

Wednesday the 27th of November, 2019

Automatic Detection of Epilepsy Seizures in NHS Electroencephalography Records (using classical machine learning models)

Presented by David Luke Elliott

Department of Psychology, D37 Fylde College, Lancaster University, Lancaster, LA1 4YF

My work focuses on developing hardware, software, and algorithms for Electroencephalography (EEG) monitoring of patients with epilepsy.

Introduction

I am a psychology methods researcher, with the emphasis on the methods (Data Scientist?).

Focus of Today's Talk

Epilepsy

Clinical Decision Support

Classification

Imbalanced Labels Classical Methods Bayesian Optimization

What is Epilepsy

Epilepsy is the tendency to have unprovoked and recurrent seizures.

Seizures are caused by neuronal hyperexcitability and excessive electrical discharges.

There are over 40 types of epilepsy and seizures, of which individuals may experience several.

Absence Epilepsy

Absence seizures can develop during childhood (6- to 7-years) or early adolescence (~12-years).

Constitutes around 10% of paediatric epilepsy patients.

Clinical symptoms include…

- **Blank stare**
- Interrupted activities
- Slowed speech
- Upward rotation of the eyes

Diagnosing an epilepsy syndrome is primarily reliant on:

- Patient report
- Identification of clinical features in diagnostic imaging

○ **Electroencephalography (EEG)**

- Magnetic Resonance Imaging (MRI)
- Computed Tomography (CT)
- Video recordings

NHS Epilepsy Diagnosis

A patient's medical history, along with ~30-minute scalp EEG assessment (sometimes also measuring heart rate and blood oxygen saturation), is commonly first assessed.

During the assessment, the patient may be asked to hyperventilate or exposed to flashing lights (photic stimulation) to provoke a seizure.

The patient is monitored by staff, who note events on the records to aid retrospective analysis. If a diagnosis is suspected, but not gained, a patient may then have a longer EEG assessment.

https://kidshealth.org/en/parents/eeg.html

Manual review of EEG is

- Time consuming
- **Expensive**
- Prone to error

95-99% of the recorded data is useless for diagnosis

Data Analysis

Algorithms to assist medical practice have been around for decades.

- Computer aided ECG's have been around since the 1970's.
- Use static rule-based models (heuristics) with limited accuracy.

Machine learning models are increasingly being applied to diagnostic imaging:

- **Radiology**
- Dermatology
- Clinical pathology

DEEP MEDICINE

HOW ARTIFICIAL **INTELLIGENCE CAN MAKE HEALTHCARE HUMAN AGAIN**

ERIC TOPOL

With a foreword by ABRAHAM VERGHESE. value of Cutting for Stone

Pre-processing

Prepare the raw signal

Feature extraction

Quantify values or features of the signal (e.g. biomarkers or artefacts)

Classification

Applying a threshold or model-based criteria

● Model-based classification requires additional feature reduction or extraction, and a training or supervised learning step

Expert System

The global strategy that is developed

- Which features to select
- How to combine features
- Account for contextual information

Algorithms generally can be designed for efficiency (online) or accuracy (offline)

Seizure-event detector

Aim

● Identify seizures with the greatest possible sensitivity/specificity/precision

Use

● Provide a summary of frequency, duration, and time of a patient's seizures to enable physicians diagnose and better titrate therapy

Seizure predictors

Aim

● Predict seizures with the greatest accuracy and time in advance

Use

- Trigger neurostimulators to prevent a seizure
- Provide warning that a patient may have a seizure

Seizure-onset detector

Aim

Detect the onset of a seizure with the shortest possible delay

Use

- Initiate functional neuroimaging to localise the cerebral origin of a seizure
- Trigger neurostimulators to affect seizure progression
- Alert a carer to the patient's condition or call emergency response

Algorithms generally can be designed for efficiency (online) or accuracy (offline)

Seizure-event detector

Aim

● Identify seizures with the greatest possible sensitivity/specificity/precision

Use

● Provide a summary of frequency, duration, and time of a patient's seizures to enable physicians diagnose and better titrate therapy

Seizure predictors

Aim

● Predict seizures with the greatest accuracy and time in advance

Use

- Trigger neurostimulators to prevent a seizure
- Provide warning that a patient may have a seizure

Seizure-onset detector

Aim

● Detect the onset of a seizure with the shortest possible delay

Use

- Initiate functional neuroimaging to localise the cerebral origin of a seizure
- Trigger neurostimulators to affect seizure progression
- Alert a carer to the patient's condition or call emergency response

Models can be trained and tested in various ways for different use cases

Patient-General

Training

Models are trained on records from a number of patients and tested on a separate test group

Use

● Clinical decision making (diagnosis, treatment)

Patient-Specific

Training

- Trained only on data from an individual patient to detect/predict future seizures
- A patient general algorithm is adapted to fit an individual patient (e.g. Semi-supervised Reinforcement Learning/Transfer Learning)

Use

• Ambulatory (home) patient monitoring

Models can be trained and tested in various ways for different use cases

Patient-General

Training

Models are trained on records from a number of patients and tested on a separate test group

Use

● Clinical decision making (diagnosis, treatment)

Patient-Specific

Training

- Trained only on data from an individual patient to detect/predict future seizures
- A patient general algorithm is adapted to fit an individual patient (e.g. Semi-supervised Reinforcement Learning/Transfer Learning) Use
	- Ambulatory (home) patient monitoring

Study

- Dataset with Ecological Validity
- Large Feature Space
- **Classical Models**
- **Exploration Over Pipeline Components &** Hyperparameters (Bayesian Optimisation)

Data Collection

EEG records from 21 pediatric patients (ages 4-13) diagnosed with absence epilepsy (~11hrs).

Patients underwent a routine clinical EEG assessment, lasting approximately 30 minutes, and were asked to hyperventilate or exposed to photic stimulation to provoke a seizure.

Data from these sessions were anonymized and burned to a CD by a clinical physiologist after being used for diagnostic purposes.

Baseline (47.60%)

All data that was not marked represents interictal EEG with no content of interest

AMPSAT (27.41%)

Segments with amplifier saturation, mostly at the start of the recordings where the signals data quality is being improved

Artefact (22.96%)

Electrical phenomena which distorts the neural signal such as respiratory, eye movement, muscle, or environmental sources

Generalized Epileptiform Discharge (1.45%)

Spike-and-wave discharges which are sometimes proceeded by polyspikes

Notched Rhythmic Waveforms (0.54%)

Benign activity likely a result of the patient being in a state of drowsiness

Spikes (0.04%)

Events that in isolation would be unlikely to be used as a diagnostic marker

Binary

Ictal

Generalised Epileptiform Discharge

Inter-ictal

- **Baseline**
- **Artefact**
- Notched Rhythmic Waveforms
- **Spikes**

Multiclass

Ictal

● Generalised Epileptiform Discharge

Inter-ictal

- Baseline
- Notched Rhythmic Waveforms

● Spikes

Artefact

Feature Extraction

Quantify values or features of the signal (e.g. biomarkers or artefacts)

The data was epoched into window sizes of 2 seconds with a 1 second overlap (most records were sampled at 256Hz). In each epoch, for each channel, the following features were extracted…

Ratio

To get all these features for the full dataset (11hrs) takes around 6:03 mins on my laptop

Dimension Reduction **Principal Component Analysis (PCA)**

Dimensionality reduction algorithms remove multicollinearity and retain important information by creating new synthetic features through combining features

PCA aims to separate a set of mixed signals into their component sources.

PCA aims to find vectors that best explain a data's variability by transforming data onto an equal or lower dimensional subspace, combining features that are highly correlated.

PCA can reduce a model's complexity, run time, and potential for overfitting to the training data.

SVMs are discriminative algorithms that distinguish classes of objects by finding a hyperplane that provides the maximum margin of separation from classes.

If data can be linearly separated, then a 'hard' margin of separation can be used; whereby a point on the edge of a class is used as the support vector for the decision boundary.

However 'hard' margins are sensitive to outliers, so often a 'soft' margin is used to allow for some errors (*C*).

If classes cannot be linearly separated, the input feature space can be projected to higher dimensions to create a nonlinear separation boundary

```
pipe svc rbf = Pipeline([('scl', StandardScaler()),
                             ('c)f', SVC(C=100,
                                         kernel='rbf',
                                         class weight = 'balanced',
                                         random state=RANDOM STATE))])
   pipe svc rbf.fit(vis data, y train)
  plot decision regions (vis data,
                          v train.
11
                         c1f = pipe svc rbf)
12
13 plt.xlabel(x axis label)
14 plt.ylabel(y axis label)
15 plt.xlim(0, .6)16 plt.ylim(0, 1.)17 plt.show()
```


KNN is a lazy learner that memorizes training data, rather than learning a discriminative function, assigning data points to the class with the greatest number of "nearest neighbors.

The number of nearest neighbors (*k*) and a distance metric, to measure the distance between samples, need to be specified.

```
I from sklearn.neighbors import KNeighborsClassifier
  pipe knn = Pipeline([('scl', StandardScaler()),
                        ('clf', KNeighborsClassifier(n neighbors=2))])
  pipe knn.fit(vis data, y train)
  plot decision regions (vis data,
                         y train,
                         clf = pipe knn)
10
11 plt.xlabel(x axis label)
12 plt.ylabel(y axis label)
13 plt.xlim(0, .6)14 plt.ylim(0,1.)15 plt.show()
```


Classification **Classification Decision** Tree

Decision trees split the data based on the features that best separates data into the class labels.

Data is split until all the samples within each node all belong to the same class or a maximum depth is reached.

```
DT = DecisionTreeClassifier(criterion='qini',max depth = None,
                               random state=RANDOM STATE)
  DT.fit(vis data, y train)
  dot data = export graphviz (DT, out file=None,
                        feature names=[x axis label, y axis label],
                        class names=feature reduced['class'].unique(),
                        filled=True, rounded=True,
                        special characters=True)
10
11
12 graphviz. Source (dot data)
```


A RF is an ensemble of multiple decision trees which are averaged together.

A random forest draws a random bootstrap sample of data and features to grow individual decision trees on. This process is repeated *n* times and the prediction of each tree is aggregated to assign class labels.

A Bayesian optimization method was used to search over classification pipeline components and model hyperparameters for each classifier. The search space begins with a random combination of components and hyperparameters, which are optimized over 1000 iterations.

Optimisation and Cross-Validation

The objective function is used at each iteration to update a prior from a history of model configuration and score pairs. The probability model P(score|configuration) is used to search for the most promising candidates and is therefore quicker than evaluating all possible combinations (e.g. GridSearch).

There are a few different algorithms for bayesian optimisation, such as gaussian processes and tree-structured-parzen-estimators.

Fig. 3: SVM parameter optimization using Bayesian optimization algorithm.

Nandy, A., Alahe, M. A., Uddin, S. N., Alam, S., Nahid, A. A., & Awal, M. A. (2019, January). Feature Extraction and Classification of EEG Signals for Seizure Detection. In 2019 International Conference on Robotics, Electrical and Signal Processing Techniques (ICREST) (pp. 480-485). IEEE.

Gaussian Mixture Model's (GMM) or regression models can be used for modelling the probability.

For TPE's a prior distribution needs to be defined for the hyperparameters, although these can just be uniformly distributed if there is little previous guidance.

The first few iterations just perform a random search to build a distribution of the best observations for each hyperparameter. A GMM l(x) is fitted to parameters associated with the smallest loss function values, and another GMM g(x) to the remaining values to choose a parameter value x that maximizes the ratio $I(x)/g(x)$.

http://neupy.com/2016/12/17/hyperparameter_optimization for neural networks.html

The distributions are modelled using parzen-window density estimators so that each sample defines a gaussian distribution which can be stacked together and normalised to give a probability density function.

The tree structure refers to the fact parameters can have tree-structured dependencies; for example, the Gamma parameter of a SVM can only be selected if the kernel is chosen to be a RBF rather than linear.

Optimisation and Cross-Validation Tree of Parzen Estimators (TPE)

```
\bullet1 from hyperopt import fmin, tpe, hp, STATUS OK, Trials
       2 from sklearn.preprocessing import StandardScaler
       \frac{1}{2} PARAM DIST = {
       5' 'C': hp.uniform('C', 0, 8),
          'kernel': hp.choice('kernel',
               {'ktype': 'linear', 'qamma': 'auto'}, # qamma ignored
               {'ktype': 'sigmoid', 'gamma': hp.uniform('sig_gamma', 0, 1) },
               ['ktype':'poly', 'gamma': hp.uniform('poly gamma', 0, 1) },
               {'ktype': 'rbf', 'gamma': hp.uniform('rbf gamma', 0, 1)}]),
      1011
           'scale': hp.choice('scale', [0, 1])
      121314 def hyperopt_train_test(params):
      15X = X train[:]16
      17if 'scale' in params:
      18
          if params['scale'] == 1:
      19
               sc = StandardScale()20
              X = sc.fit transform(X)2122 clf = SVC(C = params['C'],23<sup>1</sup>\texttt{kernel} = \texttt{params['kernel']['ktype'],
      24
                     gamma = params['kernel']['gamma'],
      25
      26
     27
           return cross val score(clf, X, y train, cv = 5). mean()
      28
      29 def objective(params):
      30acc = hyperopt train test(parg)31return ('loss': -acc,
                                             # minus because we need to reduce
      32
                   'status': STATUS OK)
      33
      34 trials = Trials()
      35 best = fmin(objective, PARAM DIST,
      36
                    algo=tpe.suggest, max evals=500,
      37.trials=trials)
      38
      39 print ('best:')
      40 print (best)
    100%
                       500/500 [01:02<00:00, 8.06it/s, best loss: -0.9875]
B
    best:
    {'C': 0.7576142466789729, 'kernel': 0, 'scale': 1}
```


Optimisation and Cross-Validation

Optimisation and Cross-Validation

Pipelines were cross-validated using a 5-fold StratifiedKFold so each fold had a similar proportion of seizure and non-seizure data to the full data.

Each fold was undersampled to balance the number of ictal and interictal data for training.

Separately for each classifier, at each trial of the Bayesian optimization training, features could be selected using a random forest, extracted using PCA, or both.

Training (1 Bayes Iteration)

Question: How can I get 98.55% accuracy using 1 rule/line of code on a 20 minute EEG record where a patient has 3 seizures each lasting 5.8 seconds?

Question: How can I get 98.55% accuracy using 1 rule/line of code on a 20 minute EEG record where a patient has 3 seizures each lasting 5.8 seconds?

Question: How can I get 98.55% accuracy using 1 rule/line of code on a 20 minute EEG record where a patient has 3 seizures each lasting 5.8 seconds?

Answer: Just always predict a patient is never having a seizure > *predictions = [0]*len(patient_record)*

(Also I find that weighting classes or up-sampling tends to perform worse as the imbalance is huge in this case)

Performance Evaluation

Patient-specific leave-one-out cross-validation

Performance is assessed in a manner that is like how the models would be used in practice

Performance Evaluation

The best pipelines for each classifier (SVM, RF, KNN) on each held-out dataset were selected and re-trained on an undersample of the full held-out dataset it was previously cross-validated on. This is because during cross-validation it was only trained on $4/5$ th of data.

These models were then also grouped into a soft voting ensembles (SVE's) for each patient.

Training

Training

SVM Hyperparameters on data where P2 was left out (random state = 1)

SVM Hyperparameters on data where P2 was left out (random state = 2)

Training Training

Training Training

P20_KNeighborsClassifier

Accuracy = $1 - \frac{FP+FN}{FP+FN+TP+TN}$

 $Metric = F1-score$

General Conclusions

Datasets with lots of artifactual (noisy) data, means there's likely to be increased instances of false positives.

Some authors…

…group detection's together. …remove artefacts before training and testing models. …do not consider a detection false if within 1 minute of a seizure!

Features selected by random forests reflect the presentation of absence seizures. This may enable…

…a seizure specific EEG channel profile based on the focal area of seizures.

…patient specific limited channel EEG for long term monitoring based on their unique seizure topography.

Finding optimal parameters is important… … for model fit

… to ensure differences between models are not because of default/selected parameters

Model performance tends to be worse on records with no seizures present.

- Algorithms could assist with collecting longer EEG records.
- Another study found 30% of children who had no clinically detected seizures in a standard recording procedure had them detected in 1hr EEG recordings.

Use of Bayesian hyperparameter optimisation

● Authors often do not make it clear how they arrived at certain hyperparameters

Most complete descriptions of the models performance in raw seconds

General Conclusions

Comparison of Binary and Multiclass models with a new dataset marked freely rather than in windowed bins

First use of NHS clinic data scans collected during diagnostic routine

They tend to be noisy at the start of the record and while they are asking the patient to breathe heavily.

Whats Next?

Larger datasets

- NHS: Increase to 37 Patients (26hrs) with absence seizures
- TUH: 11 Patients (6hrs) with absence seizures
- TUH: 65 Patients (47hrs) with generalised seizures
- CHB: 24 Patients (980hrs) with generalised seizures

Ensemble Models

- **Balanced Bagged KNN**
- **Balanced Random Forest**
- Randomly Undersampled Boosted Trees (RUSBoost)
- **LightGBM**

Whats Next?

Deep learning architectures

- **Multilayer Perceptron (MLP)**
- Convolutional Neural Network (CNN)
- **Recurrent Neural Network**

BOHB – Bayesian Optimization and Hyperband

Varying window sizes based on data (Changepoint)

Computing hardware and software

Hardware

Dell XPS 13 9370 laptop Lancaster High End Computing Cluster Google Colab (GPU & TPU)

Software

Python 3

- Numpy, Pandas
- PyWavelets, SciPy
- Scikit-learn
- Imbalanced-learn
- Hyperopt, HpBandSter
- **LightGBM**
- Tensorflow 2.0 (Keras API) Jupyter Notebooks

GitHub

Project
Team

Clinical Application

- Prof. Vincent Reid (Professor of Psychology)
	- David Elliott (PhD Student)
	- Aidan Moutrey (Undergraduate Student)
- . Dr. Judith Lunn (Lecturer in Medical School)
- Dr. Christian DeGoede (Consultant Paediatric Neurologist)
- Dr. Munni Ray (Consultant Paediatric Neurologist)
- Dr. Rosemary Belderbos (Consultant Paediatrician)
- Staff from Preston, Blackburn, and Leeds NHS Hospitals
	- Dr. Nicholas Combes
	- Gemma Wilkinson
	- **Andrew Lancaster**
	- Heather Collier

Hardware

- Barrie Usherwood (Electronics/Research Technician)
- Dr. Peter Tovee (Electronics/Research Technician)

□ Software

- Dr. Abe Karnik (Lecturer in Computing and Communications)
	- Kristoffer Geyer (PhD Student)
	- Nathan Rutherford (Undergraduate Student)

Data Analysis

- Dr. Rebecca Killick (Senior Lecturer Statistics)
	- David Elliott (PhD Student)

Thanks to our sponsors!

MIRALIS

Digital
Lancashire/