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Theoretical & Experimental Analysis of the Non Markov Parameter to Detect Low Frequency Synchronisation In Time Series Analysis

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Abstract— **A theoretical investigation into the behaviour of the Non-Markov Parameter is performed from a signal processing perspective in contrast to previous methodologies based on stochastic processes theory. The results indicate that the NMP can be regarded as an informational metric which is indicative of the degree of low frequency synchronisation in a complex system. These results have deep implications for physiological analysis of biological systems where the presence of sychronisation is often a marker of pathological functioning. The NMP measure is then applied to in vivo micro-electrode recordings from the subthalamic nucleus.**

I. INTRODUCTION

Treatment of Parkinson's disease beyond pharmacological therapy is moving towards a neurosurgical treatment known as Deep Brain Stimulation (DBS). In DBS the location of the candidate neural structures for stimulation are verified by Micro Electrode Recordings (MER) in addition to standard imaging techniques. The presence of the MER probes in deep brain structures of the Basal Ganglia (BG) in conjunction with an awake cognitive patient (as is required for the DBS procedure) provides a unique opportunity to perform linguistic tests to directly 'see' how certain neurons deep in the brain behave during cognitive processing.

Signal processing metrics are frequently employed in investigative signal analysis in conjunction with statistical tests to detect quantitative changes in the behaviour of neurons when the brain performs different cognitive processes. The task of understanding qualitatively what these changes suggest about the underlying biology of the neuronal behaviour is very important but more difficult. The key to the success of this hinges largely on having a good conceptual understanding of the metrics applied to the neural signals in order to link the quantified changes observed to the physiological changes which are veiled.

In recent research [1] the *unfiltered* neural signals from the subthalamic nucleus (STN) were analysed using the Non Markov Parameter (NMP) as a signal processing metric. The unfiltered data was analysed on the hypothesis that the 'neural noise' often discarded with spike sorting algorithms was removing important neural interactions vital for decoding the behaviour of STN neural clusters. The application of the unorthodox NMP metric was motivated largely by the failure of previous studies using classical signal processing metrics to show that the STN activity was modulated with the changes in linguistic stimuli [2]. The success of the NMP metric to detect these changes [1] where others had not is of interest.

The results from applying the NMP metric to the unfiltered STN MER signals indicated that the STN changes its neural firing patterns when presented with different stimuli but gave no indication about the nature of this different behaviour. The central problem was that the NMP was defined from the abstract fields of non equilibrium statistical mechanics and stochastic processes where it is very difficult to draw out a conceptual understanding of what the NMP changes physically represented. In effect, using the NMP significant changes were observed, but understanding what these changes were was unknown.

To provide more insight into the NMP existing theory is reviewed and then extended to show that the NMP can be related to standard spectral functions in signal processing theory. The link between the NMP and detection of synchronicity is then explored by analysing how the NMP varies for a system which acts as a simplified model with variable synchronicity. The conceptual understanding of the NMP is then applied to the results of neuro-linguistic experiments [1] to provide insight into the physiological changes in the behaviour of STN neurons when processing different linguistic tasks.

II. NMP METHODOLOGY

Consider a swarm of interacting objects with defined observables which *describe the phase space* of the system. The objects could range in complexity from the positions and momenta of the balls in a game of snooker after a break to the voltage and conductance of the ionic gating variables of the 10^{11} neurons in the human brain when an action potential fires. Often the evolution of all the system variables is not of concern. For example one may only care about the trajectory of the black ball in a game of snooker or the voltage changes of a cluster of neurons near an electrical probe. The evolution of these variables of interest ($\mathcal{G}_\mu$) are described by an integro-differential equation which is forced by a noise term $\mathcal{F}_\mu(t)$:

$$\dot{\mathcal{G}}_\mu(t) = \sum_\nu \Omega_{\mu\nu}\mathcal{G}_\nu(t) - \int_0^t \sum_\nu M_{\mu\nu}(t')\mathcal{G}_\nu(t-t')dt' + \mathcal{F}_\mu(t), \tag{1}$$

where $\Omega_{\nu,\mu}$ is the coupling matrix between the different observables of interest and $M_{\mu\nu}(t')$ is the abstract memory kernel which also allows coupling between the different observables of interest.

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The contribution of the neglected variables is buried in the memory kernel (convolution) and stochastic forcing terms. The convolution term causes the evolution of the observables to depend on their past history and is a general consequence of describing a history independent process as a history dependent process with reduced degrees of freedom [3]. The stochastic force can conceptually be understood as the contribution of the neglected variables which are not being observed, but will still be effecting the dynamics, perturbing the observables in a stochastic fashion.

For simplicity the evolution of a single observable is considered and the commutative property of the convolution operator is invoked. The coupling matrix is reduced to the scalar known as the first relaxation parameter λ. In addition the memory kernel is multiplied by the second relaxation parameter Λ:

$$\dot{\mathcal{G}}(t) = \lambda G(t) - \Lambda \int_0^t M(t-t')\mathcal{G}(t')dt' + \mathcal{F}(t). \qquad (2)$$

The relaxation parameters are normalisation factors defined in terms of the derivative of the normalized autocorrelation function of the observable c(t) and the memory function at time zero which satisfy:

$$\lambda = \frac{dc(t)}{dt}\Big|_{t\to 0^+}, \qquad \Lambda = \frac{1}{M(t)}\Big|_{t=0}. \qquad (3)$$

The problem with the ZM chain (2) is that the presence of the noise term makes the system a *stochastic* integro-differential equation which are mathematically difficult to solve and analyse. The equation can be reduced to a standard integro-differential equation by removing the noise term by projecting the observable at time zero, $\mathcal{G}(0)$, onto the evolution equation and averaging:

$$\frac{dc(t)}{dt} \;=\; \lambda c(t) - \Lambda \int_0^t M(t-t')c(t')dt', \qquad (4)$$

where:

$$\langle \mathcal{F}(t)\mathcal{G}(0)\rangle = 0 \quad , \quad \langle \mathcal{G}(t)\mathcal{G}(0)\rangle = c(t). \qquad (5)$$

Another problem with the ZM chain formalism is the difficulty in conceptually understanding the memory kernel. The second fluctuation dissipation theorem shows (in the one dimensional case) that the memory kernel can be written in terms of the autocorrelation functions of the stochastic force and the system observable [4]:

$$M(t) = \frac{\langle f(t)f(0)\rangle}{\langle \mathcal{G}(0)\mathcal{G}(0)\rangle} \qquad (6)$$

The consequences of this result are not immediately clear in the sense that it is difficult to translate knowledge about the autocorrelation structure of the neglected variables perturbing the relevant observables to knowledge about the system and observables of interest. This theorem is nonetheless of fundamental importance because it identifies that both the memory kernel and stochastic force, which arise from applying the ZM chain framework to the full (all observables considered) dynamical system, are intrinsically linked and not independent variables.

Numerical solutions of equation 4 (or its multi-dimensional analogues) have been applied to data sets as diverse as wind speeds to stock prices [5] in order to estimate the 'memory length' of these complex systems. Care must be exercised in interpreting the memory kernel as it has been shown [6] that it can generate periodic structure with no connection to the physical system in addition to the solution depending on the discretisation process. It has also been shown [6] that the ZM chains form a true subclass of Auto Regressive Moving Average models, which helps indicate how the ZM chains analyse a system in a linear signal processing framework.

A different approach to applying ZM chains to interpret data sets from complex systems has been undertaken [7]. In this approach a metric, the NMP, is established to indicate when a complex system is operating in different states. This metric [1] has successfully been applied in biological systems to show the difference in cardiac R-R interval behaviour between a healthy heart and one undergoing myocardial infarction [8]. The NMP is defined as:

$$NMP = \lim_{\omega\to 0}\frac{\mathcal{F}\left[c(t)\right](\omega)}{\mathcal{F}\left[M(t)\right](\omega)} = \frac{\int_{-\infty}^{\infty} c(t)dt}{\int_{-\infty}^{\infty} M(t)dt}. \qquad (7)$$

It can be seen that the NMP is a ratio of the 'L_0 norms' of the autocorrelation function and memory kernel. The NMP will be maximised for a memory kernel described by the Dirac delta distribution at zero (conditional on the autocorrelation function not also being described by a Dirac delta distribution). The structure of this memory kernel (i.e. no memory except at zero time) indicates that the NMP is maximal for regular Markov processes. More generally it can be shown [5] that the NMP is the ratio of the correlation time of the system to the correlation time of the random forces acting on the system and an "informational measure of chaosity and randomness" [8]. In the next section the NMP described by equation (7) will be expressed in simpler signal processing terms using equation 4.

III. NMP Results

In this section frequency domain analysis is applied to equations (4) and (7) to express the NMP in terms of well known spectral functions. From the Wiener-Khintchine theorem it is known that the Fourier Transform (FT) of the normalised autocorrelation function is simply the normalised Power Spectral Density (PSD). It is less clear what the FT of the memory function represents. Understanding this is key to understanding the NMP in a signal processing framework.

In order to determine a functional form for the memory function in frequency space we take the FT of both sides of the 1-D ZM chain (equation 4). In taking the FT of these signals there is an immediate problem: the time series observed from any signal probe must be causal (i.e. only exist from the time the recordings start at t = 0 to some future finishing time t = T) but the FT is defined over all positive

[1]This article looked at the full NMP spectrum, not just the zero frequency value

and negative time. In order to remedy this the Fourier kernels are multiplied by the Heaviside function centered at zero:

$$\mathcal{F}\left[\frac{dc}{dt}\theta(t)\right] = \lambda\mathcal{F}\left[c(t)\theta(t)\right] - \Lambda\mathcal{F}\left[\int_0^t M(t-\tau)c(\tau)\theta(t)d\tau\right]. \tag{8}$$

These Fourier transforms will be considered individually:

$$\mathcal{F}\left[\frac{dc(t)}{dt}\theta(t)\right](\omega) = i\omega\mathcal{F}\left[c(t)\theta(t)\right] - 1, \tag{9}$$

Where integration by parts has been used and it is recognised that the definite integral component vanishes, and then the sifting property of the Dirac delta distribution has been applied.

The convolution term can be determined by writing the double integral as the product of two FT with an additional Heaviside function in the kernel, using the variable substitution $p = t - \tau$, and then applying the convolution theorem:

$$\begin{aligned}&\mathcal{F}\left[\Lambda\int_0^t M(t-\tau)c(\tau)d\tau\theta(t)\right](\omega)\\ =\ &\Lambda\cdot\mathcal{F}\left[M(p)\right]*\mathcal{F}\left[\theta(p)\right]\cdot\mathcal{F}\left[c(\tau)\right]*\mathcal{F}\left[\theta(\tau)\right]\end{aligned} \tag{10}$$

Applying these FTs and Re-arranging the ZM chain (4) for the memory kernel term yields:

$$\begin{aligned}&\mathcal{F}\left[M(p)\right](\omega)*\mathcal{F}\left[\theta(p)\right](\omega)\\ &= \frac{1}{\Lambda}\left(\lambda - i\omega\right) + \frac{1}{\Lambda}\cdot\frac{1}{\mathcal{F}\left[c(\tau)\right](\omega)*\mathcal{F}\left[\theta(\tau)\right](\omega)}\end{aligned} \tag{11}$$

This equation can be simplified by using the following identity [9]:

$$\mathcal{F}\left[f(t)\right](\omega)*\mathcal{F}\left[\theta(t)\right](\omega) = \frac{1}{2}\left(F(\omega) - i\mathcal{H}\left[F(\omega)\right](\omega)\right), \tag{12}$$

where $\mathcal{H}\left[F(\omega)\right](\omega)$ is the Hilbert transform of the Fourier transform of the signal. Applying this identity to (11) and taking the real component of the memory function yields:

$$M(\omega) = \frac{2\lambda}{\Lambda} + \frac{4}{\Lambda}\left(\frac{P(\omega)}{|V(\omega)|^2}\right). \tag{13}$$

By substituting equation (13) into equation (7) the NMP can be expressed as;

$$NMP = \lim_{\omega\to 0}\frac{1}{2}\left(\frac{\Lambda P(\omega)|V(\omega)|^2}{\lambda|V(\omega)|^2 + 2P(\omega)}\right). \tag{14}$$

The expression $|V(\omega)|^2 = P(\omega)^2 + \mathcal{H}\left[P(\omega)\right]^2$ is known in communications theory as the square of the Complex Envelope (CE) [10], which as the name suggests, envelopes the function. PSDs which are monotonically decreasing or flat (i.e. white noise) will be perfectly tracked by the CE of the PSD. Conversely for PSDs which oscillate with local maxima and minima (i.e. exhibit synchoronisation frequencies) the CE will not perfectly track the PSD in these regions.

Hence the NMP defined in [8] can be understood from equations (13) and (14) as a measure of how much oscillatory behaviour occurs at low frequency. For flat spectral behaviour near zero the NMP will be approximately unity, for oscillatory spectral behaviour near zero the NMP will be larger than unity. In the next section the conceptual understanding of the NMP is applied to the archetypal example of the forced harmonic oscillator to explore how the NMP varies with spectral parameters and to identify a possible link to the detection of synchronicity.

IV. Analytical Application of NMP Results

In this section of the paper the NMP for a damped harmonic oscillator driven by white noise is analysed. The natural frequency for this one dimensional oscillator can be considered as the frequency that the components of a multi-dimensional complex system synchronise at, with the damping factor indicating how sharply the components synchronise about this frequency. A particularly salient example for this paper is to consider this as a model for the aggregate output electrical behaviour of a collection of neurons.

The autocorrelation structure of a damped harmonic oscillator driven by white noise is given by [11]:

$$c(t) = e^{-a|t|}cos(\omega_0 t). \tag{15}$$

Where a is the damping constant and ω_0 is the natural frequency. The Laplace transform of the autocorrelation function is given by:

$$C(s) = \mathcal{L}\left[e^{-a|t|}cos(\omega_0 t)\right](s) = \frac{s+a}{(s+a)^2+\omega_0^2}. \tag{16}$$

The memory kernel as a function of time can be determined by taking the Laplace transform of both sides of equation (4), applying the convolution theorem, recognising that the normalised auto correlation function is unity at time zero, re-arranging for the memory kernel and taking the inverse Laplace transform of the result:

$$M(t) = \mathcal{L}^{-1}\left[\frac{1}{\Lambda}\left((\lambda - s) + \frac{1}{C(s)}\right)\right], \qquad t \geq 0. \tag{17}$$

Using equations (16) and (17) the memory kernel of the white noise driven harmonic oscillator can be expressed as:

$$M(t) = \frac{\omega_0^2}{\Lambda}e^{-a|t|}. \tag{18}$$

This immediately shows that the relaxation parameters λ and Λ are given by the damping constant and natural frequency squared respectively. The normalized PSD of this process is given by the FT of the normalized autocorrelation function (equation 15):

$$P(\omega) = \frac{a}{a^2+(\omega_0-\omega)^2} + \frac{a}{a^2+(\omega_0+\omega)^2}. \tag{19}$$

The memory kernel in frequency space is given by taking the Fourier transform of equation (18):

$$M(\omega) = \mathcal{F}\left[e^{-a|t|}\right] = \frac{2a}{a^2+\omega^2}. \tag{20}$$

Using (7), (19) and (20) The NMP is given by:

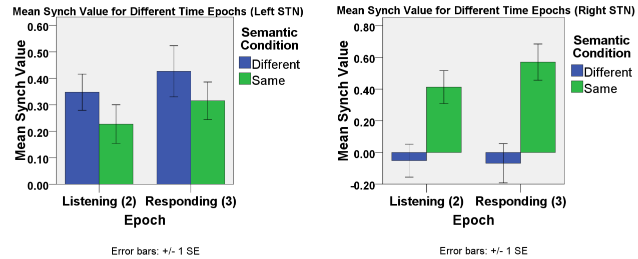
$$NMP = \lim_{\omega\to 0}\frac{P(\omega)}{M(\omega)} = \frac{a^2}{a^2+\omega_0^2}. \tag{21}$$

Equation (21) shows that the NMP depends on both the system natural frequency and damping constant. The natural frequency is the location of the local maxima in the PSD and thus the closer this is to zero the greater the difference between the PSD and its CE, giving a larger NMP, leading to unity in the limit of $\omega_0 = 0$. The heavy damping regime can be explained by the damping causing the PSD to smear out, allowing more accurate tracking by the CE, leading to an NMP of approximately unity. In the neural analogy this would correspond to the case of all the neurons in the cluster firing at a range of different frequencies from one another. The zero damping case is trivially explained by the PSD being zero everywhere except at ω_0. In the analogy this would correspond to all of the neurons perfectly synchronising by firing at the same specific frequency ω_0. It is important to note that this zero damping (perfect resonator) case is in agreement with the result that strongly non-Markov processes will have a NMP $<< 1$ [8]. The following section outlines the experimental methodology of the neuro-linguistic tests which were analysed using a variant of the NMP as a signal processing metric.

V. Experimental Methodology

The complete description of the experimental set up and methodology used in this research is provided in [1]. In essence the experiments performed were based on seeing whether the electrical behaviour of the STN, as determined by MER probes, was correlated with the patients behaviour when presented with pairs of words which were either semantically similar (n=14) or different (n=14). The words forming the pairs were drawn from either household items or animals. Thus ‘cat’ and ’dog’ would be considered semantically similar word pairs whereas ’cat’ and ’chair’ would be considered semantically different word pairs. The auditory recordings of the word pairs were presented to the patient, who responded manually using his left index finger to indicate which category the word pair belonged to. The electrical behaviour of the STN was analysed under the additional permutations of the two brain hemispheres (the left and right sides were considered in separate trials) and three time epochs. The first epoch was before the word pair was given for baseline activity, the second epoch was immediately after the word pair was given during the cognitive processing of the stimuli and the third epoch was during the motor response to the stimuli. The MER signals were taken from the STN of 7 patients (all male, non senile and right handed) comprising 666 individual trials sampled at 24 kHz which were analysed in an unfiltered form off line.

Experiments of this form allow for an examination of whether the BG may be involved in semantic processing and decision making in addition to its well known motor modulation functions [12]. One of the unique features of the current research is the use of highly localised MER recordings in contrast to the indirect methods of subcortical activity such as functional Magnetic Resonance Imaging [13]. It is important to note that [2] used MER of the BG, showing that the STN activity was not modulated with the changes in linguistic processes in contrast to recent results



(a) Left STN. No significant difference (b) Right STN. significant difference

Fig. 1. Mean Synch values *during* and *after* (Epoch 2 and 3) *same* and *different* word pair associations from the left and right STN MER recordings. Notice that there is only statistically significant differences between the semantic condition for the right brain.

which suggested a statistically significant change when using the NMP signals processing metric [1].

In addition to using highly localised MER probes the application of exotic complexity based metrics to the unfiltered neural signals is unique. Most waveform analysis is based on a subjective threshold of the recorded signal followed by ad hoc analysis of resultant inter-arrival times [14], [15]. For example, mean firing rates and a burst index (calculated by dividing the burst firing rate by the mean firing rate) were considered in [16]. The signal analysis in this experiment simply required the unfiltered MER signals which were fed into the NMP signal processing metric.

The NMP of equation (7) could not be employed directly in the statistical analysis because it violated the critical requirements that the data be normally distributed. In order to remedy this an optimal Box-Cox (power law) transformation was applied to the data of the form:

$$\text{Synch} = -2\left(\frac{1}{\sqrt{\text{NMP}}} - 1\right). \qquad (22)$$

The synch metric was applied to the MER signals and the resulting data was analysed using a Linear Mixed Model (LMM) to determine if there were any statistically significant interaction effects between the three fixed factors of brain side (left or right), semantic condition (same or different) and time epoch (before, listening and responding to stimulus). The LMM was set up such that brain side, semantic condition and time epoch were modeled as fixed effects whereas the patients were modeled as random effects and significance of interaction was set at the ($p < 0.05$) level. Statistically significant interaction effects were observed between all two and three way interactions. Interaction effects of interest were then explored with planned contrasts. The next section focuses on interpreting the results of the analysis of interaction between the brain sides and the listening and responding epochs using the conceptual understanding of the synch metric.

VI. Experimental Results

The interaction of the neural behaviour with the brain side and presentation of linguistic stimuli during the different epochs were analysed with the synch parameter using the experimental methodology described in the previous section. In particular, figure 1 shows post-hoc contrasts comparing the mean synch values with standard error as uncertainties between the listening and responding epochs on both brain hemispheres. The change in mean synch value was shown not to be statistically significant between the listening and responding epochs for the left brain, but statistically significant ($p < 0.01$) for the right brain by unpaired t-tests. Using the developed conceptual understanding of the NMP (and hence synch) it can be seen from figure 1 that the spectral firing pattern in the STN on the right side of the brain appears to lose a low frequency synchronisation and display either a monotonically decreasing or flat PSD at low frequencies when changing processing from identifying semantically similar to different word pairs. To obtain insight into this behaviour it is important to note that the in the case of a maximal NMP (minimal synch) value the memory kernel will typically be a Dirac delta distribution. By the second fluctuation-dissipation theorem the stochastic noise term in equation (2) will be a white noise process. Thus behaviour of the observable (in these experiments the aggregate output voltage) reduce to the well studied Ornstein-Uhlenbeck (OU) process. The probability evolution for an OU process is known to be a time dependent Gaussian distribution [17]. The fact that information entropy is a maximum for a Gaussian white noise process [18] may show that the low synch value is detecting the cluster of neurons firing in a manner to maximise the information entropy. This would suggest that the brain requires more information to identify semantically different word pairs compared to semantically similar word pairs.

The problem with this hypothesis is that there is little evidence that suggests that more information is required to distinguish different words than to identify similar words. From a mathematical perspective a fundamental problem is that this logic cannot be extended to determine the probability evolution for a general memory function which will be forced by a colour correlated process. A second mathematical problem is that the statement of maximal information entropy is particularly vague, not withstanding that information entropy places upper limits and not values on information transmission [18]. Thus these results need to be placed on firmer mathematical grounds, extending the probability evolution of the observable to the general case and the link to information entropy should be rigorously explored.

The discrepancy between these results and those discussed in [2] is most likely a consequence of using the synch metric. The MER signals in [2] were analysed in a linear signal processing framework by comparing whether the mean peak voltage and latency time observed between semantically different word pair experiments was significant ($p \leq 0.05$ level). These results suggest that if STN is involved in lexical processing its influence is extremely subtle, as evidenced by the need for such highly exotic parameters as the synch metric to see its effects.

VII. Conclusion

The NMP parameter has been analysed using frequency domain techniques to show that it can approximately be regarded as a measure of how much a complex envelope varies from its PSD at low frequencies. This result indicates that the NMP may be a suitable metric for detecting low frequency synchronisation in complex systems. This conceptual understanding of the NMP has been applied to deep brain structures of humans during neurolinguistic tests to suggest that the neurons in the right side STN of the brain tends to synchronise at low frequencies when presented with semantically similar word pairs. The detection of STN unfiltered signal changes with the NMP metric has broad consequences in neurophysiology and clinical neuroscience where significant effort is applied through multiple probe configurations and post processing techniques to remove the 'neural noise' which may in fact have valuable information content.

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