We have developed a high-performance real-time seizure detection system that achieves a performance of 42.05% sensitivity with 5.78 false alarm per 24 hours on the development dataset of v1.5.2 of the Temple University Hospital Seizure Detection Corpus (Figures 1-3). The system can easily run in real-time using a single core CPU, operating at 0.58 xRT on a 1.7 GHz processor in 16 Gbytes of memory with a latency of 300 msec. This system compares favorably with the best systems evaluated in the Neureka 2020 Epilepsy Challenge (which the PIs co-organized) and is the only system of those that runs in real-time and is suitable for clinical applications.

Scalp electroencephalogram (EEG) signals inherently have a low signal-to-noise ratio due to the way the signal is electrically transduced. Temporal and spatial information must be exploited to achieve accurate detection of seizure events. Most popular approaches to seizure detection using deep learning focus on modeling temporal or spatial information, but do not jointly model this information. We exploit both simultaneously by converting the multichannel signal to a grayscale image and using transfer learning approaches to achieve high performance. The proposed system is trained end-to-end with only very simple pre- and post-processing operations which are computationally lightweight and have low latency, making them conducive to clinical applications that require real-time processing.

We also demonstrated that non-real-time approaches benefitted from separating the seizure detection problem into a two-phase problem – epileptiform activity detection followed by seizure detection. In the first phase, we used a sequential neural network algorithm known as a long short-term memory (LSTM) network to identify channel-specific epileptiform discharges associated with seizures. In the second phase, the feature vector is augmented with posteriors that represent the onset and offset of ictal activities. These augmented features are applied to a multichannel convolutional neural network (CNN) followed by an LSTM network. The multiphase model was evaluated on a blind evaluation set and was shown to detect $106$ segment boundaries within a $2$-second margin of error. Our previous best system, which delivers state-of-the-art performance on this task, correctly detected only 9 segment boundaries. Our multiphase system was also shown to be robust by performing well on two blind evaluation sets. Seizure detection performance on the TU Seizure Detection (TUSZ) Corpus development set is $41.60\%$ sensitivity with $5.63$ false alarms/$24$ hours (FAs/24 hrs). Performance on the corresponding evaluation set is $48.21\%$ sensitivity with $16.54$ FAs/$24$ hrs. Performance on a previously unseen corpus, the Duke University Seizure (DUSZ) Corpus is $46.62\%$ sensitivity with $7.86$ FAs/$24$ hrs. Our previous best system yields $30.83\%$ sensitivity with $6.74$ FAs/$24$ hrs on the TUSZ development set, $33.11\%$ sensitivity with 1$9.89$ FAs/$24$ hrs on the TUSZ evaluation set and $33.71\%$ sensitivity with $40.40$ FAs/$24$ hrs on DUSZ. The multiphase system represents our best overall performance for a non-real-time system.

Finally, a major goal in this project was to develop deep learning-based architectures that capture spatial and temporal correlations in an EEG signal. We began this activity by developing a variety of architectures based on popular deep learning networks such as LSTMs and CNNs. We demonstrated that performance of a system trained only on Temple University Seizure Corpus (TUSZ) data transfers to a blind evaluation set (DUSZ) and the Emory University Seizure Corpus (EUSZ). This type of generalization is very important since complex high-dimensional deep learning systems tend to overtrain. In clinical settings, we cannot control the ambient recording conditions, so demonstrating an ability to handle previously unseen data is important. We also developed some effective visualization tools to understand exactly what the network is learning and demonstrated that encoding long-term temporal relationships is still a challenging problem. Because of the complexity of these deep learning systems, it is extremely difficult to visualize the internal states of the system and understand what it has learned relative to the problem of interest. The techniques we developed, based on a process where you maximize activations at the input layer and explore the weights of the internal connections based on density maps, are demonstrated in Figure 4.

There are three major activities associated with this project: (1) improve the performance of our seizure detection system to meet clinical targets; (2) create a real-time implementation of our best research system that has low latency and is acceptable for clinical use; and (3) continue our attempts to commercialize the technology, building on the results of our STTR Phase I grant.

With respect to the first activity, our best research system, which we refer to as the baseline system for this grant, is fully described in Vinit Shah’s PhD dissertation (Shah, 2021), which was successfully defended in May 2021. This dissertation represents the cumulative work of one of our two students who initiated our work in automatic seizure detection. The central thesis of his work is that separation of the seizure detection problem into a two-phase problem – epileptiform activity detection followed by seizure detection – should improve our ability to detect and localize seizure events. In the first phase, we used a sequential neural network algorithm known as a long short-term memory (LSTM) network to identify channel-specific epileptiform discharges associated with seizures. In the second phase, the feature vector is augmented with posteriors that represent the onset and offset of ictal activities. These augmented features are applied to a multichannel convolutional neural network (CNN) followed by an LSTM network.

The multiphase model was evaluated on a blind evaluation set and was shown to detect $106$ segment boundaries within a $2$-second margin of error. Our previous best system, which delivers state-of-the-art performance on this task, correctly detected only 9 segment boundaries. Our multiphase system was also shown to be robust by performing well on two blind evaluation sets. Seizure detection performance on the TU Seizure Detection (TUSZ) Corpus development set is $41.60\%$ sensitivity with $5.63$ false alarms/$24$ hours (FAs/24 hrs). Performance on the corresponding evaluation set is $48.21\%$ sensitivity with $16.54$ FAs/$24$ hrs. Performance on a previously unseen corpus, the Duke University Seizure (DUSZ) Corpus is $46.62\%$ sensitivity with $7.86$ FAs/$24$ hrs. Our previous best system yields $30.83\%$ sensitivity with $6.74$ FAs/$24$ hrs on the TUSZ development set, $33.11\%$ sensitivity with 1$9.89$ FAs/$24$ hrs on the TUSZ evaluation set and $33.71\%$ sensitivity with $40.40$ FAs/$24$ hrs on DUSZ.

Our second student, Meysam Golmohammadi, who pioneered our work on applying deep learning to seizure detection and was the Chief Technical Officer of our start up, Biosignal Analytics Inc., also successfully defended his dissertation (Golmohammadi, 2021) in June 2021. This dissertation represents a summary of our initial work understanding the problem and addressing it by leveraging our years of experience with other applications such as speech recognition. Automatic analysis of clinical EEGs is a very difficult machine learning problem due to the low fidelity of a scalp EEG signal. Deep learning approaches can be viewed as a broad family of neural network algorithms that use many layers of nonlinear processing units to learn a mapping between inputs and outputs. Deep learning-based systems have generated significant improvements in performance for sequence recognitions tasks for temporal signals such as speech and for image analysis applications that can exploit spatial correlations, and for which large amounts of training data exists. The primary goal of this research was to develop deep learning-based architectures that capture spatial and temporal correlations in an EEG signal. We applied these architectures to the problem of automated seizure detection for adult EEGs. The main contribution of this work is the development of a high-performance automated EEG analysis system based on principles of machine learning and big data that approaches levels of performance required for clinical acceptance of the technology.

With respect to the second goal of developing a real-time system, the process of engineering the system to be amenable to a real-time implementation is discussed in Khalkhali et al. (2021). Scalp electroencephalogram (EEG) signals inherently have a low signal-to-noise ratio due to the way the signal is electrically transduced. Temporal and spatial information must be exploited to achieve accurate detection of seizure events. Most popular approaches to seizure detection using deep learning focus on modeling temporal or spatial information, but do not jointly model this information. We exploit both simultaneously by converting the multichannel signal to a grayscale image and using transfer learning approaches to achieve high performance. The proposed system is trained end-to-end with only very simple pre- and post-processing operations which are computationally lightweight and have low latency, making them conducive to clinical applications that require real-time processing. We demonstrate the efficacy of this approach We have achieved a performance of 42.05% sensitivity with 5.78 false alarm per 24 hours on the development dataset of v1.5.2 of the Temple University Hospital Seizure Detection Corpus. The system can run easily run in real-time using single core CPU, operating at 0.58 xRT on a 1.7 GHz processor in 16 Gbytes of memory with a latency of 300 msec.

With respect to the third major activity, in Golmohammadi’s study, we used the Temple University EEG (TUEG) Corpus, supplemented with data from Duke University and Emory University, to evaluate the performance of these hybrid deep structures. We demonstrated that performance of a system trained only on Temple University Seizure Corpus (TUSZ) data transfers to a blind evaluation set consisting of the Duke University Seizure Corpus (DUSZ) and the Emory University Seizure Corpus (EUSZ). This type of generalization is very important since complex high-dimensional deep learning systems tend to overtrain.

We also investigated the robustness of this system to mismatched conditions (e.g., train on TUSZ, evaluate on EUSZ). We train a model on one of three available datasets and evaluate the trained model on the other two datasets. These datasets are recorded from different hospitals, using a variety of devices and electrodes, under different circumstances and annotated by different neurologists and experts. Therefore, these experiments help us to evaluate the impact of the dataset on our training process and validate our manual annotation process.

Further, we introduce methods to improve generalization and robustness. We analyze performance to gain additional insight into what aspects of the signal are being modeled adequately and where the models fail. The best results for automatic seizure detection achieved in this study are $45.59\%$ with $12.24$ FA per $24$ hours on TUSZ, $45.91\%$ with $11.86$ FAs on DUSZ, and $62.56\%$ with 11.26 FAs on EUSZ. We demonstrate that the performance of the deep recurrent convolutional structure presented in this study is statistically comparable to the human performance on the same dataset.

Finally, in Golmohammadi’s work, we also developed some effective visualization tools to understand exactly what the network is learning. We believe these tools will be relevant to a larger class of deep learning systems.

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