34th Annual International Conference of the IEEE EMBS
San Diego, California USA, 28 August - 1 September, 2012

Sensor Integration of Multiple Tripolar Concentric Ring Electrodes Improves Pentylenetetrazole-induced Seizure Onset Detection in Rats

Oleksandr Makeyev, *Member*, *IEEE*, Quan Ding, *Member*, *IEEE*, Steven M. Kay, *Fellow*, *IEEE*, and Walter G. Besio, *Senior Member*, *IEEE*

Abstract— **As epilepsy affects approximately one percent of the world population, electrical stimulation of the brain has recently shown potential for additive seizure control therapy. Previously, we applied noninvasive transcranial focal stimulation via tripolar concentric ring electrodes on the scalp of rats after inducing seizures with pentylenetetrazole. We developed a system to detect seizures and automatically trigger the stimulation and evaluated the system on the electrographic activity from rats. In this preliminary study we propose and validate a novel seizure onset detection algorithm based on exponentially embedded family. Unlike the previously proposed approach it integrates the data from multiple electrodes allowing an improvement of the detector performance.**

I. Introduction

Epilepsy is a neurological disorder that affects approximately one percent of the world population [1]. Recently, electrical stimulation of the brain has shown promise in reducing seizure frequency. Different forms of noninvasive electrical stimulation including transcranial magnetic stimulation [2], [3] and transcranial direct current stimulation [4] have received increasing attention compared to implantable techniques. Yet, as previously concluded in a review of various brain stimulation techniques, the best structures to stimulate and the most effective stimuli to use are still unknown [5].

Concentric ring electrodes (CREs) have unique capabilities. They perform the second spatial derivative, the Laplacian, on the surface potentials. Previously, we have shown that tEEG, Laplacian electroencephalography (EEG) with the tripolar CRE (TCRE) configuration, is superior to conventional EEG with disc electrodes because tEEG has significantly better spatial selectivity, signal-to-noise ratio, localization, approximation of the analytical Laplacian, and mutual information [6]-[8].

Unlike electrical stimulation via conventional disc electrodes applied across the head, transcranial electrical stimulation via the CRE has a much more uniform current density [9] and focuses the stimulation directly below the electrodes. In our previous works, we have achieved promising results using transcranial focal stimulation (TFS) via TCRE to attenuate acute seizures in animal models induced by pilocarpine [10], penicillin [11], and pentylenetetrazole (PTZ) [12]-[14]. For pilocarpine-induced status epilepticus TFS attenuated electrographic seizure activity and halted the progression of behavioral seizures significantly extending life and enhancing the survival of rats [10]. For severe penicillin induced myoclonic jerks (MJs) TFS significantly decreased MJs in number and duration [11]. Finally, for the PTZ-induced model, a significant increase in synchrony within the beta-gamma frequency bands during seizures was demonstrated as well as the potential of TFS to significantly reduce this synchrony [12]. We also found that TFS caused reductions of both power of electrographic seizure activity [13] and duration of behavioral myoclonic activity [14]. For all these models TFS was triggered manually immediately after the first MJ was observed.

As the next fundamental step, we demonstrated feasibility of an automatic noninvasive seizure control system in rats with PTZ-induced seizures through single and multiple TFS administrations [15], [16]. The TFS was automatically triggered by a real-time electrographic seizure activity detector based on a disjunctive combination of cumulative sum algorithm (CUSUM) and generalized likelihood ratio test (GLRT).

The detection methodologies proposed in [15]-[17] (as well as methods for this paper) are based on detecting the changes in signal power since in our previous works we found a significant increase in tEEG power corresponding to seizure onset [13], [17]. An average seizure onset detection accuracy of 76.14% was obtained for the test set (n = 13) [16]. Detection of electrographic seizure activity was accomplished in advance of the early behavioral seizure activity in 76.92% of the rats [16]. Automatically triggered TFS significantly ($p = 0.001$) reduced the electrographic seizure activity power in the once stimulated group compared to controls in 70% of the cases [16].

Unlike [15]-[17] where data from a single TCRE was used for seizure onset detection, in this study we integrate data from three TCREs using the exponentially embedded family (EEF) approach that has been recently proposed for multi-sensor (or multi-channel) detection [18], [19]. Applied to hypothesis testing EEF has been shown to have superior performance compared to existing methods for cases where

This work was supported in part by Award Number R21NS061335 from the National Institute of Neurological Disorders and Stroke. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Neurological Disorders and Stroke or the National Institutes of Health.

O. Makeyev, Q. Ding, S. M. Kay, and W. G. Besio are with the Department of Electrical, Computer, and Biomedical Engineering, University of Rhode Island, Kingston, RI 02881, USA (phone: 401-874-9208; fax: 401-782-6422; e-mail: omakeyev@ele.uri.edu, dingqqq@ele.uri.edu, kay@ele.uri.edu, besio@ele.uri.edu).

the sensor outputs are not independent [18], [19]. Such is our case since sensor measurements could be correlated due to the common source and the relative sensor locations. The proposed seizure onset detection approach has been validated on the subset of the dataset used in [16] to allow direct comparison of performance with our previous disclosed methodology.

II. Methods

A. Dataset

A short summary of the aspects of the original dataset collected in [16] that are the most relevant to the current study is presented below.

24 h before the induction of seizures adult male Sprague-Dawley rats were anesthetized, their scalps were shaved, and prepared with abrasive gel. Three custom-designed TCREs [6] were placed on the scalp with conductive paste and adhered with dental acrylic cement. One TCRE (1.0 cm dia.), used to record from and stimulate, was centered on the top of the head. Two other recording TCREs (6 mm dia.) were placed bilaterally behind the eyes, but in front of the ears. An isolated ground electrode was attached on the top of the neck behind the ears. The real-time CUSUM/GLRT based seizure detection was performed automatically using individual models i.e. detection was trained on baseline electrographic activity for each rat. All other detector parameters were selected from the training group of rats (n = 3) using grid search. Detection accuracy was calculated for the test group (n = 13) of which five rats were used as controls, five received a single dose of TFS (50 mA, 200 μs, 300 Hz, 2 m, biphasic, charge-balanced pulses) and three received two doses of TFS. Animals were divided into groups based on skin-to-electrode impedance. Lower impedances for the two TFS treated groups ensured effectiveness of TFS. Since TFS was applied between the outer ring and the central disc of the 1.0 cm TCRE the rat was given TFS if the impedance for the outer ring and the central disc to the ground electrode were both less than 10 KΩ. Otherwise, if this impedance was between 10 KΩ and 25 KΩ the animal was put into the control group (n = 5).

To validate the seizure detection data were collected for each rat in the following way: first, 5 min of baseline tEEG were recorded to train the seizure detector. Next, the seizure detector was activated for 5 min of sham seizure activity (baseline) recording. Finally, seizures were induced with PTZ (55 mg/kg i.p.) and tEEG recording continued for another 15 min with one and two TFS dose groups receiving automatically triggered TFS. For tEEG derivation the EEG signals were preamplified (gain 100 and 0.3 Hz high pass filter) with a custom built preamplifier, amplified (gain 1000 and band pass of 1.0–100 Hz with the 60 Hz notch filter), and digitized (16 bits, 256 S/s). Next, two differential EEG signals from each TCRE were combined to give Laplacian derivation of the signal as reported previously by Besio [6]. Detection accuracy was calculated for periods of sham and real seizure until the first observed MJ (first clear behavioral seizure manifestation) with an exception of a 30 s handling period corresponding to the PTZ injection. Sensitivity, specificity and overall accuracy were calculated for time windows of 5 s.

In [16] for each rat data recorded from one TCRE was selected for real-time seizure detection based on skin-to-electrode impedance and visual inspection of data. In this study we combine the data from all three TCREs using EEF for detection of a change in power as described below.

B. EEF Problem Statement

This EEF derivation is for three TCREs but it can be easily extended for any number of electrodes. Let $\{\mathbf{x}_1^b, \mathbf{x}_1^t\}, \{\mathbf{x}_2^b, \mathbf{x}_2^t\}, \{\mathbf{x}_3^b, \mathbf{x}_3^t\}$ be the de-meaned tEEG data from three TCREs respectively, where the superscript "*b*" represents the baseline data of length N_b and "*t*" represents the testing data of length N_t. In other words, $\mathbf{x}_1^b, \mathbf{x}_2^b, \mathbf{x}_3^b$ are the training data and $\mathbf{x}_1^t, \mathbf{x}_2^t, \mathbf{x}_3^t$ are the validation data for the detector. We assume that all data follow Gaussian distributions: $\mathbf{x}_i^b \sim N(\mathbf{0}, \sigma_{i,b}^2\mathbf{I})$, $\mathbf{x}_i^t \sim N(\mathbf{0}, \sigma_{i,t}^2\mathbf{I})$ for i = 1,2,3 and we want to choose between two hypotheses:

$$H_0 : \sigma_{1,t}^2 = \sigma_{1,b}^2, \sigma_{2,t}^2 = \sigma_{2,b}^2, \sigma_{3,t}^2 = \sigma_{3,b}^2$$
$$H_1 : \sigma_{1,t}^2 > \sigma_{1,b}^2, \sigma_{2,t}^2 > \sigma_{2,b}^2, \sigma_{3,t}^2 > \sigma_{3,b}^2$$

Under the null hypothesis the variances of baseline and testing segments for each TCRE are equal meaning that there is no significant change in power (equal to variance for de-meaned segments). The alternative being a significant rise in power is detected meaning detection of seizure onset.

C. EEF Implementation

We also assume that $\sigma_{1,b}^2, \sigma_{2,b}^2, \sigma_{3,b}^2$ can be estimated accurately, which is possible if we have sufficient number of samples: $\sigma_{i,b}^2 = \frac{1}{N_b}\sum_{n=1}^{N_b}\left(x_i^b[n]\right)^2$ for i = 1,2,3. Now we can re-write the hypothesis testing problem in a different way:

$$H_0 : \mathbf{x}_1^t \sim N(\mathbf{0}, \sigma_{1,b}^2\mathbf{I}), \mathbf{x}_2^t \sim N(\mathbf{0}, \sigma_{2,b}^2\mathbf{I}), \mathbf{x}_3^t \sim N(\mathbf{0}, \sigma_{3,b}^2\mathbf{I})$$
$$H_1 : \mathbf{x}_1^t \sim N(\mathbf{0}, \sigma_{1,t}^2\mathbf{I}), \mathbf{x}_2^t \sim N(\mathbf{0}, \sigma_{2,t}^2\mathbf{I}), \mathbf{x}_3^t \sim N(\mathbf{0}, \sigma_{3,t}^2\mathbf{I})$$

where $\sigma_{1,b}^2, \sigma_{2,b}^2, \sigma_{3,b}^2$ are assumed to be known and $\sigma_{1,t}^2, \sigma_{2,t}^2, \sigma_{3,t}^2$ are the unknown variances such that $\sigma_{1,t}^2 > \sigma_{1,b}^2, \sigma_{2,t}^2 > \sigma_{2,b}^2, \sigma_{3,t}^2 > \sigma_{3,b}^2$. Since under H_0 there is no seizure, we assume that $\mathbf{x}_1^t, \mathbf{x}_2^t, \mathbf{x}_3^t$ are independent. Therefore, we have for p being the probability density function (PDF):

$$p(\mathbf{x}_1^t, \mathbf{x}_2^t, \mathbf{x}_3^t; H_0) = p(\mathbf{x}_1^t; H_0)\, p(\mathbf{x}_2^t; H_0)\, p(\mathbf{x}_3^t; H_0)$$

As shown in [18] the EEF can be expressed as:

$$p_{\eta_1,\eta_2,\eta_3}(\mathbf{x}_1^t,\mathbf{x}_2^t,\mathbf{x}_3^t)$$
$$= \exp\left[\eta_1 \ln\frac{p(\mathbf{x}_1^t;H_1)}{p(\mathbf{x}_1^t;H_0)} + \eta_2 \ln\frac{p(\mathbf{x}_2^t;H_1)}{p(\mathbf{x}_2^t;H_0)}\right.$$
$$\left. + \eta_3 \ln\frac{p(\mathbf{x}_3^t;H_1)}{p(\mathbf{x}_3^t;H_0)} - K(\eta_1,\eta_2,\eta_3) + \ln p(\mathbf{x}_1^t,\mathbf{x}_2^t,\mathbf{x}_3^t;H_0)\right]$$

where $0 \le \eta_1,\eta_2,\eta_3 \le 1$ and

$$K(\eta_1,\eta_2,\eta_3) = \ln E_0\left[\exp\left(\eta_1 \ln\frac{p(\mathbf{x}_1^t;H_1)}{p(\mathbf{x}_1^t;H_0)} + \eta_2 \ln\frac{p(\mathbf{x}_2^t;H_1)}{p(\mathbf{x}_2^t;H_0)} + \eta_3 \ln\frac{p(\mathbf{x}_3^t;H_1)}{p(\mathbf{x}_3^t;H_0)}\right)\right]$$

is the normalizing factor to guarantee a valid PDF. Once we find $\hat{\eta}_1,\hat{\eta}_2,\hat{\eta}_3$ as the maximum likelihood estimates (MLEs) of η_1,η_2,η_3, we decide H_1 if $2\ln\frac{p_{\hat{\eta}_1,\hat{\eta}_2,\hat{\eta}_3}(\mathbf{x}_1^t,\mathbf{x}_2^t,\mathbf{x}_3^t)}{p(\mathbf{x}_1^t,\mathbf{x}_2^t,\mathbf{x}_3^t;H_0)} > \gamma$.

Letting $\theta_i = -\eta_i\left(\frac{1}{2\sigma_{i,t}^2} - \frac{1}{2\sigma_{i,b}^2}\right)$ for i = 1,2,3, we can re-parameterize the EEF as $p_{\theta_1,\theta_2,\theta_3}(\mathbf{x}_1^t,\mathbf{x}_2^t,\mathbf{x}_3^t)$ and equivalently find the maximum over $\theta_1,\theta_2,\theta_3$. It can be shown that the MLEs are:

$$\hat{\theta}_i = \left(\frac{1}{2\sigma_{i,b}^2} - \frac{N_t}{2\sum_{n=1}^{N_t}\left(x_i^t[n]\right)^2}\right) u\left(\frac{\sum_{n=1}^{N_t}\left(x_i^t[n]\right)^2}{N_t} - \sigma_{i,b}^2\right)$$

for i = 1,2,3 where $u(\cdot)$ is the unit step function. Note that if $\frac{\sum_{n=1}^{N_t}\left(x_i^t[n]\right)^2}{N_t} < \sigma_{i,b}^2$ then $\hat{\theta}_i = 0$ which is the case when the i-th sensor provides no information. Finally, it can be shown that the EEF decides H_1 if:

$$T(x) = 2\ln\frac{p_{\hat{\theta}_1,\hat{\theta}_2,\hat{\theta}_3}(\mathbf{x}_1^t,\mathbf{x}_2^t,\mathbf{x}_3^t)}{p(\mathbf{x}_1^t,\mathbf{x}_2^t,\mathbf{x}_3^t;H_0)}$$
$$= 2\hat{\theta}_1\sum_{n=1}^{N_t}\left(x_1^t[n]\right)^2 + 2\hat{\theta}_2\sum_{n=1}^{N_t}\left(x_2^t[n]\right)^2 + 2\hat{\theta}_3\sum_{n=1}^{N_t}\left(x_3^t[n]\right)^2$$
$$+ N_t\ln(1-2\sigma_{1,b}^2\hat{\theta}_1) + N_t\ln(1-2\sigma_{1,b}^2\hat{\theta}_2) + N_t\ln(1-2\sigma_{1,b}^2\hat{\theta}_3) > \gamma$$

where $T(x)$ is the test statistic and the threshold γ is selected for a given false alarm rate P_{FA}. It can be shown that $T(x)$ asymptotically follows chi-squared distribution with three degrees of freedom allowing one to set γ accordingly.

III. Results

For this preliminary validation of EEF we used a subset of the dataset from [16] corresponding to the control group (n = 5). The control data was selected because it does not contain automatically triggered periods of TFS that have to be excluded from accuracy evaluation. This evaluation followed the guidelines of [16] including size of testing data window N_t equal to 5 s and the three-of-three smoothing algorithm (for three consecutive detections the third one was marked as seizure onset). All the available baseline data was used for EEF training, i.e. N_b was equal to 5 min. Out of 3 rats used in [16] for detector training only two were controls and as such were used to train the EEF. No results are reported for the training set (n = 2). As in [16] training was performed using grid search maximizing the overall accuracy for a range of P_{FA} values. Suboptimal P_{FA} equal to 10^{-6} was obtained in training and used for validation.

TABLE I
Performance Metrics for CUSUM/GLRT and EEF Detectors and Their Disjunctive Combination.

Detector	Average			Rats with seizure onset detected prior to the first MJ (%)	Mean time from PTZ injection to seizure onset detection (s)
	Overall accuracy (%)	Sensitivity (%)	Specificity (%)		
CUSUM/GLRT	79.8	29.1	98.34	80	26.6
EEF	81.73	69.35	95.98	100	18.2
Disjunctive combination	82.17	72.02	94.32	100	17

The results obtained on the validation set (n = 5) are presented in Table 1. It can be seen that obtained CUSUM/GLRT results are comparable to the ones obtained for the full dataset (n = 13) in [16]. EEF outperforms CUSUM/GLRT with more than twice the sensitivity and comparable specificity, higher percentage of rats with seizure onset detected prior to MJ, and faster seizure onset detection. At the same time the disjunctive combination of CUSUM/GLRT and EEF with detections from either detector combined using logical OR fusion did not show a significant improvement over EEF. This may suggest that EEF showed near optimal performance for this particular data. Individual test statistics and detections for periods of sham seizure (5 min) and seizure (before the first MJ) are presented in Fig. 1. Rat *A* never developed a MJ even though there was

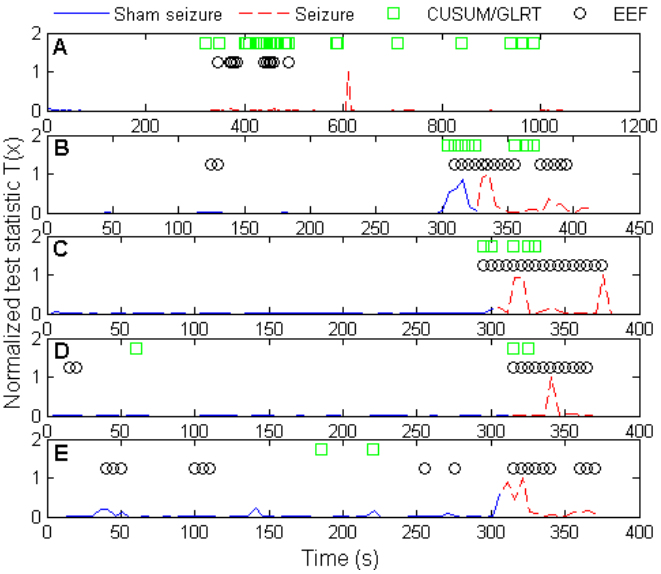

Fig. 1. Individual test statistics and detections for sham seizure (5 min) and seizure before the first MJ (n = 5; letters *A*-*E* denote individual rats).

electrographic seizure activity present so all the available data (15 min) after PTZ injection was used for accuracy assessment (time scale is different for this rat in Fig. 1). For rat *E* seizure onset was detected before the first MJ by EEF but not by CUSUM/GLRT.

IV. Discussion

We believe that the improvement achieved in seizure onset detector performance using EEF is primarily due to the fact that tEEG via TCRE decreases mutual information increasing the level of independency between electrodes compared to EEG via conventional disc electrodes [8]. Due to the significantly lowered mutual information we believe that multiple TCRE sensors collect more independent local data. Therefore, integration of multiple TCREs increases the total information and improves the seizure detection.

Furthermore, selection of EEF for detection was crucial since it combines the information from all the TCREs using an exponential family. The weights for each channel are estimated from the samples. This procedure makes the EEF a robust method. For example, in our case of performing the validation on control data no selection criteria was used to assure good quality of signal for all three TCREs since only data from a single TCRE was previously used. As a result some of the channels corresponding to TCRE elements had high (>25 KΩ) or intermittent impedance resulting in low signal to noise ratio data. Moreover, a couple of the channels were open due to loss of connector pins resulting in channels consisting of just noise. As was shown in EEF implementation (Section 2C) channels containing mostly noise and providing no useful information resulting in low power receive weights equal to zero (or close to zero in practice), i.e. for EEF the contribution of a channel is proportional to the amount of useful information it contains. Finally, EEF is also a great simplification over a previously used methodology based on a disjunctive combination of CUSUM and GLRT.

V. Conclusion

We believe that the preliminary results obtained in this study suggest the potential of the proposed approach and further investigation is needed to confirm it. Quality of the data that was used was not controlled for all the channels or TCREs and even the few controlled channels had poor impedances (10-25 KΩ). Therefore, it is likely to represent the worst case scenario and the lower bound of the detector performance. Due to its robustness to such low quality data and improved performance EEF holds great promise for sensor integration in applications not limited to seizure onset detection in rats and, potentially, humans.

References

[1] J. W. Sander, "The epidemiology of epilepsy revisited," *Curr. Opin. Neurol.*, vol. 16, no. 2, pp. 165-170, April 2003.

[2] C. A. Tassinari, M. Cincotta, G. Zaccara, and R. Michelucci, "Transcranial magnetic stimulation and epilepsy," *Clinical Neurophysiology*, vol. 114, pp. 777–798, May 2003.

[3] W. H. Theodore, K. Hunter, R. Chen, F. Vega–Bermudez, B. Boroojerdi, P. Reeves–Tyer, K. Werhahn, K. R. Kelley, and L. Cohen, "Transcranial magnetic stimulation for the treatment of seizures: A controlled study," *Neurology*, vol. 59, no. 4, pp. 560-562, August 2002.

[4] F. Fregni, S. Thome-Souza, M. A. Nitsche, S. D. Freedman, K. D. Valente, and A. Pascual-Leone, "A controlled clinical trial of cathodal DC polarization in patients with refractory epilepsy," *Epilepsia*, vol. 47, no. 2, pp. 335–342, February 2006.

[5] W. Theodore and R. Fisher, "Brain stimulation for epilepsy," *The Lancet*, vol. 3, no. 2, pp. 111-118, February 2004.

[6] W. Besio, K. Koka, R. Aakula, and W. Dai, "Tri-polar concentric electrode development for high resolution EEG Laplacian electroencephalography using tri-polar concentric ring electrodes," *IEEE Trans. BME.*, vol. 53, no. 5, pp. 926-933, May 2006.

[7] W. Besio, R. Aakula, K. Koka, and W. Dai, W, "Development of a tri-polar concentric ring electrode for acquiring accurate Laplacian body surface potentials," *Annals of Biomedical Engineering*, vol. 34, no. 3, pp. 426-435, March 2006.

[8] K. Koka and W. Besio, "Improvement of spatial selectivity and decrease of mutual information of tri-polar concentric ring electrodes," *J of Neuroscience Methods*, vol. 165, pp. 216–222, September 2007.

[9] J.D. Wiley, J.G. Webster, "Analysis and control of the current distribution under circular dispersive electrodes," *IEEE Trans. BME.*, vol. 29, pp. 381–385, 1982.

[10] W. Besio, K. Koka, and A. Cole, "Effects of noninvasive transcutaneous electrical stimulation via concentric ring electrodes on pilocarpine-induced status epilepticus in rats," *Epilepsia*, vol. 48, no. 12, pp. 2273–2279, December 2007.

[11] W.G. Besio, K. Koka, K.S. Gale, and A.V. Medvedev, "Preliminary Data on Anticonvulsant Efficacy of Transcutaneous Electrical Stimulation via Novel Concentric Ring Electrodes," in S.C. Schachter, J.V. Guttag, S.J. Schiff, D.L. Schomer, Summit Contributors, Advances in the application of technology to epilepsy: the CIMIT/NIO Epilepsy Innovation Summit, Boston, May 2008, *Epilepsy Behav.*, vol. 16, no. 1, pp. 3-46, 2009.

[12] W. Besio, X. Liu, L. Wang, A. Medvedev, and K. Koka, "Transcutaneous electrical stimulation via concentric ring electrodes reduced pentylenetetrazole-induced synchrony in beta and gamma bands in rats," *International Journal of Neural Systems*, vol. 21, no. 2, pp. 139-149, April 2011.

[13] O. Makeyev, X. Liu, K. Koka, S.M. Kay, and W.G. Besio, "Transcranial focal stimulation via concentric ring electrodes reduced power of pentylenetetrazole-induced seizure activity in rat electroencephalogram," in *Proceedings of 33rd Annual International Conference of the IEEE EMBS*, Boston, USA, August 30 - September 3, pp. 7560-7563, 2011.

[14] W.G. Besio, K.S. Gale, and A. Medvedev, "Possible therapeutic effects of trancutaneous electrical stimulation via concentric ring electrodes," Xth Workshop on Neurobiology of Epilepsy (WONOEP 2009), *Epilepsia*, vol. 51, no. 3, pp. 85–87, 2010.

[15] Makeyev O., Liu X., Luna-Munguía H., Rogel-Salazar G., Mucio-Ramirez S., Liu Y., Sun Y., Hadidi R., Kay S.M., Besio W.G., "Toward an automatic seizure control system in rats through transcranial focal stimulation via tripolar concentric ring electrodes," Proc. 65th Annual Meeting of the American Epilepsy Society, *Epilepsy Currents*, vol. 12, no. s1, pp. 29-30, January/February 2012.

[16] Makeyev O., Liu X., Luna-Munguía H., Rogel-Salazar G., Mucio-Ramirez S., Liu Y., Sun Y., Kay S., Besio W., "Toward a noninvasive automatic seizure control system in rats with transcranial focal stimulations via tripolar concentric ring electrodes," *IEEE Trans. Neural Syst. Rehabil. Eng.*, DOI: 10.1109/TNSRE.2012.2197865.

[17] W.G. Besio, X. Liu, Y. Liu, Y.L. Sun, A.V. Medvedev, and K. Koka, "Algorithm for automatic detection of pentylenetetrazole-induced deizures in rats," in *Proceedings of 33rd Annual International Conference of the IEEE EMBS*, Boston, USA, August 30 - September 3, pp. 8283-8286, 2011.

[18] S. Kay and Q. Ding, "Exponentially Embedded Families for Multimodal Sensor Processing," in *Proc. IEEE International Conference on Acoustics, Speech, and Signal Processing*, Mar. 2010, pp. 3770–3773.

[19] S. Kay, Q. Ding, and D. Emge, "Joint PDF Construction for Sensor Fusion and Distributed Detection," in *Proc. International Conference on Information Fusion*, Jun. 2010.