

PONTINE NUCLEUS AUDIO STIMULI DETECTION & MODELING FOR BRAIN MACHINE INTERFACE REHABILITATION OF CONDITIONAL LEARNING

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ABSTRACT

In order to establish a brain-machine-interface (BMI) system that rehabilitates damaged cerebellum function of discrete motor learning, the detection of conditional and unconditional stimuli (CS and US) onset times based on electro-physiology recordings analysis is necessary. These signals are relayed through brainstem areas called Pontine Nucleus (PN) and the Inferior Olive (IO) respectively. In this paper we focus on the model based analysis of the PN and compare the expected model performance with the observed one with real samples.

We suggest a model of multi-unit (MU) activity as filtered inhomogeneous Poisson pulses of evoked activity contaminated by homogenous spontaneous activity and thermal noise (Filtered Poisson-Poisson-Gaussian model). By assigning the likelihood into the generalized log likelihood test (GLRT), we show that the best expected feature is energy detection.

The model parameters were estimated based on the recorded peri-stimuli-time-histogram (PSTH) by chi-square goodness-of-fit minimization. Monte Carlo simulation showed that the thermal noise can be neglected in respect to the spontaneous activity and also predicted the order of the observed empiric detection performance in terms of detection probability and area under the receiver operation characteristic (ROC) curve (AUC).

Index Terms— Brain Machine Interface, Neural Decoding, Brainstem, Classical Conditioning, SVM, Electrophysiology, Multi Unit, Poisson Model, GLRT, Detection, ROC, AUC, Simplex, Goodness-of-fit.

1. INTRODUCTION

Brain machine interfaces (BMI) are systems that enable the interaction between a living brain tissue and an external man-made-machine. The endeavor of the field is clinical rehabilitation application [1].

There has been much progress in the field of BMI on the last decade [1] which is mainly aimed at two periphery nervous system applications: sensory rehabilitation (e.g. bionic eye research) and motor control rehabilitation (e.g.

limb prosthesis [2]). However, our research [3] is novel as we aim towards rehabilitation of a learning function in the central nervous system.

The *ReNaChip* project [3] aims to tackle conditioned motor learning of discrete motor response as it considered being simple relative to other cognitive tasks [4; 5]. Specifically, it focuses on eye-blink conditioning by an auditory tone with an animal model (rats). In order to rehabilitate a malfunction cerebellum circuit, first we need to peak up the signals from the brainstem areas of the inputs and deliver them into the biomimetic chip that will reproduce the natural missing motor response (see Fig. 1). Here we focus on the estimating the onset time of the CS and US from the electro-physiological data (Fig 1).

In this paper we suggest a Filtered Poisson-Gaussian model for the measurements and derived an optimal detector to find the discrimination performance sensitivity to the model's parameters using Monte Carlo simulations. Then, we estimated the model parameters which fit the observed. This allowed us to compare performance of feature based [5] detection of the real data. Moreover we could estimate upper bounds on performance from the model and compare it to real data.

In section 2 we present the proposed model while in section 3 we derive its upper bound for performance in the homogenous or short time non-homogenous cases together with the necessary performance for our application. Section 4 describes the results of the empiric detection performance on real data (using features based supervised classifier), and compare it to simulation of the model. In section 5, we summarize and discuss the results.

2. MODELING OF THE MEASURED SIGNALS

In the *ReNaChip* project, the data is collected by a multiunit electrode, due to the requirement for robustness and reliable operation over a long period (which supports possible clinical use). Oppose to single unit electrodes that aim to capture activities of a single or few neuron, such electrodes collect data from several neurons and integrate over their activities.

We suggest to model the multi unit response activity $r(t)$ as the sum of three components $r(t) = n(t) + s(t) + e(t)$,

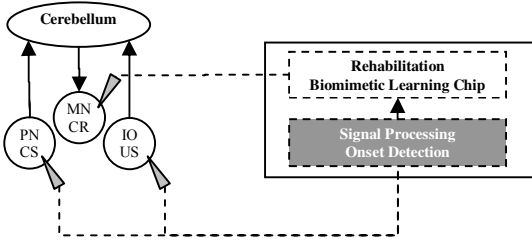


Fig 1. Block Diagram of discrete motor learning rehabilitation in the cerebellum. The CS and US are naturally relayed into the cerebellum from the PN and IO respectively (solid lines). Once rehabilitation takes place, electrodes interfaces collect the extra cellular signals (dashed) into an "onset detection" algorithm (gray). The detected onsets time tags are then propagated into a learning algorithm that mimics the cerebellum circuit. The output of the prosthesis drives the appropriate motor (M) neuron to produce a conditional desired response (CR).

where: $n(t) \sim N(0, \sigma_n^2)$ is the thermal noise; $s(t) = \sum_i \delta(t - t_i^s) * p(t)$ is the spontaneous baseline activity, modeled as a filtered homogeneous Poisson process with pulse shapes $p(t)$ and time events t_i^s with rate λ_s ; and $e(t)$ is an evoked response, modeled as a filtered inhomogeneous Poisson process with time events t_i^e with rate $\lambda_e(t - t_i)$, triggered to the stimuli onset (Fig 2).

In MU recording, the signals is usually assumed to be multiplied with a multiplicative noise, thus it is a common preprocessing procedure to rectify the recorded signal in order to enable incoherent integration. We chose to simplify our model and thus disregard this noise source. We claim that a similar result could be derived for multiplication noise, but this is currently under investigation

The pulse shape $p(t)$ served as an approximation to a biological spike and is modeled as a sum of two Gaussians, one STD apart with relative weights of 1 and -0.3 (Fig 3).

We denote the Rate Ratio as the ratio between the evoked and spontaneous rates $\eta_{rate} = \lambda_e / \lambda_s$ and the SNR as the signal to noise ratio of the spike power relative to the noise floor.

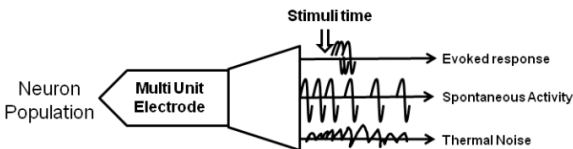


Fig 2. A cartoon schematic of the multi unit activity toy model (filtered Poisson-Poisson-Gaussian). The recorded signal is a sum of the evoked response which is a stationary triggered inhomogeneous filtered Poisson process contaminated with spontaneous activity (homogenous Poisson process) and thermal noise (Gaussian noise).

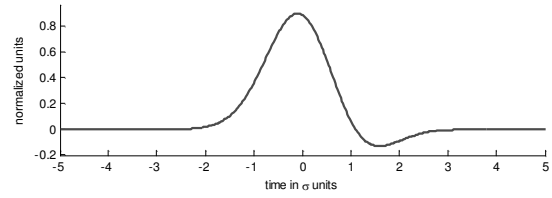


Fig 3. Model's pulse shape was composed of two Gaussians $p(t, t_0) = G(t, t_0, \sigma) - 0.3G(t, t_0 + \sigma, \sigma)$ where each was defined as $G(t, t_0, \sigma) = \exp[-(t - t_0)^2 / 2\sigma^2]$

3. OPTIMAL STIMULI DETECTION

According to Hero et al [7; 8], the likelihood function for the time of arrival time τ for our model equals to an expression that can be interpreted as process where the signal is first correlated with the pulse shape (matched filter), then emphasized using an exponential (weighted with an SNR factor) and finally correlated it again with the rate profile function of the evoked response (1).

$$L(x | \tau) = e^{\left\{ \int_0^T [\exp(\alpha x(t) * p(-t) - \beta) - 1] \lambda_e(t - \tau) dt \right\}} \quad (1)$$

The α, β constants relate to the SNR ratio.

We used (1) to find the statistical sufficient feature for detection basing on GLRT. We assume that the rate profile function is constant in short time scales such that are needed for online detection. Hypothesis H_0 is spontaneous activity (λ_s) while H_1 stands for the hypothesis that the rate is higher and caused by the evoked response ($\lambda_e + \lambda_s$):

$$GLRT = \log \frac{L(x | \tau, H_1)}{L(x | \tau, H_0)} = \int_0^T \left[e^{(\alpha x(t) * p(-t) - \beta) - 1} \right] \lambda_e dt$$

The GLRT is proportional to the integrand and thus to the exponent power which is just the mean signal value:

$$GLRT(H_1, H_0 | \tau) \propto \int_0^T x(t) * p(-t) dt \quad (2)$$

The last approximation (2) indicates that the GLRT detector is simply the pulse shape match filter output. Note that usually in the pre-process stage the signals are filtered with a pass band at spike-band frequencies (1-3 KHz). The latter actually approximates the pulse-shape match filter, so the best feature would become just the mean value of the rectified filtered signal is spike-band. This result was observed by feature based detection (see Results).

The constraint in the PN's onset detection is that the false alarm rate (FAR) is considerably smaller than the true detection rate (TDR) and that the detection latency will be much smaller than the inter-stimuli-interval. This condition is necessary for the learning of the higher hierarchy in the chip since otherwise, he cerebellum will have no information about the association between the CS and the US or the US will not be associated with the CS.

The FAR can be expressed in terms of FA probability as $FAR = P_{FA} f_{step} = P_{FA} / \tau_{step}$, where τ_{step} is the offset between successive testing for onset existence. Similarly, the TDR can be related to the true detection probability $TDR = P_d / ITI$, where ITI is the inter-trial-interval time. Thus, the constraint can be transformed into probability terms such as: $P_{FA} \ll \tau_{step} / (ITI(1 - P_{MD}))$ and after assigning the problem specific values, we get $P_{FA} |_{P_{MD} \sim 1, \tau_{step} \sim 0.1 \text{ sec}, ITI \sim 10 \text{ sec}} \ll 1\%$.

We have built a feature extraction analysis and testing framework that allows us to evaluate the performance of different features in different scenarios and settings in a synchronous scenario (known possible onset times). The full details of the framework are described in a paper under preparation [9]. In the following we demonstrate the results using measurements from the PN only and we compare them with the model prediction.

4. RESULTS

We used grid search together with Simplex [9] search for estimating the different parameters setting (see model description above) to find parameters settings that minimize the χ^2 goodness-of-fit [10] error in several (6) time regions of the model's PSTH (3 STD threshold spikes and raw waveform) relative to the observed one. We are aware that the fit is ambiguous, since different parameter setting will produce similar PSTHs (especially η_{rate} & η_{amp} can commute). The problem of estimating the model parameters in a Maximum Likelihood (ML) fashion is under investigation. Fig 4 describes the details of the best fit parameter set found compared with a real data example and shows high resemblance in value distribution both for averaged waveform and spike rate.

We investigated the performance of the GLRT detector on different SNR and rate-ratio scenarios and discovered first, that the thermal noise has little effect above SNR of 5dB and secondly, that the current signal model parameters are close to a cut-off point in the performance curve both in SNR and in rate ratio. This can be seen clearly since both the ROC area (AUC) and probability of detection (P_d) at low false alarm ($P_{FA} \sim 10^{-3}$) fall dramatically below $\eta_{rate}^{cutoff} \sim 4$ (Fig 5).

The cutoff value in rate ratio and SNR dimensions are of the same order of magnitude as of the estimated model parameters that fit real data (4 and 5dB respectively). Moreover, the analysis also predicts similar detection performance to empiric estimation in the real data (Fig 6).

This finding can also explain the large variability we saw in the real data set (Fig 6). If different samples are different slightly in parameters, it influences the detection performance dramatically around the cut-off working point.

Additionally, the best feature in the PN was found to be a simple mean and standard deviation of the spike-band waveform. This was expected from the multi-unit model detection performance analysis we derived.

The summary of performance of the different features, setting and the benefit of multi electrode array can be found in [3; 9].

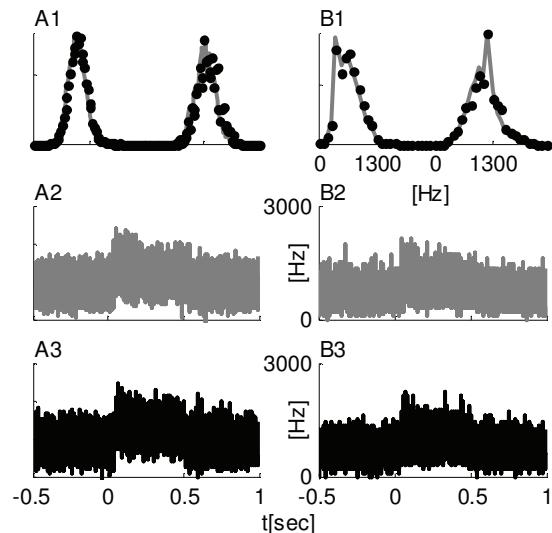


Fig 4. Model fit of the averaged response waveform (A) and spike (threshold over 3 STD) PSTH (B). The top panel (1) shows the data value distribution (black dots) and the model fit (solid gray line) within response (left) and outside (right) ($R^2 \sim 0.85$). The middle panel (2) shows the averaged response of the model, compared with the real data (typical best case) at the bottom row (3). The model parameters were set to minimize the chi-square goodness-of-fit (panel 1) by a grid search and Simplex algorithms [9] and were finally set to sampling rate ~ 11.11 KHz, response duration ~ 0.5 sec, SNR ~ 5.2 dB, evoked rate ~ 224 Hz, $\eta_{rate} \sim 3.9$, $\eta_{amp} \sim 1.2$ and pulse duration ~ 0.6 msec.

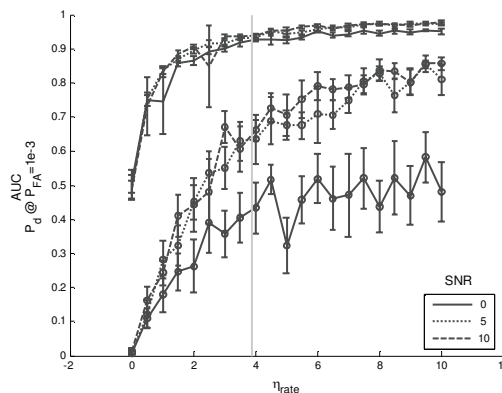


Fig 5. Performance curve of model simulation measured by AUC (no markers) and P_d at low P_{FA} (circles) as function of rate ratio and for different SNR (0-10dB). Performance has a cut of both in the SNR dimension (below 5dB) and rate ratio dimension (below 4) where the performance slope is steep. The best fit model rate ratio (vertical gray line) falls around these cut-off values, thus predicting high variability in detection performance between samples. Moreover, it predicts high AUC values of around 0.9 while P_d around 0.5. This performance values confirms the observed empiric detection (see Fig. 6). Error bars are STD over 10 repetitions.

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7. REFERENCES

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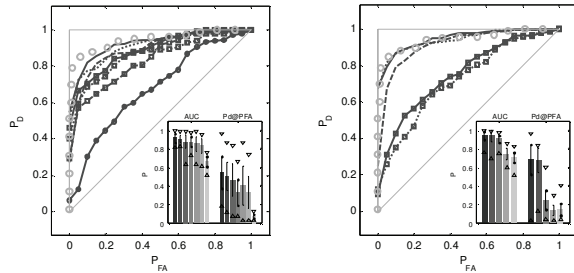


Fig 6. PN spike-band features receiver operation curve (ROC) averaged over (N=5) samples for different features (left panel) and averaged over (K=7) features for different samples (right). The grey circle represent the model best-fit ROC of the best case sample. The area under curve (AUC) and the probability of detection at low false alarm are presented on the bottom right panel as bar plots for each ROC trace. Due to high amount of details we present the error bars only on these last measurements where the bar represent the mean, the error bar the standard deviation and the small triangle the minimum and maximum value respectively. The features on the left are ordered in descending order (AUC wise) when the best was the waveform mean-value and standard deviation (as was expected from our derivation). The features used (from best AUC to worst) were (1) mean and standard deviation, (2) cumulants, (3) inter-spike-interval distribution (4) mean & standard deviation of spike counts, (5) power spectrum density estimation with 32 bins, (6) same as (5) but with 64 bins, (7) distribution of values.

5. DISCUSSIONS & SUMMARY

The MU activity model proposed here was fitted to real PN recording via comparison of the simulated and real PSTH value distribution, using goodness-of-fit test with high correlation between model and data distribution values ($R^2=0.85$). The feature-based detection showed that the best feature (tested) is the mean and STD which related to mere energy detection. This coincided with our derivation of the GLRT rule of two different rate, which showed that the mean is statistical sufficient for testing between different rate hypothesis. Moreover, simulation of the optimal detector on generated model samples, showed similar detection performance as well as predicting high within sample performance variance due to the fact that the model parameters are close to cutoff point in performance.

Therefore, we believe that no improvement of the detection performance in the given measurements can be done based on signal processing alone. Improvement of the detection performance, however, can be done by the usage of multi-array as we show in [8]. Additionally, we plan to consider reverse-correlation techniques in order to learn what is the 'best stimulus', that creates the most energetic response (e.g. evoke with white noise auditory signal, and use system identification and de-convolution techniques in order to learn what is the matched input). Finally, deriving GLRT detector for a model that includes multiplicative noise might help in offering a better detector and maybe higher performance bound.