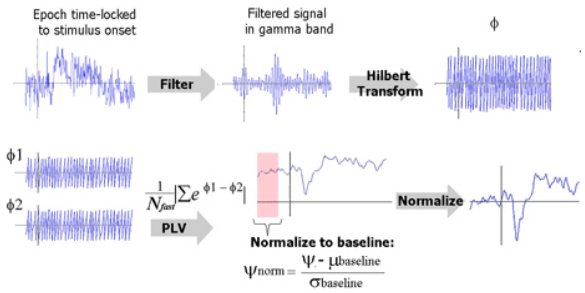


Figure 5: There are several steps involved in computing phase-locking value for a pair of time-series.

Questions

(a) Look up the `filter` and `filtfilt` commands in MATLAB documentation. Which command do you think is more suitable for filtering the data for the PLV analysis? Why?
(b) What is the purpose of baseline-normalizing the results as the final step of the PLV analysis?
(c) Recall the concept of shuffle correction. Can one use shuffle correction instead of baseline-normalization?
(d) Using the description of this problem and the equation stated earlier, implement the PLV metric and apply it on the LFP recordings contained in the provided dataset (`lfp.mat`). This dataset contains a matrix of size $N_{channels} \times N_{time} \times N_{trials}$. Each row corresponds to the recordings of one trial. The first channel contains the recordings of V4 and the second channel is associated with recordings of FEF. Neural activities are recorded at a sampling rate of 1kHz.
(e) Do you observe any increase in connectivity strength? If positive, try to assess its statistical significancy. We propose two different test and ask for implementing only the latter. First, Rayleigh test over the evaluated Von-Mises distribution and second, permutation test with the null-hypothesis of no locking between two regions. Although you can look up the former method and summarize its procedure in your report as a bonus question.

2.2. Linear Granger Causality (LGC) Analysis

The Granger causality test is a statistical hypothesis test for determining whether one time series is useful in forecasting another. A time series X is said to Granger-cause Y if it can be shown, usually through a series of t-tests and F-tests on lagged values of X (and with lagged values of Y also included), that those X values provide statistically significant information about future values of Y. Here, using the term ”causality” might be a misnomer, as Granger-causality is better described as “precedence”, or, as Granger himself later claimed in 1977, “temporally related”. Rather than testing whether X causes Y, the Granger causality tests whether X forecasts Y. As depicted in Figure 6, when a time series (here, X) Granger-causes another time series (here, Y), the patterns in former are approximately repeated in the later time-series after some time lag (two examples are indicated with arrows in Figure 6). Thus, past values of the first time-series can be used for the prediction of future values of the second one.

Sir Clive William John Granger (1934 – 2009) was a British econometrician known for his contributions to nonlinear time series analysis. Granger was awarded the Nobel Memorial Prize in Economic Sciences in 2003 in recognition of the contributions that he and his co-winner, Robert F. Engle, had made to the analysis of time series data. This work fundamentally changed the way in which economists analyse financial and macroeconomic data.

(a) Describe the assumptions of the LGC method. In other words, what are the preconditions that the input time-series must meet in order for the results to be considered dependable?

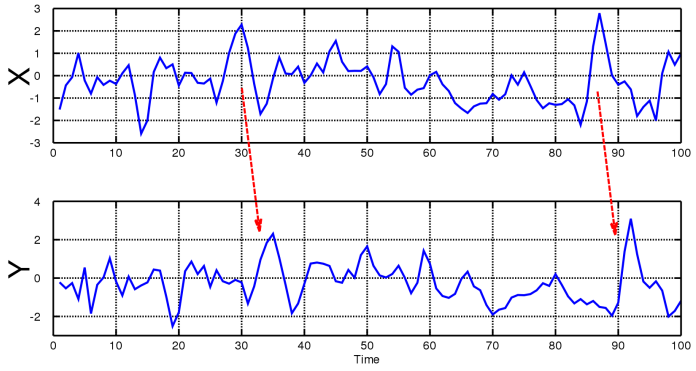


Figure 6: An example of one time-series (X) predicting the fluctuations of another time-series (Y).

(b) Load the dataset (`lfp.mat`) and examine whether the data meets the preconditions of the LGC analysis? Justify your answer by plotting proper diagrams and performing statistical tests on the data.

(c) Perform the following pre-processing steps on the data:

  (i) Filtering: Apply a High-pass filter at 0.5Hz to remove any irrelevant low-frequency oscillations. Followed by that, apply an additional notch filter at 60Hz to remove noises incurred by the power line nearby the recording chamber.

  (ii) Normalization: In each trial, find the mean (μ) and standard deviation (σ) of all samples associated with that trial. Then, following the equation below, normalize the data for each individual trial.

$$X_{\text{norm}}(t) = \frac{X(t) - \mu}{\sigma}$$

  (iii) Stationarity: To make sure that recordings of each trial behaves as a stationary time-series, apply a first-order differentiation on each individual trial. In MATLAB, you can simply use the following command: `y = diff(x)`.

(d) LGC Analysis: By applying the LGC method on the data, plot the time-course of connectivity strength in both directions (i.e. V4 $\longrightarrow$ FEF and FEF $\longrightarrow$ V4). To calculate this time-course, you must employ the LGC method on smaller windows and slide that window from $t = 0s$ to $t = 4s$. For this analysis, you may use window size of 150ms. [2]

(e) Do you observe any increase in connectivity strength? How can you statistically assess the significance of your observations? Propose a method for evaluating your results and examine them by applying the proposed method on the results.

(f) Do you see any congruence between the results of PLV analysis and LGC analysis? Explain.

2: For this part, you are **not** required to implement the LGC method yourself. There are great MATLAB toolboxes such as FieldTrip and MVGC (GCCA mode) that you may use for this question.

3. Data Modality: Functional Magnetic Resonance Imaging

FMRI is one of the most recently developed forms of neuroimaging but the idea underpinning the technique - inferring brain activity by measuring changes in blood flow - is not new. The following account of an experiment performed by the Italian scientist Angelo Mosso can be found in William James' The Principles of Psychology, published in 1890:

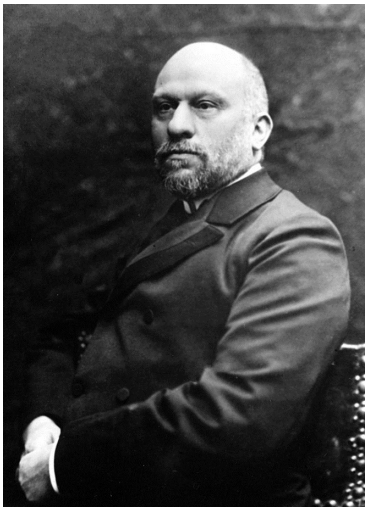
"The subject to be observed lay on a delicately balanced table which could tip downwards either at the head or the foot if the weight of either end were increased. The moment emotional or intellectual activity began in the subject, down went the balance at the head-end, in consequence of the redistribution of blood in his system..."

The reported success of this early experiment can only have been wishful thinking on the investigators behalf. But the suggestion that blood flow is coupled to neural activity was insightful. In 1890 the prevailing view was that since the brain is encased by the skull, local increases in blood flow and volume would be impossible. It was thought instead that any changes in blood flow were caused by systemic changes in blood pressure or cardiac output.

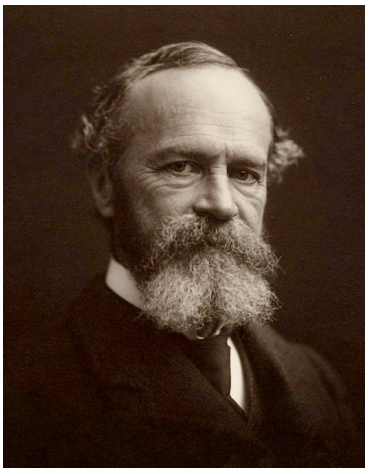
Toward the end of the nineteenth century, Charles S. Roy and Charles S. Sherrington provided the first evidence supporting a coupling between energy metabolism and blood flow in the brain. In their experiments, a monitoring device was placed on the brain surface of anesthetized dogs, which measured fluctuations in blood volume (Sherrington Starling kymograph, left). They showed that blood volume (and presumably flow) does change locally in the brain. However it was still unclear whether the brain itself was responsible for mediating these changes

It was not until 1948 in a seminal experiment measuring oxygen metabolism and blood flow in the brain that Seymour Kety and Carl Schmidt confirmed that blood flow in the brain is regionally regulated by the brain itself. They demonstrated that when neurons use more oxygen, chemical signals cause nearby blood vessels to dilate. The increase in vascular volume leads to a local increase in blood flow. At the time of these publications Kety and Schmidt were considered vascular physiologists more than brain scientists. Nevertheless the ability to measure CBF, a proven correlate of brain metabolism, opened up the remarkable possibility of studying brain function in humans.

The development of FMRI in the 1990s, generally credited to Seiji Ogawa and Ken Kwong, is the latest in long line of innovations, including positron emission tomography (PET) and near infrared spectroscopy (NIRS), which use blood flow and oxygen metabolism to infer brain activity. As a brain imaging technique



Angelo Mosso (1846 – 1910) is the 19th century Italian physiologist who invented the first neuroimaging technique ever, known as 'human circulation balance'



William James (1842 – 1910) was an American philosopher, historian, and psychologist, and the first educator to offer a psychology course in the United States. James is considered to be a leading thinker of the late 19th century, one of the most influential philosophers of the United States, and the "Father of American psychology". James is famous for helping to found psychology as a formal discipline, for establishing the school of functionalism in psychology, and for greatly advancing the movement of pragmatism in philosophy.

FMRI has several significant advantages:

- It is non-invasive and doesn't involve radiation, making it safe for the subject.
- It has excellent spatial and good temporal resolution.
- It is easy for the experimenter to use.

The attractions of FMRI have made it a popular tool for imaging normal brain function – especially for psychologists. Over the last decade it has provided new insight to the investigation of how memories are formed, language, pain, learning and emotion to name but a few areas of research. FMRI is also being applied in clinical and commercial settings. [1]

1: For more info refer to this link.

Although the statistical concepts behind fMRI analysis are similar to the ones of other modalities, data structures and methods used in this context are somewhat different (and some of the toolboxes are only available distribution). These methods are comprehensively covered in other coursewares and it seemed sufficient to just demonstrate a basic analysis via computation framework provided by Google (Colab). Problem description is provided within the attached python notebook file and further explanations are to be delivered in online workshops.

4. Submission

For each of your 3 questions, submit a single jupyter notebook (`ipynb`) or Matlab livescript (`mlx`). In any case, separate your codes for each section properly and make sure to annotate your codes with comments about your implementation. Keep in mind that your codes must be runnable on our machines with ZERO modifications.

For this assignment, there is no need for separate pdf report, although it is preferred that you export each of your handouts as a pdf file and attach to your original files. Respond to the questions in the livescript or notebook. The solutions should not include any explanation about the coding logic. It should contain your insights about the results.

Assignment deadline is announced via elearn modules.

If there was a question about EEG section refer to N. Darjani. For LFP analysis you might consult with R. Abolhasani. Refer to Y. Bagheri for fMRI questions.

A. Rapid Serial Visual Presentation

You walk into a bookshop and notice, among all the books on display, one whose cover design or title suggests that it might be of interest to you. So you pick it up, flex it somewhat and then riffle fairly quickly through its pages to get a first glimpse of its contents. Are there many pictures? What about equations? Probably in the course of four or five seconds you will know whether further, and more detailed, inspection is warranted. Because the action of riffling is essentially a rapid one, and the pages are viewed in sequence, we say that you are experiencing a Rapid Serial Visual Presentation of the pages or, for short, RSVP. Nowadays, of course, both computation and graphical processing are developed to such a degree that this means of presentation can be achieved by computer. What is more, many variants of RSVP can be contemplated that would be difficult or impossible to achieve by physical means. As a consequence, RSVP can support a wide variety of common and not-so-common tasks in a wide range of domains. it is useful briefly to identify certain aspects of RSVP that make it so attractive.

This book's exclusive focus on images that are presented in rapid succession is exemplified by the riffling of the pages of the book you picked up in the bookshop: you probably saw each page for about one-fifth to one-tenth of a second. Nevertheless, if your interest was in the History of Art, you would immediately recognise the Mona Lisa or one of Mondrian's distinctive paintings well within that short exposure. That's a very short time in which to do something useful! What's more, you didn't have to pay any conscious attention in order to identify those images of interest. That is why we refer to pre-attentive visual processing, of which more later. Therefore, two good reasons for exploring the potential offered by RSVP are that something of interest (either detailed or generic) can be identified very quickly and without conscious cognitive effort. For those two simple but profound reasons the potential of RSVP certainly deserves exploration. First, though, we need to ask a question about its use. [2]

In the literature, RSVP tasks that use image stimuli are designed either passively (without need for subject's response) or actively (in which the subject has to report something from presented stimuli or answer a question about identity of presented stimulus). Either way, it's a rather fast paradigm, consisted of brief stimuli presentation followed by a blank period in which a gray or black image is represented (or in some cases, frames of white noise).

B. Memory Guided Saccade

Memory Guided Saccade is a common task paradigm, generally used for working and short-time memory research. The task consists of a period of fixation at the center of a monitor screen, followed by a peripheral visual cue is presented on the screen. After that, a period of delay starts during which the subject maintains fixation while remembering the cue location (1s), and after the fixation point disappears, executes a saccadic eye movement to the remembered. Assuming that the subject is a non-human primate, performing precise saccade to stimulus location yields reward like drops of juice.

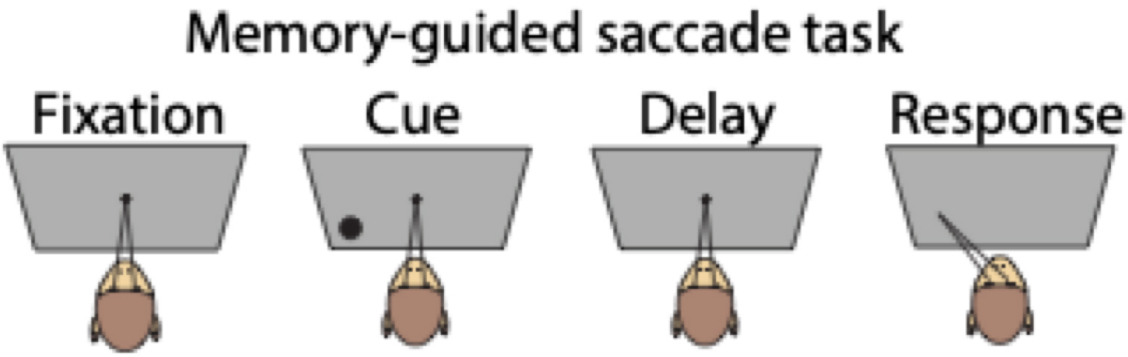


Figure 7: Memory-guided saccade (MGS) task paradigm.

References

[1] Nikolaus Kriegeskorte, Marieke Mur, and Peter A Bandettini. 'Representational similarity analysis-connecting the branches of systems neuroscience'. In: *Frontiers in systems neuroscience* 2 (2008), p. 4 (cited on page 2).

[2] Robert Spence and Mark Witkowski. *Rapid serial visual presentation: design for cognition*. Springer, 2013 (cited on page 10).

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