NEURAL CELL TYPE RECOGNITION BETWEEN GLOBUS PALLIDUS EXTERNUS AND GLOBUS PALLIDUS INTERNUS BY GAUSSIAN MIXTURE MODELING

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ABSTRACT

This paper proposes a new application of Gaussian Mixture Modeling (GMM) for neural cell type classification between globus pallidus externus (GPe) and globus pallidus internus (GPi). Our work is motivated by the results of previous research in which different neural cell types could be identified by their discharge patterns. It is critical for surgeons to distinguish between these two cell types to identify brain nuclei during the procedure known as a pallidotomy, a treatment for Parkinsons disease. Currently, skilled surgeons rely on discharge patterns converted to sound. In this study, performance evaluations are conducted based on a labeled database recorded during previous neural surgeries. The GMM achieves better than 92% correct recognition using 10-second segments, which demonstrates the best performing classifier to date.

1. INTRODUCTION

Parkinson's disease is a progressive neurological disorder that results from degeneration of neurons in a region of the brain that controls movement. This degeneration causes the movement impairments that characterize the disease. A pallidotomy is a neuro-surgical treatment which may reduce the symptoms of the disease dramatically [1]. During the surgery, accurate targeting is required to precisely localize the region of interst – the globus pallidus internus (GPi) [1]. Since different parts of the brain consist of neurons with different firing patterns, it is reasonable to attempt to localize the region by analyzing microelectrode recordings [1, 2]. Conventionally, professional neurologists listen to the neural recordings and make decisions based on their experience. This subjective method is less than ideal in that it is difficult to train new practitioners and it often suffers from lack or repeatability. In this paper, we introduce a recognition framework using Gaussian Mixture Modeling (GMM) to accomplish objective neural cell type classification.

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Objective classification has two specific tasks: (1)*Neural spike detection from a noisy recording environment*. There is much literature in this area which proposes a number of approaches ranging from on-line real-time algorithms with higher detection speed [3] to off-line schemes which are time-consuming but more accurate [4]. In this paper we present a novel on-line neural spike extraction method, which achieves a good trade-off between speed and accuracy. (2) *Identification of the type of the neural cell which generated the spike train*. It has been proposed by physiologists that neurons convey information mainly through timing within their spike trains (i.e., the intervals between neural spikes). Previous research has reported failure in cell type identification based on spike shapes [5]. Therefore, we use only features that contain timing information. The most difficult task in neural cell type classification for the pallidotomy is differentiating between cells from the globus pallidus internus (GPi) and the globus pallidus externus (GPe). Generally speaking, cells in GPe fire in a relatively "tonic" way while GPi cells fire more irregularly. In this paper, all experiments are evaluated based on neural signals recorded from GPe or GPi.

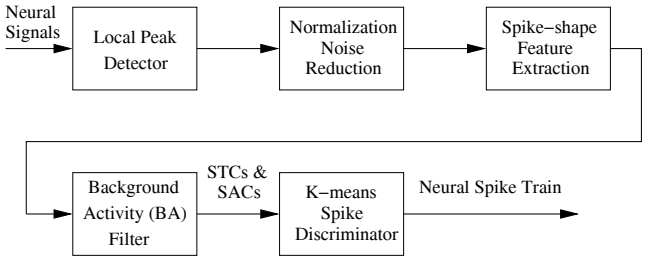

Fig. 1. The diagram of the neural spike detection algorithm.

The reason for the selection of the Gaussian Mixture Model (GMM) [6, 7] is motivated by its excellent ability to model complex probability density functions. Further more, we were prompted by certain similarities in cell type

classification and speaker identification. Using a feature set extracted from spike trains, the GMM can provide a good trainable probabilistic model of the underlying cell type.

The rest of paper is organized as following. We introduce the neural spike detection algorithm in section 2. In section 3, the GMM model and feature set are described. Experimental evaluation is presented in section 4, where we compare the performance of a GMM, a uni-model Gaussian model, a VQ codebook, and a Radial Basis Function(RBF) neural network. Finally, we conclude with possible continuations to our work.

2. NEURAL SPIKE DETECTION

A segment of a neural signal recording usually consists of four components: (1) The spikes from the target cell (STC), (2) the spikes from adjacent cells (SAC), (3) background activity (BA), and (4) microphonics and other noise artifacts (e.g., the patient talking or electrical noise from medical equipment). The objective is to isolate the first component (STC) from the others. The approach used in our framework can be described as a cascade of a "local peak" detector, a block of normalization and noise reduction, a spike-shape feature extractor (note that features used here are different with ones in GMM training), a background activity filter, and a spike discriminator. The diagram of our detection algorithm is shown on the Figure 1.

As shown in the diagram, we first define a sample in the input segment as a "local peak" if its amplitude is beyond that of its 79 neighbors (39 samples before it and 40 after it). All these local peaks are found after the original data block has gone through the local peak detector. After the second step, depicted as the block named normalization and noise reduction, the input data is separated into small "clips." Every clip is a segment of length 80 and there is one local peak at the 40th sample. These clips are saved as raw material for subsequent spike-shape feature extraction. One clip may be STC, SAC, background activity (BA), or noise. Empirically, three reliable features for isolating STC are selected: (1) the time between spike peak and trough (peak-trough time), (2) the amplitude difference between spike peak and trough (peak-trough amplitude difference), and (3) the energy of the total clip. These features are measured or calculated for BA rejection and spike discrimination based on each clip. The first feature is employed in the "Background Activity (BA) Filter" block and the last two are selected to construct a 2-dimensional feature space in the final spike discriminator. At the output of the BA filter, all the clips identified as background activity will be rejected and only qualified clips containing either STC or SAC are left. The last step is the spike discriminator, which uses the k-means algorithm [6] to train discrimination between STC and SAC.

3. GMM MODELING AND FEATURE INTRODUCTION

In this section we first review the background of the Gaussian mixture model (GMM) under a Bayesian decision rule. This will serve as motivation for its application to neural cell's firing type characterization. The GMM is adopted not only for its ability to approximate complex distributions smoothly, but also due to its great success in tasks such as automatic speaker recognition. Close examination shows many of the characteristics used in the latter task are analogous to the former. Similar to non-stationary cell firing, pitch and spectral features of a speaker may be affected by factors of time, mood, or health conditions. The GMM has proven to be efficient and robust model in the speaker identification [7], and is naturally considered a promising scheme for cell type classification.

The probabilistic model for a Gaussian mixture density is a weighted sum of N Gaussian components, which is described as follows:

$$p(\mathbf{x}|\Theta) = \sum_{k=1}^{N} p_i \alpha_i(\mathbf{x}) \tag{1}$$

where $\mathbf{x}$ is a D-dimensional random vector, $\alpha_i(\mathbf{x}), i = 1, 2, \ldots$ are the component densities and $p_i, i = 1, 2, \ldots, N$ are the mixture weights. Each component density function is a D-dimensional Gaussian distribution defined as

$$\alpha_i(\mathbf{x}) = \frac{1}{(2\pi)^{D/2}|\Sigma_i|^{1/2}} \exp\{-\frac{1}{2}(\mathbf{x}-\mu_i)^T {\Sigma_i}^{-1}(\mathbf{x}-\mu_i)\}$$

where the weights p_i satisfy the condition $\sum_{i=1}^{N} p_i = 1$. One Gaussian mixture model can be characterized by its parameter vector, represented by the notation $\Theta = \{p_i, \mu_i, \Sigma_i\}$, $i = 1, 2, \ldots, N$ with weights p_i, mean vector μ_i and covariance matrix Σ_i. The model is trained by the standard EM algorithm[6].

Suppose there is a group of cell types which is labelled as $\{1, 2, \ldots, S\}$. Each element of this group is represented by a GMM $\Theta_i, i = 1, 2, \ldots, S$. Note that in this paper $i = 1, 2$ since it is a two-class problem. We will label an incoming unknown cell as the type for which the *posteriori* probability is maximized. From Bayes' rule, we can write the *a posteriori* probability as

$$\begin{aligned} \hat{S} &= \mathbf{argmax} Pr(\Theta_k|\mathbf{X}) \\ &= \mathbf{argmax} \frac{p(\mathbf{X}|\Theta_k)Pr(\Theta_k)}{p(\mathbf{X})}, 1 \leq k \leq S \end{aligned}$$

If we assume equal *a priori* probability (i.e., $Pr(\Theta_k) = 1/S$), the equation above can be simplified as

$$\hat{S} = \mathbf{argmax} p(\mathbf{X}|\Theta_k), 1 \leq k \leq S \tag{2}$$

Note that the assumption of equal a priori probabilities may not be appropriate in real cases. We may obtain extra information about the a priori probability in the surgery if we integrate our method with MRI and other mapping-aid methods. Hence the performance is expected to be improved in the future.

We use 14 features computed from Inter-Spike Interval(ISI) vectors in building the feature space. Those ISI vectors are generated by our spike detection algorithm described above. The selection of features is motivated by [8], in which the features are demonstrated to be effective descriptors for the study of neural activity. The features are listed below:

1. **Average length of Inter-Spike Interval(MeanISI):**
2. **Standard deviation of Inter-Spike Interval(StdISI):**
3. **Maximum length of Inter-Spike Interval(MaxISI):**
4. **Minimum length of Inter-Spike Interval(MinISI):**
5. **Mean Instantaneous Frequency (MeanIF):** The Instantaneous Frequency(IF) is defined as the value of the reciprocal of ISI values(i.e., $IF = \frac{1}{ISI}$). Each ISI value in a data block is inverted to an equivalent instantaneous frequency. The Mean Instantaneous Frequencies (MeanIF) are then calculated by averaging of the IF values.
6. **Standard Deviation of the Instantaneous Frequency (StdIF):**
7. **High Frequency Content Ratio (HFCR):** The HFCR is the total number of ISI data less than the HFCR parameter (defined as 5ms in the simulation) divided by the total number of ISI data in one ISI vector.
8. **Low Frequency Content Ratio (LFCR):** The LFCR is the total time of Low Frequency ISI values divided by the total low frequency equivalent time (LFCR-Time). A low frequency ISI is defined as three sequential ISIs greater than the LFCR parameter (defined as 300ms in the simulation). A 3-pulse interval between each pulse and the third pulse later is calculated. If a 3-pulse interval is longer than LFCR parameter it is cumulated to the LFCRTime. The total time is computed by the summation of all ISI values. LFCR is obtained by dividing LFCRTime by total time.
9. **Dispersion (D):** The dispersion is the variance of the ISI values divided by the value of MeanISI.
10. **Dispersion Index (DI):** The Dispersion Index is the difference between MaxISI and MinISI divided by MeanISI.

Table 1. The recognition performance table

Training data	Model order	Recognition ratio		
		3s	5s	10s
5 sec	M = 2	76.04	80.50	74.13
	M = 8	82.66	86.72	82.86
	M = 16	80.89	88.67	85.37
	M = 64	74.98	89.06	85.19
10 sec	M = 2	86.55	83.64	78.42
	M = 8	82.69	88.32	86.49
	M = 16	81.19	89.44	89.84
	M = 64	78.05	92.43	92.78

11. **Burst Index (BI):** Burst Index is the number of ISI values less than the burst index parameter (defined as 10ms in the simulation) divided by the number of ISI values greater than burst index parameter.
12. **Asymmetry Index (AI):** The mode of ISI is defined by the histogram of the ISIs using a bin width of the asymmetry index parameter (defined as 1ms in the simiulation). The bin with the most ISI values is the mode. Asymmetry Index is the mode of the ISI divided by MeanISI. If more than one bin has the same number of ISI values the AI is 0.
13. **PauseIndex (PI):** PauseIndex is the number of ISI values greater than the pause index parameter (defined as 50ms in the simulation) divided by the number of ISI values less than the pause index parameter.
14. **PauseRatio (PR):** Pause Ratio is the cumulative time of ISI values longer than the pause ratio parameter (defined as 50ms in the simulation) divided by the cumulative time of ISI values less than the pause ratio parameter.

4. EXPERIMENTAL EVALUATION

The training and testing sets for the neural signals were recorded in an actual clinical environment with a sampling rate of 20kHz. They were stored and maintained in the Department of Neurology, Emory University. All files have been labelled as "GPe," or "GPi" indicating the recording area by professional neurologists. For simplicity, all training and test segments were set to be 3, 5 or 10 seconds in length. The recognition results are listed in Table 1. The experimental results in this paper are averaged values based on 150-time simulations and the number of total training files are fixed at 2000. A number of observations can be made from this table. First, it appears that the information included in 3-second segments is not sufficient to provide robust cell type identification. The correct recogni-

Table 2. The performance comparison

Model	Parameters	Recognition ratio
GMM-nv	1856	89.06±2.44
VQ-128	1793	65.35±3.15
GMM-gv	974	60.40±3.07
VQ-64	897	62.03±2.72
RBF network	513	54.37±3.08
UGM	210	54.25±3.27

tion ratio with 3-second testing segment is much lower than those with 5 and 10 second segments. We may conclude, data segments of length less than 3 seconds may not contain enough reliable information to identify the cell type. Hence the discussion and analysis below are only for the 5-second and 10-second data segments. Second, as we increase the model order, the performance increases. The the best recognition performance is 92.78% and is obtained using 10-second training data and 10-second test data under the largest model order (64) in our simulation. Third, as we increase the length of the training data, the performance increases. All of the values in the table belonging to 10-second training length are better than those corresponding to 5-second training data. This is also as expected since longer training lengths "teach" more to the classifier.

In Table 2, we compare the recognition performance of the GMM with some other widely-used pattern recognition techniques: specifically, a vector quantization (VQ) code book, the uni-model Gaussian model (UGM), and the radial basis function (RBF) neural network. Two kinds of GMM model are used in the comparison. The first one (GMM-nv) has 64 components with nodal variance and the second one (GMM-gv) also has 64 components but only with one grand variance per model. At the same time, the UGM uses a 14×14 full covariance matrix. The performance of the VQ code book is demonstrated also by two forms of VQ models(VQ-64 and VQ-128), with 64 and 128 vectors per code book, respectively. Both of them are trained by the LBG algorithm [9] using Mahalanobis distance and a global diagonal covariance matrix. Finally, the design of RBF network is based on the Neural Network Toolbox in Matlab, with 512 basis functions.

In Table 2, the training and test data length are both set to be 5 seconds. As in the top level of classifier, the GMM-nv obviously has a superior performance to any other model. However, the GMM-nv has the most parameters per cell pattern. VQ-128, VQ-64 and GMM-gv are at the second level, which can achieve higher than 60% correct identification rate. The RBF and UGM are at the third level, producing a ratio less than 60%, possibly due to the small number of trained parameters.

5. CONCLUSIONS AND FUTURE WORK

Our current work has illustrated that the GMM is an effective tool in differentiating signals from GPe and GPi cells. In the future, we may extend our work into other areas of human brain, helping surgeons not only in treatment of Parkinson's disease but also other type of diseases. In this paper, we assume equal *a priori* probabilities. Nevertheless, we may obtain extra information by incorporating other tools such as MRI to improve performance more.

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