HAMLET: Interpretable Human And Machine co-LEarning Technique

Olivier Deiss¹, Siddharth Biswal¹, Jing Jin², Haoqi Sun², M. Brandon Westover² and Jimeng Sun¹

¹Georgia Institute of Technology
²Massachusetts General Hospital

March 26, 2018

Abstract

Efficient label acquisition processes are key to obtaining robust classifiers. However, data labeling is often challenging and subject to high levels of label noise. This can arise even when classification targets are well defined, if instances to be labeled are more difficult than the prototypes used to define the class, leading to disagreements among the expert community.

Here, we enable efficient training of deep neural networks. From low-confidence labels, we iteratively improve their quality by simultaneous learning of machines and experts. We call it Human And Machine co-LEarning Technique (HAMLET). Throughout the process, experts become more consistent, while the algorithm provides them with explainable feedback for confirmation. HAMLET uses a neural embedding function and a memory module filled with diverse reference embeddings from different classes. Its output includes classification labels and highly relevant reference embeddings as explanation.

We took the study of brain monitoring at intensive care unit (ICU) as an application of HAMLET on continuous electroencephalography (cEEG) data. Although cEEG monitoring yields large volumes of data, labeling costs and difficulty make it hard to build a classifier. Additionally, while experts agree on the labels of clear-cut examples of cEEG patterns, labeling many real-world cEEG data can be extremely challenging. Thus, a large minority of sequences might be mislabeled. HAMLET has shown significant performance gain against deep learning and other baselines, increasing accuracy from 7.03% to 68.75% on challenging inputs. Besides improved performance, clinical experts confirmed the interpretability of those reference embeddings in helping explaining the classification results by HAMLET.

1 Introduction

For a wide spectrum of real-world applications, ranging from image classification (K. He et al., 2015 He et al. (2015)), face and speech recognition (A. Y. Hannun et al., 2014 Hannun et al. (2014)), and bioinformatics (A. Esteva et al., 2017 Esteva et al. (2017)), to speech synthesis (A. van den Oord et al., 2016 van den Oord et al. (2016)) and even game playing (V. Mnih et al., 2015 Mnih et al. (2015)), deep learning has become one of the most powerful tools. Convolutional Neural Networks (CNNs), which are biologically-inspired models (Y. LeCun et al., 1989 LeCun et al. (1989)) able of reaching great performance in image classification (A. Krizhevsky et al., 2012 Krizhevsky et al. (2012)), natural language processing (W. Yin et al., 2017 Yin et al. (2017)) or analysis of time-series data, are a great example of successful models. However in supervised learning, excellent performance always comes with the same burden, regardless of the field of research: the need of large quantities of high-quality labeled data. The problem of detecting events in electroencephalograms (EEG) belongs to this class of applications where deep learning can achieve excellent results but requires large amounts of labeled data.

However, in many real world applications, the labels are difficult to acquire. Either the acquisition costs are too high to make it possible to collect enough data, or events of a certain label are simply too rare to
be observed enough times. In both situations, it becomes hard to apply deep learning algorithms. In other recurring situations, there is an abundance of raw data, but a lack of high quality labeled data, again due to either high labeling costs or the difficulty of the labeling task. In biomedical applications, data acquisition is a first challenge to be overcome. First, for privacy reasons, it can be difficult to obtain patient data. Second, labeling is often expensive in that it requires availability of a domain expert who can dedicate enough time to the dataset creation. Third, tasks can become challenging to the point where even domain experts cannot readily come to an agreement on some or many sample points (N. Gaspard et al., 2014 Gaspard et al. (2014)). For a classification task, they might often disagree on difficult sample points at the boundaries of multiple classes, or have different interpretations of the established concepts. For these reasons, obtaining a large dataset with high-quality labels is quite challenging.

As an example, one great challenge in biomedicine is related to the classification of seizures, which are the result of abnormal electrical activity in the brain. There exist multiple types of seizures, and classifying them allows to study their respective impact on health, as well as how to effectively cure or treat them. A recent study by Ruiz et al. (2017) showed that the analysis of continuous electroencephalography (cEEG) signals can help predict the risk of seizures in critically ill patients. cEEG is a non-invasive method to monitor the electrical activity of the brain. In the critical care setting, cEEG monitoring is typically performed for 24-72 hours at a time, providing large volumes of data. However, manually labeling the events is a tedious task for the human expert, both due to the high volumes of data and the difficulty of the task.

Deep learning models could advance both the clinical value of brain monitoring and provide valuable scientific tools for studying seizures and related pathological cEEG events. Deep neural networks have already been used to study EEG patterns (P. W. Mirowski et al., 2008 Mirowski et al. (2008); P. Bashivan et al., 2015 Bashivan et al. (2015)), so they are a model of choice in our study. The issue here is the costs related to labeling data, making it hard to rely on a standard learning framework. In addition, EEGs are difficult for experts to label consistently due to the frequent overlap between classes (JJ. Halford et al., 2015 Halford et al. (2015); H. A. Haider et al., 2016 Haider et al. (2016)). The standard solution to this problem in the medical literature is to have each sample reviewed and labeled independently – or in a committee – by multiple human experts before a decision on the class label is taken. This approach is however not scalable. Overall, this situation makes it challenging to obtain a labeled dataset suitable for proper training of deep neural networks, and therefore is a great application of our work on label acquisition.

With the help of active learning, it has been shown that a classifier can be trained on a judiciously selected subset of the available data while performing as accurately as models trained with a much larger set of randomly selected training examples (K. Wang et al., 2017 Wang et al. (2017)). Such efficient methods for selecting sample points for human labeling allow to cope with budget restrictions with no or limited trade-off on performance. However, although a similar framework could help us efficiently grow our dataset, all active learning methods start with the assumption that they can query an “Oracle”, a human expert who can label any sample point – the query – with no risk of misclassification. In many studies, the “Oracle” is a human, expert in the field, and the correct class label leaves no room for doubt. In other studies, like ours, the problem is so challenging that fully relying on human experts in order to obtain ground truth class labels is not enough. Indeed, the task is so difficult that there is a great risk that the label given by the human expert may still be wrong. Therefore, although active learning remains attractive for our study, using it would not solve our issues.

Instead, we first acknowledge that in an increasing number of studies, although the model can be seen as being taught by humans, it is not uncommon that the overall accuracy of the model is better than that of all human teachers combined (V. Gulshan et al., 2016 V et al. (2016); D. Silver et al., 2017 Silver et al. (2017)). In this work, we use this fact as a way to improve the human raters’ performance and consistency in the labeling task, especially when labeling data that spans multiple different patients, and we propose HAMLET, a Human And Machine co-LEarning Technique to efficiently bypass this label acquisition difficulty. We apply HAMLET to train a classifier for various types of non-convulsive seizures, based on continuous EEG recordings. HAMLET helps us face the above mentioned issues, while making use of the great performance of deep learning models at challenging tasks to improve label quality in a feedback-loop fashion. HAMLET fully integrates the limiting constraint of lacking an “Oracle” or absolute source of truth. With HAMLET, we were
able to improve our dataset, ultimately obtaining higher classification accuracies. Our contributions can be summarized as follow:

- Design of an algorithm for efficient label improvements.
- Increased interpretability of our classifier with the use of a separate memory module hosting representative reference embeddings.
- Successful application of our method to the challenging task of seizure classification.

In this article, we first survey related work in EEG classification, deep learning for health informatics, active learning and co-training. Our co-learning technique and the architecture of our classifier are introduced in section 3. Finally, in section 4 we present our dataset, methods for pre-processing, and results.

2 Related Work

2.1 EEG Classification

2.1.1 Using Feature Extraction

The topic of EEG classification is a fertile area of research. Most methods traditionally rely on feature selection combined with a classifier, such as Support Vector Machines (SVM), Linear Discriminant Analysis (LDA) or k-Nearest Neighbors (k-NN) (M. H. Alomari et al., 2013 Alomari et al. (2013); H. Shoeb et al., 2010 H. Shoeb and V. Guttag (2010)). Relevant features include Common Spatial Patterns (CSP), Filter-Bank Common Spatial Patterns (FBCSP), and Logarithmic Band Power (BP) (X. Yong et al., 2015 Yong and Menon (2015)). Seizure classification has also been approached with feature engineering (F. Fürbass et al., 2015 Fürbass et al. (2015)) for instance using signal amplitude variation (AV) and a regularity statistic (PMRS) (J. C. Sackellares et al., 2011 Sackellares et al. (2011)). Although careful feature engineering can lead to great performance, it is not be strictly necessary.

2.1.2 Deep Learning

Classification of EEG data can be seen as a multivariate time-series classification problem (P. Bashivan et al., 2015 Bashivan et al. (2015)). Furthermore, one advantage of CNNs is the automated feature selection that happens during the training process. Without additional work, the model learns the features that it finds most relevant for its given task, from the raw signals given as input. This has been shown with great success for sleep staging (S. Biswal et al., 2017 Biswal et al. (2017)) as well as seizure classification (U. Rajendra Acharya et al., 2017 Acharya et al. (2017)). However, all these deep models require high volumes of labeled data for training, which is the bottleneck in our application. Therefore, CNNs remain a model of choice but we cannot use them directly in the present study due to the label limitation.

2.2 Convolutional Auto-Encoders (CAEs)

CNNs can be used in a supervised learning framework, but cannot benefit from the large amounts of unlabeled data. Traditionally, auto-encoders (AEs) have been widely used to extract meaningful features in the absence of labels even on biomedical data (J. Tan et al., 2015 Tan et al. (2015)). However, in their simplest form, AEs cannot be efficiently applied to time-series as they ignore their bi-dimensional structure. Convolutional Auto-Encoders (CAEs) bring together the advantages of using convolutions and auto-encoders (X. Mao et al., 2016 Mao et al. (2016); Masci et al. Masci et al. (2011)). However, seizures are typically relative rare events, whereas CAEs tend to learn to represent the dominant statistical structure of the underlying data, which is not directly relevant for seizure classification. Therefore using CAEs alone is not sufficient in our classification task.

3
2.3 Co-Training

Co-training is a semi-supervised machine learning algorithm, where two models can be concurrently trained, each with its own set of features. Additionally, the predictions of one model on an unlabeled dataset are used to enlarge the dataset of the other model. The algorithm has originally been introduced for the classification of web pages (A. Blum et al., 1998 Blum and Mitchell (1998)). Here we do not focus on increasing dataset size but rather label quality within the labeled dataset. Although the standard setting for co-training includes unlabeled data that models can benefit from, it has been shown that co-training can still save labeled samples even in a strictly supervised setting (M. Darnstädt et al., 2009 Darnstädt et al. (2011)) which we use. In the original co-training algorithm, there is the possibility that the training set of a model is augmented with wrong labels from the other model. COTRADE improves on this idea by only allowing models to share labels they are confident about (M. L. Zhang et al., 2011 Zhang and Zhou (2011)). This notion of labeling confidence is at the center of HAMLET, however, there are some differences in our approach to co-training. Indeed, one of the two entities at the center of the algorithm is the human expert. The expert knowledge helps training the algorithm by updating the labeled dataset, while the model feedback helps improving the consistency of the expert at the classification task. Because of the human learning dimension, we use the term co-learning instead.

2.4 Active Learning

In situations where unlabeled data is abundant, but labeled data is scarce due to a restricted labeling budget, active learning offers a way to select the most informative sample points in order optimize labeling resources on the data that is most helpful for the model. Heuristics for active learning include Query by Committee (QBC), uncertainty sampling, margin sampling, entropy or Expected Gradient Length (EGL) (B. Settles, 2010 Settles (2010)). Although these methods might reduce the need for large label sets, this still is not enough for deep learning models like CNNs. For such models, including pseudo-labeled high-confidence data into the training set is a possible approach (K. Wang et al., 2017 Wang et al. (2017)). Unfortunately, active learning implies the existence of a source of truth that is not available in our challenging classification task, since in our study, even humans find it difficult to label many of the patterns commonly encountered in EEGs of critically ill patients.

2.5 Using Memory Modules in Neural Networks

Recently, researchers have been experimenting with augmenting neural networks with memory modules. For instance, a memory module is present in the architecture of Matching Networks (O. Vinyals et al., 2016 Vinyals et al. (2016)). In their model, the module is used together with an attention mechanism, however without interpretability in mind. Our design, presented in the following section, emphasizes interpretability thanks to an external memory module.

3 HAMLET Method

3.1 Co-learning Framework

3.1.1 Architecture of the Classifier

One important part of our HAMLET framework is the classifier, that is used to both improve the human expert through re-labeling suggestions, and of course the classification task itself, the ultimate goal of the whole process. Its architecture is shown in figure[1] It is based on a combination of the following three components:

- Embedding function $f$
- Memory module containing $N$ reference embeddings
- Dense layer $g$
One key novelty of our model lies in what we call a memory module. In this separate module, a set of $N$ reference embeddings is stored. For a given input $i$, the encoder creates an embedding $e_i = f(i)$ that is compared to each reference embedding $r_j$ using cosine similarity, giving $N$ similarity scores $s_j$. These similarity scores and the current embedding $e_i$ are concatenated to form the immediate representation fed to the classifier function $g$, typically a multilayer perceptron (MLP). We will explain in further sections how using reference embeddings enhances interpretability.

In our experiments, we used $N = 512$, and a dense layer $g$ with one hidden layer of $n = 1024$ neurons. We propose two different embedding functions $f$: 1) a supervised alternative that is trained with the available labeled dataset; and 2) a Convolutional Auto-Encoder (CAE), which allows to benefit from the whole dataset.

3.1.2 Algorithm

Our co-learning framework is best described with the following algorithm. We start with a first dataset with low quality labels, and iterate through the following steps:

1. Fine-tuning (pre-training for the first iteration) of the embedding function $f$.
2. Selection of reference embeddings.
3. Learning of the dense layer $g$.
4. Label improvement through machine feedback.

The procedure is illustrated on figure 2. By going through multiple runs of the above algorithm, the model is iteratively improved thanks to the increase in label quality. Concurrently, the expert learns from past classification mistakes and becomes more consistent at the labeling task. Each phase of the algorithm is described in the following sections.

3.2 Fine-Tuning (or Pre-Training) of the Embedding Function $f$

In this step, either a supervised or unsupervised approach can be taken. During the first iteration, the function $f$ is trained from scratch on the dataset. Further iterations of this algorithm only fine-tune $f$ and no pre-training is required.

3.2.1 Supervised Embedding Function $f$

For the supervised approach, we experimented with a CNN. In this case, $f$ corresponds to the first layers of the model up until the start of the dense layer. After training is complete, the dense layer is dropped.
Figure 2: Co-Learning algorithm with machine feedback. The model is first trained on the original training set TR\(_1\) and evaluated on the testing set TE\(_1\), keeping track of training and testing scores Sc\(_1\). The expert evaluates the results, and updates a subset of both TR\(_1\) and TE\(_1\). A more robust model is obtained by fine-tuning the original one using the newer version of the dataset. Throughout the process, the model improves and the expert becomes more consistent.

The architecture of our CNN is shown at the top of figure 3. The first layer uses a depth-wise separate convolution in order to better handle the high dimensionality of input data in EEG studies – 16 montages – a practice inspired by recent work on EEG classification (R.T. Schirrmeister et al., 2017). The depth-wise separate convolution first performs a convolution through time (per channel), followed by a convolution across all electrodes (also known as 1x1 convolution). The following blocks are standard groups of convolution, max-pooling, and dropout layers. We have used a dropout rate of \( p = 0.2 \) and batch normalization, which has been shown to improve generalization (S. Ioffe et al., 2015).

We use Exponential Linear Units (ELU) which provide faster learning (D-A Clevert et al., 2015) as our activation functions. The dense layer has 1024 neurons in the hidden layer, and ends with 5 softmax units corresponding to our class labels. We also use this CNN as a baseline for classification accuracy.

### 3.2.2 Unsupervised Embedding Function \( f \)

In the unsupervised approach, a Convolutional Auto-Encoder (CAE) is a great choice for \( f \). A CAE is made of an encoder, which creates an embedding, and a decoder that takes this embedding and reconstructs the original sequence. After the CAE is trained on the whole dataset, the decoder is dropped, and \( f \) is the encoder.

Our CAE architecture is shown at the bottom of figure 3. In the CAE, there is no dense layer. Instead all the operations are reversed in the decoder after the last max-pooling layer. To build the decoder, we use un-pooling layers which increase the sequence size from encoded representation to input length, and transposed convolutions (sometimes called de-convolutions) in order to keep the overall structure completely symmetric.

### 3.3 Selection of the Reference Embeddings

The reference embeddings are selected right after the embedding function \( f \) is learned. It is crucial that they are a close representation of the input data, and diverse enough to allow the model to use the module for all the classes present in the dataset. To ensure diversity, we use \( k \)-means among inputs of a same class, giving equal space in the memory module to all classes. Compared with a \( k \)-means on all available inputs, some reference embeddings might not be as useful for the model, or might even be redundant for rare classes, but this ensures that embeddings are always available for the model to learn from. For interpretability purposes, we keep track of the labels and sequences that correspond to the selected embeddings.
Figure 3: Embedding functions $f$. Each input channel is 1D and parameters are indicated as \{width, stride\}. Top: supervised embedding function. Not shown on the figure, batch-normalization is applied after convolutions and dropout after max-pooling layers with a rate of $p = 0.2$. The dense layer is only used for training, then dropped when used in HAMLET. Bottom: unsupervised embedding function. The first layers (before red boxes) are the encoding part of the network. They build the embedding (shown in red). The following layers are part of the decoder, which is only used for training, then dropped when used in HAMLET.
3.4 Learning of the Dense Layer $g$

The next step is to teach the model to correctly classify sequences of EEG, using both the embedding function $f$ and the memory module. The outputs of both components are concatenated and fed to the classifier $g$. The model is then trained on the labeled dataset in a supervised manner.

3.5 Label Improvement with Machine Feedback

The final step of training is where machine feedback comes into play. Using one of the machine feedback strategies described in 3.6, we suggest new labels for some sequences that the model mis-classified with high certainty. These suggestions are likely to propose sequences that have been mis-classified by the human grader. They are given to an expert for re-evaluation.

After a portion of the dataset has been re-labeled, the model is fine-tuned and new tests can evaluate performance increases. The labeling effort should be shared between samples from the training and testing sets. Although updating the testing set does not improve the model, it improves the quality of the experiment as a whole. A reasonable choice is to share this effort proportionally to each dataset size. However, in our experiments we also include results showing improvements on re-evaluated testing sequences only, to better display the improvements brought to the labels.

3.6 Machine Feedback Strategies

In traditional active learning, various heuristics can be used for suggesting new data to be labeled, with the intent of increasing the labeled dataset size. This is called uncertainty sampling. These heuristics include Least Confidence (D.D. Lewis et al., 1994 [Lewis and Gale (1994)])], Margin Sampling (T. Scheffer et al., 2001 [Scheffer et al. (2001)]) and entropy (C. E. Shannon, 1948 [Shannon (1948)]). Each heuristic outputs samples that would be most informative for the model. Here, we are looking for misclassification points that our model is most confident about, in order to suggest potential label errors by humans. Therefore we modify the active learning heuristics for improving label quality during the co-learning process. Below is a description of the various strategies for co-learning.

3.6.1 Highest Confidence

Using the confidence of the model accuracy on each piece of input data, we can select inputs that the model is most confident about. For each input $i$, the confidence $c_i$ is directly given by the probability of the class with highest probability according to the model: $c_i = \max_j p(y_i = j)$ for each class $j$. After all confidence values $c_i$ are obtained, they are ranked in decreasing order. For inputs $i$ with high confidence values $c_i$ that were wrongly classified by the model, a mistake on the original label is very likely. Therefore, those points will be provided as machine feedback to human experts for relabeling.

3.6.2 Margin Sampling

The margin sampling heuristic is also based on confidence values. Inputs with the highest difference between the confidence values of their two most likely classes indicate high confidence. For input $i$: $m_i = p(y_i = j_1) - p(y_i = j_2)$, where $j_1$ and $j_2$ are the two most likely labels, according to the model. The misclassification points with large margin will be used as machine feedback.

3.6.3 Entropy

Finally, entropy can also be used as a measure of the certainty for each input sequence. The entropy of all sequences are sorted in increasing order, the lowest values being the least informative ones – i.e. those the
model is most confident about. For a given input sequence \( i \), the entropy \( e_i \) is given by:

\[
e_i = -\sum_{j=1}^{C} p(y_i = j) \log(p(y_i = j))
\]

### 3.7 Interpretability of the Model

When using the model to perform a classification task on new data, the memory module can be used to explain the reasoning of the model. For a given input \( i \), \( N \) similarity scores \( s_k \) will be generated from the memory module, one per reference embedding \( r_k \).

In our experiments, we show that \texttt{HAMLET-CNN} learns to effectively use the reference embeddings for classification. However, we expect \texttt{HAMLET-CAE} to lack interpretability, as unsupervised training only teaches the model to recognize features that are only relevant to sequence encoding. As a result, \texttt{HAMLET} uses the memory module as a bank of features more than as a way to discriminate between classes. Therefore, interpretability can only be claimed for the supervised \texttt{HAMLET-CNN}.

Model interpretability allows to better justify the label suggestions in the last phase of the algorithm. For a given input sequence, if we look at the closest embeddings within the memory module – those with highest similarity scores \( s_k \) – we will most likely reach a reference sequence that shows a similar pattern to the current one. Formally, to justify the decision of the model to classify \( i \) into class \( c \), we can look at the reference embedding \( r^* \) with highest similarity score among reference embeddings for the same class \( c \):

\[
r^* = \arg\max_{r_k \in C} s_k, \quad s_k = \text{cosine_similarity}(r_k, f(i)).
\]

At this point, we can show the labels previously assigned to that reference sequence – preferably by the same expert – and explain why the model made such a suggestion. This increased interpretability enhances co-learning in the two following ways:

- First, the expert knows the model did not randomly happen to output a given class label. This decision is supported by interpretability and is far less likely to be ignored by the expert.

- Second, by reminding experts how they previously labeled similar sequences, they can learn much faster and become more consistent while labeling.
4 Experiments

4.1 Dataset

4.1.1 Acquisition of Continuous EEG Recordings

EEG recordings are multivariate time-series describing the electrical activity of the brain. In this study, they are recorded in a non-invasive manner by affixing 19 small metallic (silver/silver chloride) electrodes directly to the scalp. The EEG electrodes were placed in standardized locations, following the international 10-20 system, with locations and labels of electrodes as shown in figure 4.

Our original dataset, provided by the Neurosciences ICU at Massachusetts General Hospital (MGH), contains multiple hour-long (generally >24 hours) recordings of EEG for 155 different patients, sampled at $f = 200$ Hz. There is a plan to release the de-identified dataset to the public in the near future. In this dataset, we denote the EEG of patient $i$ by $X_i \in \mathbb{R}^{d_e \times m_i}$, with $d_e = 19$ the number of electrodes and $m_i$ the length of the given EEG.

4.1.2 Pre-processing

After acquisition, the raw EEG data goes through the following pre-processing pipeline:

- Low-pass filtering: the raw signals are first filtered with a 60.0 Hz low-pass filter, so that high-frequency noise and electrical artifacts are reduced.

- Computation of montages: it is usual to work with a bipolar montages instead of the raw data from the electrodes, to reduce interference from electrocardiogram (EKG) signals. This is done according to the table in figure 4. Let $M_i \in \mathbb{R}^{d_m \times m_i}$ be the montages for $X_i$ for patient $i$, with $d_m = 16$ the number of montages generated in the process – i.e. channels.

- Splitting of recordings: all EEG recordings are split into 16-second sequences. We denote each sequence from $X_i$ and $M_i$ by $s_{i,j}$ and $m_{i,j}$, respectively. Because the patterns representative of each class are usually clear only within a larger contextual time window, experts look at an additional 6 seconds of signal on each side of the sequence when labeling.

4.1.3 Initial Labeling Process

We have obtained the initial labeled recordings of 155 patients, for a total of 4176 hours, or an average of 27 hours per patient. Each sequence from these recordings has been manually labeled by a clinical expert. As we described about this task, high error rate is expected in these initial labels.

Each sequence of EEG can be given one of six class labels, where five correspond to the patterns of brain activity of primary interest (Seizure, Lateralized Periodic Discharges (LPD), Generalized Periodic Discharges (GPD), Generalized Rhythmic Delta Activity (GRDA), Lateralized Rhythmic Delta Activity (LRDA)), and the last one corresponds to Other/Artifacts (O/A). A great majority of the recordings is made of either background activity, noise, and non-physiological artifacts (O/A), so we put such sequences aside. In real-life, we can easily automate this selection step with a binary classifier. Let $D$ be the labeled dataset we obtain at this stage, without O/A ($D$ contains 5 classes).

4.1.4 Creation of Balanced Datasets

For our experiments, we created three datasets from all the available 16-second sequences $s_{i,j}$ in $D$. The class distribution in the full dataset $D$ is highly skewed, as shown in table[1] so we keep the datasets balanced in terms of class labels to ensure the models do not learn trivial frequency bias:

- $D^{unseen}_{20k}$: 20,000 sequences (89 hours of EEG data), split into a training set (80%) and a testing set (20%). Patients in the testing set are not present in the training set (testing is performed on unseen patients).
Table 1: Number of 16-second sequences from each class in the full labeled dataset $D$.

| Class Label | Sequence Count | Percentage |
|-------------|----------------|------------|
| Seizure     | 128,691        | 33%        |
| LPD         | 115,729        | 30%        |
| GPD         | 84,168         | 22%        |
| GRDA        | 32,566         | 8%         |
| LRDA        | 29,332         | 7%         |
| **Total**   | **390,486**    | **100%**   |

Table 2: Accuracy obtained on testing set of $D_{20k}^{\text{known}}$ (known patients) or $D_{20k}^{\text{unseen}}$ (unseen patients). Classifying EEGs of new patients is significantly more challenging.

| Model | Unseen Patients | Known Patients |
|-------|-----------------|----------------|
| HAMLET-CNN | 39.36%          | 75.91%         |
| HAMLET-CAE  | 38.46%          | 75.07%         |
| CNN         | 38.89%          | 74.93%         |
| MLP         | 21.04%          | 20.05%         |

- $D_{20k}^{\text{known}}$: 20,000 sequences (89 hours of EEG data), split into a training set (80%) and a testing set (20%). Patients in the testing set are also present in the training set (testing is performed on known patients).
- $D_{100k}$: made of 100,000 sequences from $D$ that are not in the previous two datasets. This larger dataset represents 445 hours of recordings and is only used for unsupervised training of the embedding function $f$ (CAE). Patients in the testing set are not present in the training set.

4.1.5 Dataset Augmentation

In this classification task, the most challenging issue is to make the model learn how to generalize across new patients. During training, in order to simulate different patients, the electrodes from the left and right side of the brain can be flipped, while the three reference electrodes in the middle of the scalp – Fz, Cz and Pz – remain unchanged. Our classification task being a symmetric problem, which particular side of the brain exhibits a pattern does not affect classification. This simple technique almost duplicates the training dataset in terms of the number of patients.

4.2 Setup

The model has been trained using a server with Intel(R) Xeon(R) CPUs E5-2630 v3 running at 2.40 GHz, 32 cores, with 256 Gb of RAM and 4 GPUs Tesla K80, NVIDIA Corporation GK210GL, with CUDA v8.0. Training has been performed with Python version 2.7, using version 1.4.1 of Tensorflow. Other libraries needed for HAMLET include numpy and scipy. With the above configuration, training HAMLET-CNN during 100 epochs on $D_{20k}^{\text{unseen}}$, with a batch size of 128, took thirteen hours. We used the Tensorflow implementation of the stochastic optimizer Adam (D.P. Kingma et al., 2014 [Kingma and Ba (2014)])
Table 3: Accuracy obtained on the testing set of $D_{20k}^{unseen}$. Accuracies are shown before and after re-evaluation. During co-learning, 837 sequences (4.18% of the dataset $D_{20k}^{unseen}$) have been re-evaluated by an expert. Results are shown for the full testing set, as well as on the subset of sequences re-evaluated during co-learning. We note a clear increase in model performance after this first iteration alone.

| Model      | Before re-labeling | After re-labeling |
|------------|--------------------|-------------------|
|            | full test | re-eval only | full test | re-eval only |
| HAMLET-CNN | 39.36%    | 7.03%      | 40.75%    | 68.75%      |
| HAMLET-CAE | 38.46%    | 10.94%     | 39.06%    | 67.97%      |
| CNN        | 38.89%    | 6.25%      | 41.58%    | 68.75%      |
| MLP        | 21.04%    | 0.78%      | 23.14%    | 14.06%      |

4.3 Evaluation

Next, we evaluate our classification models and HAMLET technique. For each experiment, we have trained our models for 100 epochs, saving the model with highest accuracy on the testing set.

4.3.1 Classification

To get a sense of the difficulty of the task, the performance of our models and various baselines has been evaluated in the following two scenarios:

- Known patients: with $D_{20k}^{known}$, where patients in the training are also present in the testing set, we first assess the ability of the model to classify known patients, which can be useful in some clinical situations such as long-term monitoring at ICU. In this setting, clinicians wish to capture seizure patterns similar to those observed previously, or in long-ambulatory long-term monitoring settings with implantable electrodes where there is the opportunity to fine-tune the system based on previous seizures.

- Unseen patients: using $D_{20k}^{unseen}$, we evaluate the performance of the model at generalizing across patients. It is important to ensure the model can classify EEG from different brains. This is an obviously harder task, leading to an understandable drop in accuracy when evaluating in this setting.

For each scenario, we have experimented with two variations of HAMLET with each $N = 512$ reference embeddings, either with supervised embedding (HAMLET-CNN) or unsupervised embedding (HAMLET-CAE), as well as the following baseline models:

- Convolutional Neural Network (CNN): this baseline is the model that we use as a supervised embedding function $f$, introduced in 3.2.1. Therefore, the complexity of this baseline is comparable to that of HAMLET-CNN.

- MultiLayer Perceptron (MLP): we have trained an MLP with 1024 neurons in the hidden layer to perform the same classification task.

The results of this experiment, shown in table 2, confirm the existence of inconsistencies within the dataset. When labeling the sequences, experts usually remain consistent for sequences coming from the same patient. However, it is hard for them to remain consistent when labeling sequences from new patients having their own specific patterns. This is where re-labeling with machine feedback will show how HAMLET can be used to drastically improve performance.

4.3.2 Co-Learning

Results on the original $D_{20k}^{unseen}$ dataset (before label re-evaluation) from the previous experiment are again shown on the first two columns of table 3. These accuracies set the starting point for improvements using co-learning.
Figure 5: Confusion matrices of HAMLET-CNN trained and tested on the original testing set (top) and after fine-tuning, with training and testing on the improved datasets (bottom). Each row shows, for a given expert-provided class label, how it has been classified and in what proportions by the model (a diagonal matrix is ideal). After co-training, although seizures are not as clearly classified as before, LRDA and LPD are not as confused with seizures anymore.

In order to evaluate our co-learning framework, we ran one iteration of our algorithm, providing a suggestion of sample points to be re-labeled by a human expert, using the highest confidence heuristic introduced in section 3.6. Results show that after this first iteration alone, during which 837 sequences (4.18% of the dataset \( D_{unseen} \)) have been re-evaluated by an expert, accuracy on the testing shows great improvement. The results are shown on table 3. We note that in most scenarios, HAMLET-CNN performs better than the unsupervised embedding alternative HAMLET-CAE, and also better than MLP which cannot learn properly, as expected. Our CNN has good performance overall, but cannot claim to be interpretable like HAMLET-CNN.

The confusion matrices for HAMLET-CNN in the first iteration and after re-labeling are shown together on figure 5. It is interesting to notice how the model improves based on these confusion matrices: although after co-learning, seizures are not as clearly recognized by the model as before, the model now better classifies LRDA and LPD, leading to overall better accuracy and classification performance of the model.

4.3.3 Interpretability

Finally, we analyzed how the model uses the reference embeddings when making decisions. This can be done by looking at the weights of the dense layer that are applied to the reference embeddings. For each output class label \( c \), we selected the 16 reference embeddings with biggest weights in the dense layer, among the 512 available embeddings. We then computed what percentage of these 16 embeddings have the same class
Table 4: Interpretability scores for HAMLET-CNN. Each percentage shows, out of the 16 reference embeddings with highest weights in the model, how many belong to the target class.

| Class | LRDA | GRDA | LPD | Seizure | GPD |
|-------|------|------|-----|---------|-----|
| Interpretability | 75.00% | 68.75% | 62.50% | 37.50% | 25.00% |

Table 5: Percentage of expert agreement on suggestions from HAMLET-CNN for various machine feedback strategies.

| Method            | Agreement |
|-------------------|-----------|
| High Confidence   | 92.19%    |
| Margin Sampling   | 91.41%    |
| Entropy           | 93.75%    |

label $c_i$ as $c$. Each percentage gives an interpretability score for label $c$.

The results presented in table 4 for HAMLET-CNN show that for most classes, the model is really able to learn how to use the similarity scores. Interestingly, the less interpretable classes in the model also are the ones with worst classification performance according to the confusion matrices. One reason could potentially be that the set of patterns that represent such classes is really diverse, preventing the model from efficiently using similarity scores.

Knowing that the model knows how to make use of reference embeddings, the expert re-evaluation task can benefit from interpretability outputs from the model. For a given input sequence that our model suggests as needing re-evaluation, the embeddings with highest similarity scores are selected and displayed next to the sequence, explaining why the model made that particular decision.

4.3.4 Comparison of Machine Feedback Strategies

Finally, we compared the three different strategies introduced in 3.6. For each strategy, HAMLET suggested 128 samples with new labels. We counted how many the expert agrees with in each case. The results in table 5 show that entropy might be a better indicator of misclassified inputs, although all methods perform almost equally well.

5 Conclusion

By acknowledging the difficulty of label acquisition in new domains for both human experts and machine algorithms, we have reached with HAMLET multiple advances in deep learning for healthcare applications. To summarize, first, we have introduced a novel technique, HAMLET, for human and machine co-learning that is suited for creating high-quality labeled datasets on challenging tasks with a limited budget. This technique has benefits that can appreciated in many deep learning applications. We have shown how this technique applies to the classification of seizures from continuous EEG, a challenging task for both machines and human experts. Finally, we have designed a new kind of network with increased interpretability potential. During the dataset improvement phase, this interpretability via similar reference examples can assist experts re-evaluating sample sequences by explaining the reasons why the algorithm came up with a given output.

Ultimately, this work can benefit others domains that share similar difficulties when it comes to efficiently labeling large volumes of data for challenging applications of deep learning.
References

Rodriguez Ruiz A, Vlachy J, Lee J, and et al. 2017. Association of periodic and rhythmic electroencephalograpic patterns with seizures in critically ill patients. *JAMA Neurology* 74, 2 (2017), 181–188. DOI: [http://dx.doi.org/10.1001/jamaneurol.2016.4990](http://dx.doi.org/10.1001/jamaneurol.2016.4990)

U. Rajendra Acharya, Shu Lih Oh, Yuki Hagiwara, Jen Hong Tan, and Hojjat Adeli. 2017. Deep convolutional neural network for the automated detection and diagnosis of seizure using EEG signals. *Computers in Biology and Medicine* (2017). DOI: [http://dx.doi.org/https://doi.org/10.1016/j.compbiomed.2017.09.017](http://dx.doi.org/https://doi.org/10.1016/j.compbiomed.2017.09.017)

Mohammad H. Alomari, Aya Samaha, and Khaled AlKamha. 2013. Automated Classification of L/R Hand Movement EEG Signals using Advanced Feature Extraction and Machine Learning. *CoRR* abs/1312.2877 (2013). [http://arxiv.org/abs/1312.2877](http://arxiv.org/abs/1312.2877)

Pouya Bashivan, Irina Rish, Mohammed Yeasin, and Noel Codella. 2015. Learning Representations from EEG with Deep Recurrent-Convolutional Neural Networks. *CoRR* abs/1511.06448 (2015). [http://arxiv.org/abs/1511.06448](http://arxiv.org/abs/1511.06448)

Siddharth Biswal, Joshua Kulas, Haoqi Sun, Balaji Goparaju, M. Brandon Westover, Matt T. Bianchi, and Jimeng Sun. 2017. SLEEPNET: Automated Sleep Staging System via Deep Learning. *CoRR* abs/1707.08262 (2017). [http://arxiv.org/abs/1707.08262](http://arxiv.org/abs/1707.08262)

Avrim Blum and Tom Mitchell. 1998. Combining Labeled and Unlabeled Data with Co-training. In *Proceedings of the Eleventh Annual Conference on Computational Learning Theory (COLT’ 98)*. ACM, New York, NY, USA, 92–100. DOI: [http://dx.doi.org/10.1145/279943.279962](http://dx.doi.org/10.1145/279943.279962)

Djork-Arne Clevert, Thomas Unterthiner, and Sepp Hochreiter. 2015. Fast and Accurate Deep Network Learning by Exponential Linear Units (ELUs). *CoRR* abs/1511.07289 (2015). [http://arxiv.org/abs/1511.07289](http://arxiv.org/abs/1511.07289)

Malte Darnstädt, Hans Ulrich Simon, and Balázs Szürényi. 2011. Supervised Learning and Co-training. In *Algorithmic Learning Theory*, Jyrki Kivinen, Csaba Szepesvári, Esko Ukkonen, and Thomas Zeugmann (Eds.). Springer Berlin Heidelberg, Berlin, Heidelberg, 425–439.

Andre Esteva, Brett Kuprel, Roberto A. Novoa, Justin Ko, Susan M. Swetter, Helen M. Blau, and Sebastian Thrun. 2017. Dermatologist-level classification of skin cancer with deep neural networks. *Nature* 542 (25 Jan 2017), 115 EP -. [http://dx.doi.org/10.1038/nature21056](http://dx.doi.org/10.1038/nature21056)

F Fürbass, MM Hartmann, JJ Halford, J Koren, J Herta, A Gruber, C Baumgartner, and T Kluge. 2015. Automatic detection of rhythmic and periodic patterns in critical care EEG based on American Clinical Neurophysiology Society (ACNS) standardized terminology. *Neurophysiologie Clinique/Clinical Neurophysiology* 45, 3 (2015), 203–213.

Nicolas Gaspard, Lawrence J Hirsch, Suzette M LaRoche, Cecil D Hahn, and M Brandon Westover. 2014. Interrater agreement for critical care EEG terminology. *Epilepsia* 55, 9 (2014), 1366–1373.

Ali H. Shoeb and John V. Guttag. 2010. Application of Machine Learning To Epileptic Seizure Detection. In *ICML 2010 - Proceedings, 27th International Conference on Machine Learning*. 975–982.

Hiba A Haider, Rosana Esteller, Cecil D Hahn, M Brandon Westover, Jonathan J Halford, Jong W Lee, Mouhsin M Shafi, Nicolas Gaspard, Susan T Herman, Elizabeth E Gerard, and others. 2016. Sensitivity of quantitative EEG for seizure identification in the intensive care unit. *Neurology* 87, 9 (2016), 935–944.

JJ Halford, D Shiau, JA Desrochers, BJ Kolls, BC Dean, CG Waters, NJ Azar, KF Haas, E Kutluay, GU Martz, and others. 2015. Inter-rater agreement on identification of electrographic seizures and periodic discharges in ICU EEG recordings. *Clinical Neurophysiology* 126, 9 (2015), 1661–1669.
Awni Y. Hannun, Carl Case, Jared Casper, Bryan Catanzaro, Greg Diamos, Erich Elsen, Ryan Prenger, Sanjeev Satheesh, Shubho Sengupta, Adam Coates, and Andrew Y. Ng. 2014. Deep Speech: Scaling up end-to-end speech recognition. *CoRR* abs/1412.5567 (2014). [http://arxiv.org/abs/1412.5567](http://arxiv.org/abs/1412.5567)

Kaiming He, Xiangyu Zhang, Shaoqing Ren, and Jian Sun. 2015. Deep Residual Learning for Image Recognition. *CoRR* abs/1512.03385 (2015). [http://arxiv.org/abs/1512.03385](http://arxiv.org/abs/1512.03385)

Sergey Ioffe and Christian Szegedy. 2015. Batch Normalization: Accelerating Deep Network Training by Reducing Internal Covariate Shift. *CoRR* abs/1502.03167 (2015). [http://arxiv.org/abs/1502.03167](http://arxiv.org/abs/1502.03167)

Diederik P. Kingma and Jimmy Ba. 2014. Adam: A Method for Stochastic Optimization. *CoRR* abs/1412.6980 (2014). [http://arxiv.org/abs/1412.6980](http://arxiv.org/abs/1412.6980)

Alex Krizhevsky, Ilya Sutskever, and Geoffrey E. Hinton. 2012. ImageNet Classification with Deep Convolutional Neural Networks. In *Proceedings of the 25th International Conference on Neural Information Processing Systems - Volume 1 (NIPS’12)*. Curran Associates Inc., USA, 1097–1105. [http://dl.acm.org/citation.cfm?id=2999134.2999257](http://dl.acm.org/citation.cfm?id=2999134.2999257)

Y. LeCun, B. Boser, J. S. Denker, D. Henderson, R. E. Howard, W. Hubbard, and L. D. Jackel. 1989. Backpropagation Applied to Handwritten Zip Code Recognition. *Neural Computation* 1, 4 (Dec 1989), 541–551. DOI: [http://dx.doi.org/10.1162/neco.1989.1.4.541](http://dx.doi.org/10.1162/neco.1989.1.4.541)

David D. Lewis and William A. Gale. 1994. A Sequential Algorithm for Training Text Classifiers. In *Proceedings of the 17th Annual International ACM SIGIR Conference on Research and Development in Information Retrieval (SIGIR ’94)*. Springer-Verlag New York, Inc., New York, NY, USA, 3–12. [http://dl.acm.org/citation.cfm?id=188490.188495](http://dl.acm.org/citation.cfm?id=188490.188495)

Xiaojiao Mao, Chunhua Shen, and Yu-Bin Yang. 2016. Image Restoration Using Very Deep Convolutional Encoder-Decoder Networks with Symmetric Skip Connections. In *Advances in Neural Information Processing Systems 29*, D. D. Lee, M. Sugiyama, U. V. Luxburg, I. Guyon, and R. Garnett (Eds.). Curran Associates, Inc., 2802–2810.

Jonathan Masci, Ueli Meier, Dan Cireşan, and Jürgen Schmidhuber. 2011. *Stacked Convolutional Auto-Encoders for Hierarchical Feature Extraction*. Springer Berlin Heidelberg, Berlin, Heidelberg, 52–59. DOI: [http://dx.doi.org/10.1007/978-3-642-21735-7_7](http://dx.doi.org/10.1007/978-3-642-21735-7_7)

P. W. Mirowski, Y. LeCun, D. Madhavan, and R. Kuzniecky. 2008. Comparing SVM and convolutional networks for epileptic seizure prediction from intracranial EEG. In *2008 IEEE Workshop on Machine Learning for Signal Processing*. 244–249. DOI: [http://dx.doi.org/10.1109/MLSP.2008.4685487](http://dx.doi.org/10.1109/MLSP.2008.4685487)

Volodymyr Mnih, Koray Kavukcuoglu, David Silver, Andrei A. Rusu, Joel Veness, Marc G. Bellemare, Alex Graves, Martin Riedmiller, Andreas K. Fidjeland, Georg Ostrovski, Stig Petersen, Charles Beattie, Amir Sadik, Ioannis Antonoglou, Helen King, Dharshan Kumaran, Daan Wierstra, Shane Legg, and Demis Hassabis. 2015. Human-level control through deep reinforcement learning. *Nature* 518 (25 Feb 2015), 529 EP -. [http://dx.doi.org/10.1038/nature14236](http://dx.doi.org/10.1038/nature14236)

J Chris Sackellares, Deng-Shan Shiau, Jonathon J Halford, Suzette M LaRoche, and Kevin M Kelly. 2011. Quantitative EEG analysis for automated detection of nonconvulsive seizures in intensive care units. *Epilepsy & Behavior* 22 (2011), S69–S73.

Tobias Scheffer, Christian Decombein, and Stefan Wrobel. 2001. Active Hidden Markov Models for Information Extraction. In *Proceedings of the 4th International Conference on Advances in Intelligent Data Analysis (IDA ’01)*. Springer-Verlag, London, UK, UK, 309–318. [http://dl.acm.org/citation.cfm?id=647967.741628](http://dl.acm.org/citation.cfm?id=647967.741628)
Robin Tibor Schirrmeister, Jost Tobias Springenberg, Lukas Dominique Josef Fiederer, Martin Glassstetter, Katharina Eggensperger, Michael Tangermann, Frank Hutter, Wolfram Burgard, and Tonio Ball. 2017. Deep learning with convolutional neural networks for EEG decoding and visualization. Human Brain Mapping (aug 2017). DOI:http://dx.doi.org/10.1002/hbm.23730

Burr Settles. 2010. Active learning literature survey. Technical Report.

C. E. Shannon. 1948. A mathematical theory of communication. The Bell System Technical Journal 27, 3 (July 1948), 379–423. DOI:http://dx.doi.org/10.1002/j.1538-7305.1948.tb01338.x

David Silver, Julian Schrittwieser, Karen Simonyan, Ioannis Antonoglou, Aja Huang, Arthur Guez, Thomas Hubert, Lucas Baker, Matthew Lai, Adrian Bolton, Yutian Chen, Timothy Lillicrap, Fan Hui, Laurent Sifre, George van den Driessche, Thore Graepel, and Demis Hassabis. 2017. Mastering the game of Go without human knowledge. Nature 550 (18 Oct 2017), 354 EP -. http://dx.doi.org/10.1038/nature24270 Article.

Jie Tan, Matthew Ung, Chao Cheng, and Casey Greene. 2015. Unsupervised feature construction and knowledge extraction from genome-wide assays of breast cancer with denoising autoencoders. 20 (01 2015), 132–43.

Gulshan V, Peng L, Coram M, and et al. 2016. Development and validation of a deep learning algorithm for detection of diabetic retinopathy in retinal fundus photographs. JAMA 316, 22 (2016), 2402–2410. DOI: http://dx.doi.org/10.1001/jama.2016.17216

Aäron van den Oord, Sander Dieleman, Heiga Zen, Karen Simonyan, Oriol Vinyals, Alex Graves, Nal Kalchbrenner, Andrew W. Senior, and Koray Kavukcuoglu. 2016. WaveNet: A Generative Model for Raw Audio. CoRR abs/1609.03499 (2016). http://arxiv.org/abs/1609.03499

Oriol Vinyals, Charles Blundell, Timothy P. Lillicrap, Koray Kavukcuoglu, and Daan Wierstra. 2016. Matching Networks for One Shot Learning. CoRR abs/1606.04080 (2016). http://arxiv.org/abs/1606.04080

Keze Wang, Dongyu Zhang, Ya Li, Ruimao Zhang, and Liang Lin. 2017. Cost-Effective Active Learning for Deep Image Classification. CoRR abs/1701.03551 (2017).

Wenpeng Yin, Katharina Kann, Mo Yu, and Hinrich Schütze. 2017. Comparative Study of CNN and RNN for Natural Language Processing. CoRR abs/1702.01923 (2017). http://arxiv.org/abs/1702.01923

Xinyi Yong and Carlo Menon. 2015. EEG Classification of Different Imaginary Movements within the Same Limb. PLOS ONE 10, 4 (04 2015), 1–24. DOI: http://dx.doi.org/10.1371/journal.pone.0121896

M. L. Zhang and Z. H. Zhou. 2011. CoTrade: Confident Co-Training With Data Editing. IEEE Transactions on Systems, Man, and Cybernetics, Part B (Cybernetics) 41, 6 (Dec 2011), 1612–1626. DOI: http://dx.doi.org/10.1109/TSMCB.2011.2157998