Machine Learning and its Potential to Improve Epilepsy Diagnosis

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Introduction

I am currently employed by the University of Edinburgh as a University Teacher in Mathematical Sciences Computing.

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

Outline

- Introduction
    - Epilepsy
- Current Diagnosis
- Problems with seizure detection
- Opportunities

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.

NHS Epilepsy Diagnosis

Diagnosing an epilepsy syndrome is primarily reliant on:

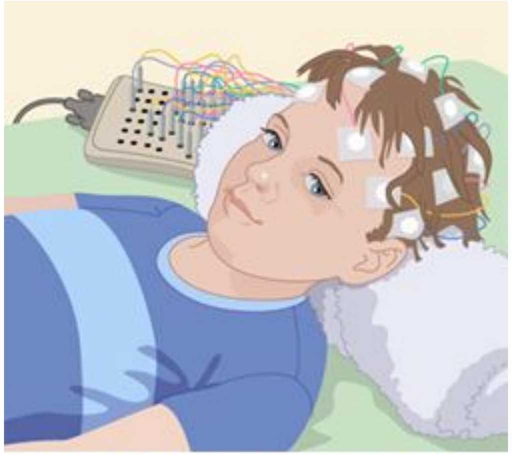
- Patient report
- Identification of clinical features in diagnostic imaging
    - **Electroencephalography (EEG)**
    - Magnetic Resonance Imaging (MRI)
    - Computed Tomography (CT)
    - Video recordings

NHS Epilepsy Diagnosis (Example)

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.

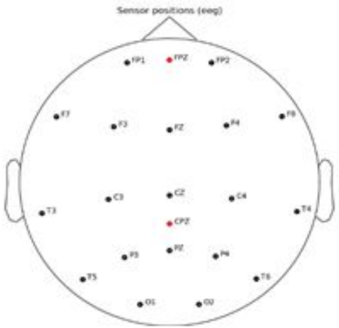


https://kidshealth.org/en/parents/eeg.html

NHS Epilepsy Diagnosis

Neurologists/physiologists qualitatively assess the EEG record, along with session notes and video, to identify the presence and type of epilepsy based on…

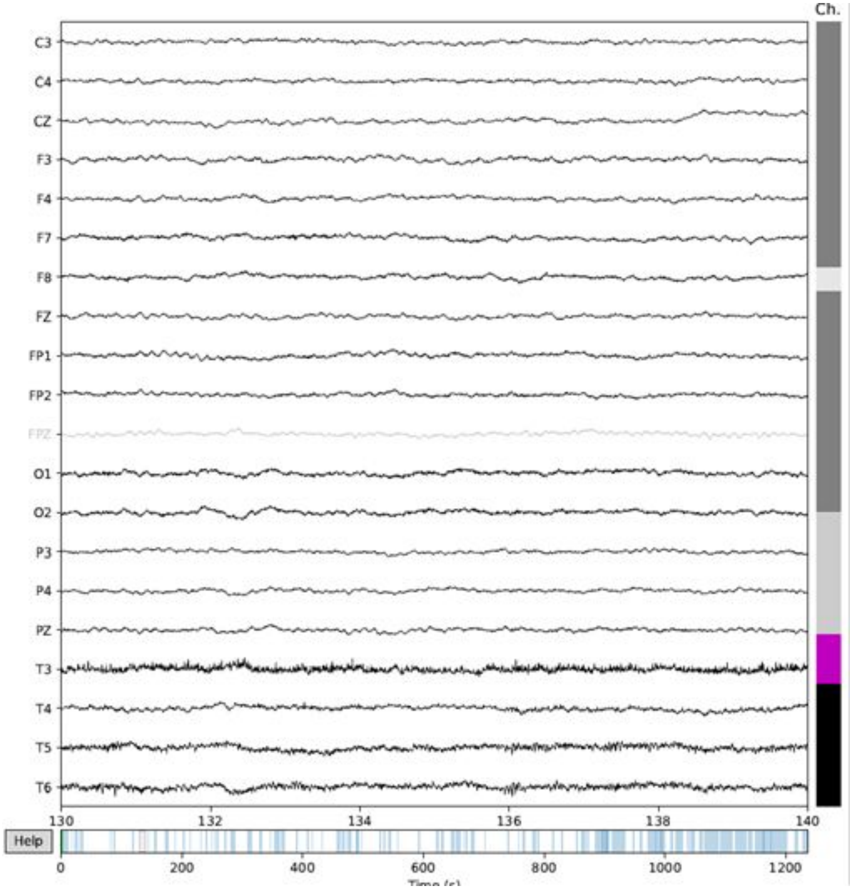
1. **Spatial and temporal information** when the EEG appears to have seizure-like oscillations over a long duration and several channels.
2. The pattern is **defined from background activity**, taking into consideration the difference of awake and asleep background EEG.
3. **Accumulated knowledge** regarding the appearance of epileptic events, noise, and benign rhythmic activity.



Pre-processing

Baseline (47.60%)

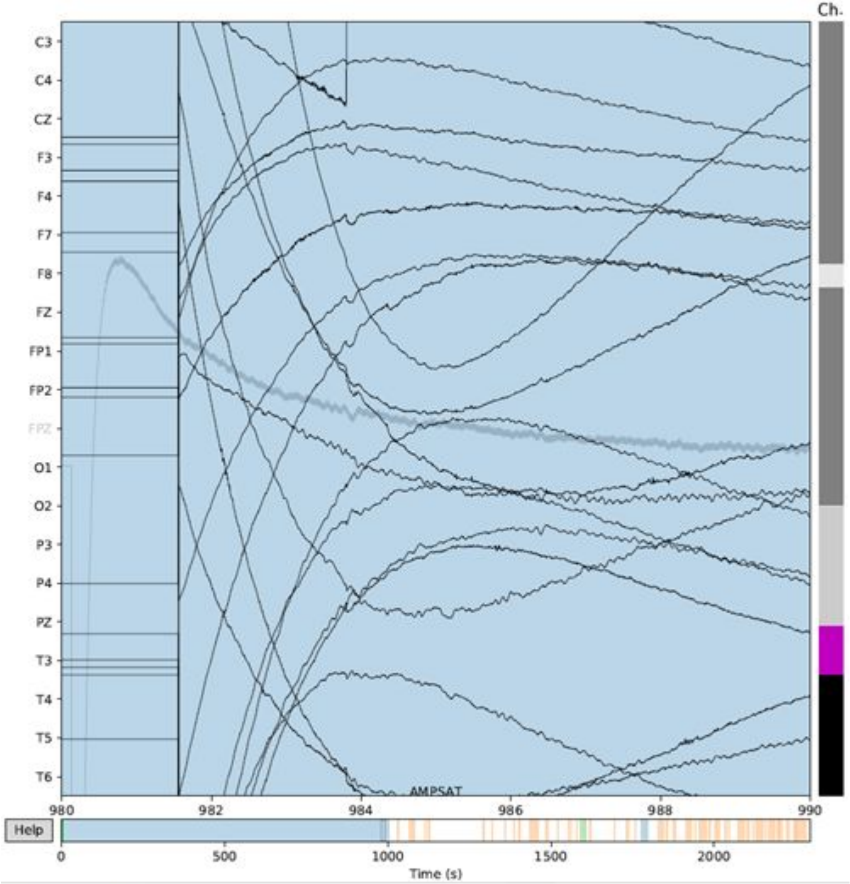
All data that was not marked represents interictal EEG with no content of interest



Pre-processing

Amplifier Saturation (27.41%)

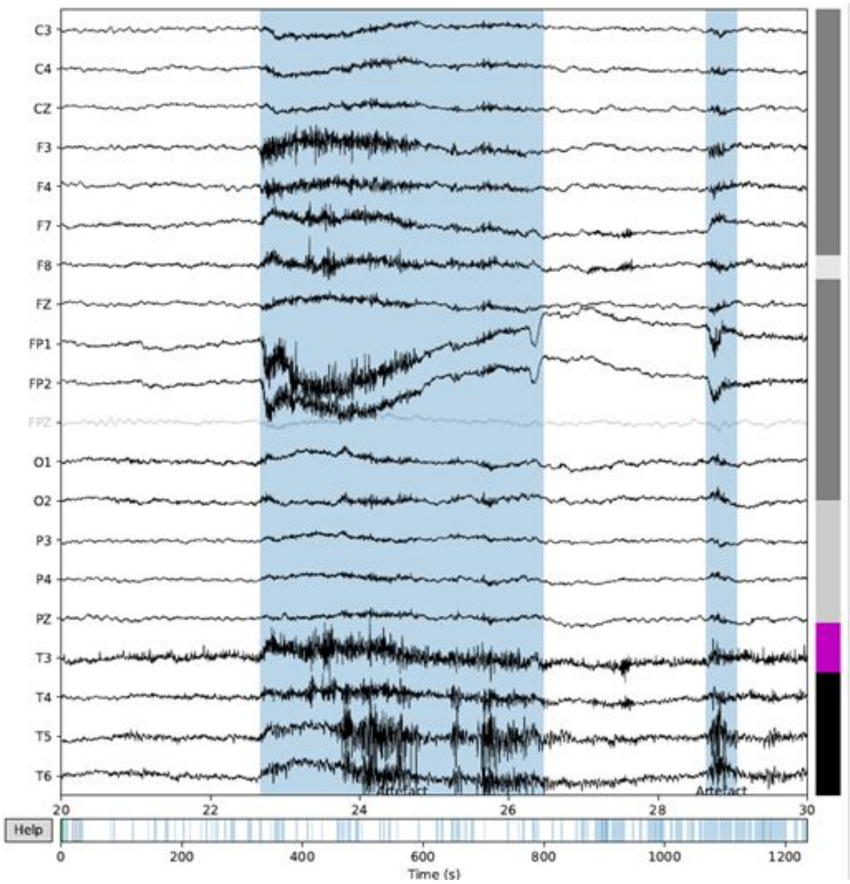
Segments with amplifier saturation, mostly at the start of the recordings where the signals data quality is being improved



Pre-processing

Artefact (22.96%)

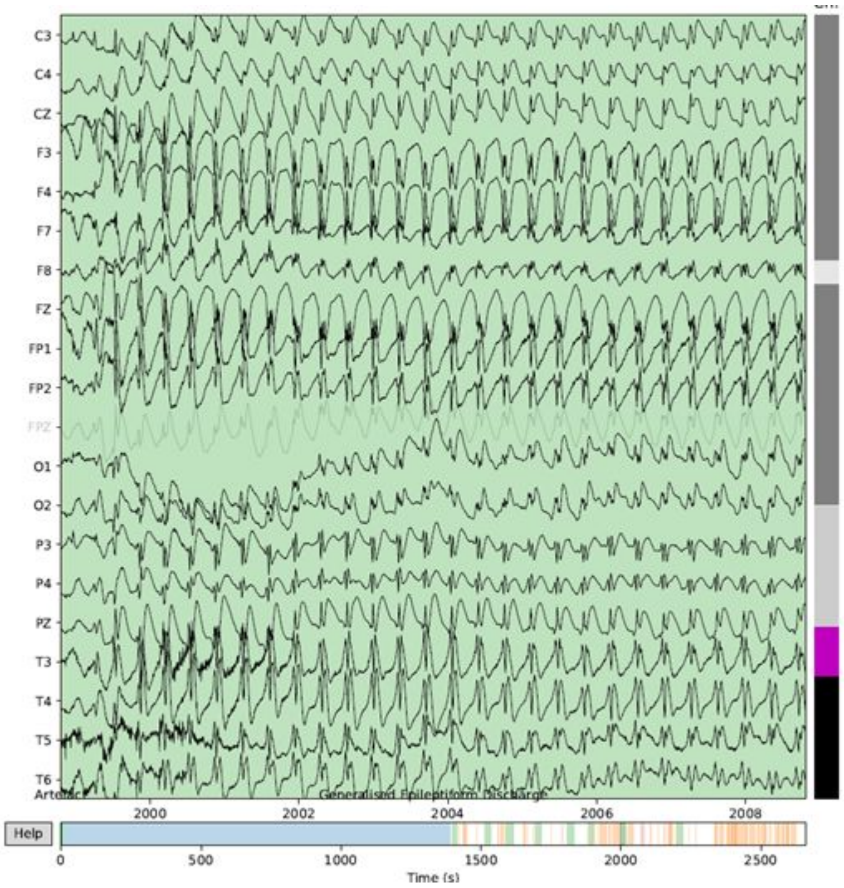
Electrical phenomena which distorts the neural signal such as respiratory, eye movement, muscle, or environmental sources



Pre-processing

Generalized Epileptiform Discharge (1.45%)

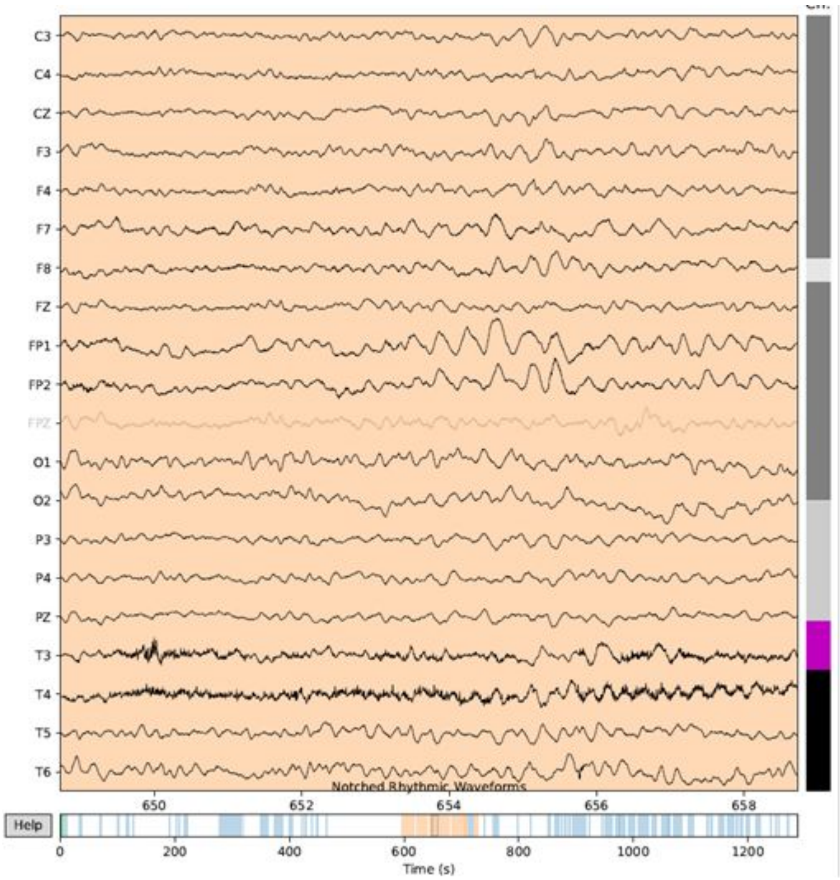
Spike-and-wave discharges which are sometimes proceeded by polyspikes



Pre-processing

Notched Rhythmic Waveforms (0.54%)

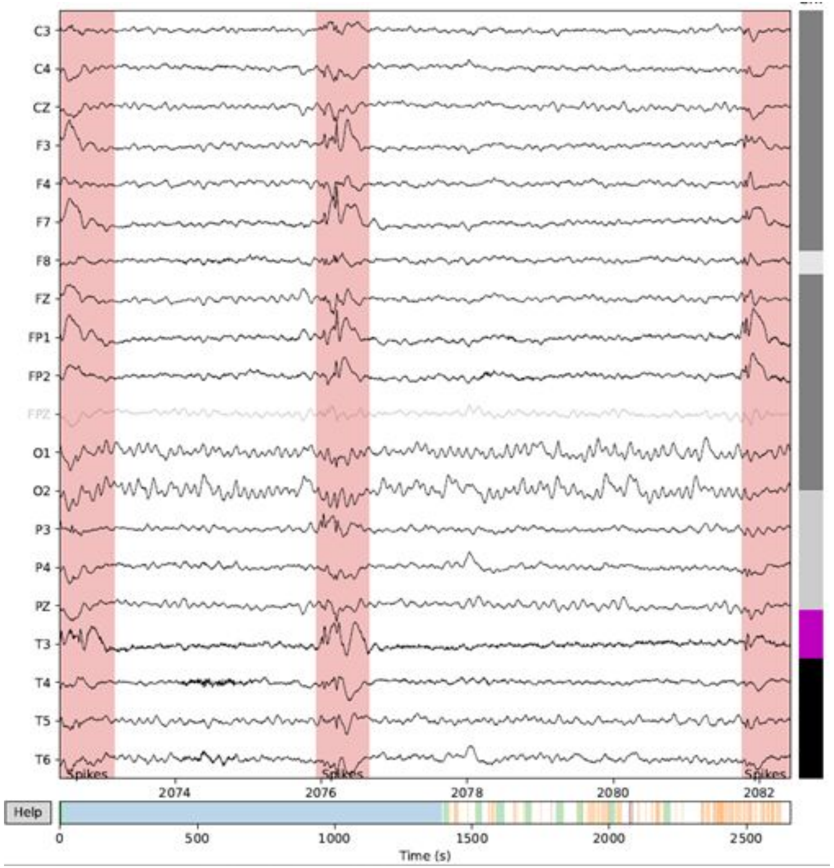
Benign activity likely a result of the patient being in a state of drowsiness



Pre-processing

Spikes (0.04%)

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



Manual review of EEG

Time consuming

The results from outpatient studies typically take within seven days to return to the patient.

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

Prone to error

Pediatric: False positive rate of 5% for the initial diagnosis of epilepsy and a false negative rate of 7.4% for children who had a previous unclear event (Stroink et al., 2003)

Adults: Misdiagnosis rates generally are estimated to be between 20-30% in developed countries (NICE Clinical Guidelines and Evidence Review for the Epilepsies, 2004).

Expensive(ish)

Pediatric: “conventional" or long-term pediatric EEG outpatient studies cost on average between £105 to £270 (NHS, 2020).

Adults: Typically these patients are under long-term monitoring which can cost on average anywhere between £1,382 to £5,947 depending on the level of the complication or comorbidities (NHS, 2020).

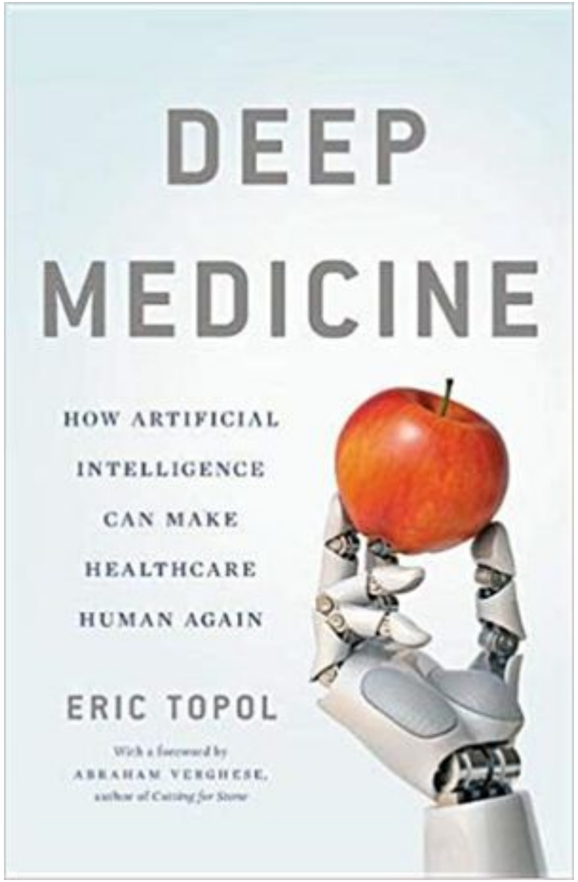
Data Analysis

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



Where is semi-automated EEG scoring in healthcare practice?

- Difficulties and inconsistencies in EEG scoring
- Technical limitations of current models
- Security and privacy issues
- The lack of friendly user interfaces
- New technology aversion

Fiorillo et al. (2019)

Where is semi-automated EEG scoring in healthcare practice?

Difficulties and Inconsistencies in EEG Scoring

High inter- and intra-scorer variability in scoring between neurologists (Wilson et al., 2003; Younes et al., 2018).

- Inter-rater agreement can be poor where there are complex and abnormal background activities (Ronner et al., 2009), or regarding subtle or brief events (Halford et al., 2015).
- Current clinical transcriptions lack information/format required for ML classification training.
- There is typically no definitive onset and offset for a seizure (Fisher et al., 2014). This is unlike other clinical data where labels are more concrete e.g. time of patient death.

Where is semi-automated EEG scoring in healthcare practice?

Technical Limitations of Current Models

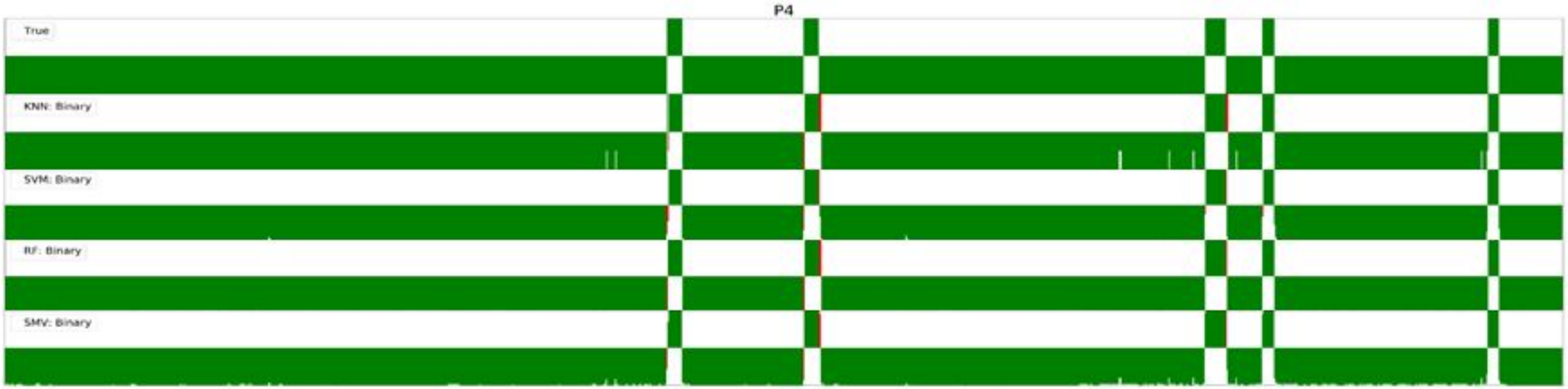
- Data with seizures is highly imbalanced which affect models performance and assessment.

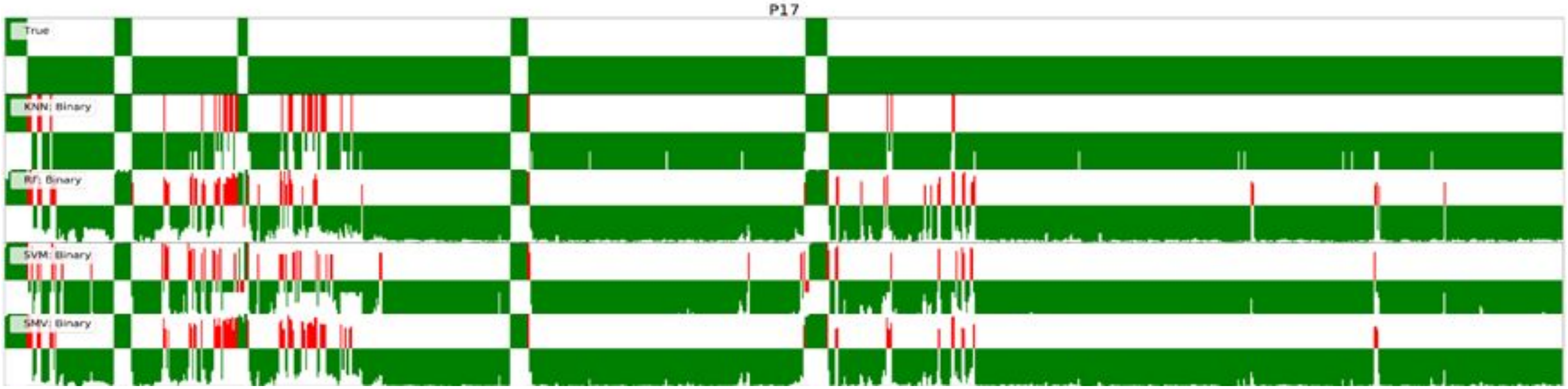
No one-size-fits-all

- Classical Algorithms (e.g. KNN) potentially better for marking the full length of a seizure.
- Balanced ensembles (e.g. LightGBM) potentially better for detecting the number of seizures in a record.
- Different seizures have different best “post-processing” window sizes used to remove false positives.
- Similar to manual coding, classification performance varies between different types of seizures.
- Multiple models trained to detect a particular type of seizure maybe better than a general multi-class?

(Based on results from my Thesis)

Automated/Semi-Automated Opportunities





No One-Size-fits all!

Technical Limitations of Current Models

What about deep learning?

- Deep learning probably best for individualised modelling (transfer learning).

Problems

- High computational complexity (Coleman et al., 2017) - meaning long training times.
- Large financial costs: the best performing models cost between $7,000 to $12 million to train (Synced, 2019). Most organizations continue to commit 25-75% of development/deployment resources to maintain the project (Dimensional Research, 2019).
- Large common DL models can emit five times the lifetime emissions of the average American car (Strubell et al., 2019).
- Ideal for running on large computing clusters, which require data transfer (see next slide).
- DL may not currently be optimal for EEG processing, as unlike its other successful applications it has comparatively limited available data, a low signal-to-noise ratio, and little empirical work addressing class imbalance (Johnson and Khoshgoftaar, 2019).

Where is semi-automated EEG scoring in healthcare practice?

Security and Privacy Issues

Some current automated EEG sleep scoring software requires the uploading of recordings to the cloud (e.g. Tay et al., 2017) or external servers (e.g. Younes et al., 2015), which can conflict with data protection policies of healthcare providers (Ali et al., 2018).

Healthcare information is highly personal, therefore any transfer of information between parties involves risks; both actual and perceived (Fichman et al., 2011).

Different models have different hardware requirements:

Good CPU Methods

KNN, SVM, GBT

Good GPU Methods

GBT, CNN

Basic Signal Processing System

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

Automated/Semi-Automated Opportunities

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

Automated/Semi-Automated Opportunities

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

Automated/Semi-Automated Opportunities

Reduce Assessment Time

Algorithms could reduce the time taken for EEG technicians to assess an EEG record. Allowing for…

- …greater involvement from in patient focused treatment plans (see Topol, 2019).
- …broader range of assessment options less constrained by the mark-up time.

- In study 1, algorithms reduced the need to review the full 11 hours of EEG across all 21 patients down to only 14 minutes of EEG segments.

Automated/Semi-Automated Opportunities

Enables the Collection of Longer EEG Records

- ~40% of patients in our NHS (Preston) dataset did not have any identifiable seizures in the 30-minute records, but were later diagnosed with absence epilepsy.
    - Another study found 30% of children who had no clinically detected seizures in a standard recording procedure had them detected in 1hr EEG recordings.

- Algorithms could be combined with portable EEG to monitor patients out of the clinic.

Automated/Semi-Automated Opportunities

Portable EEG

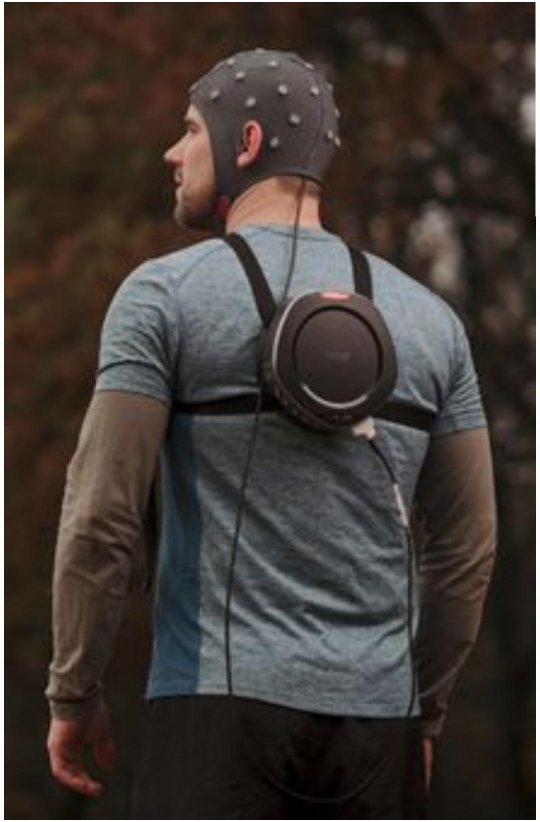
Cost Effective

- Computer-assisted outpatient EEG is around 50% to 60% cheaper per day than 24-hour hospital EEG.

More Data

- Clinical and subclinical EEG is more likely to be observed.
- Currently reliant on random sampling of a fraction of overall activity.
- Can observe typical provoking factors.

Portable EEG Hardware



Automated/Semi-Automated Opportunities

Seizure Tracking Apps

Advantages

- Improve seizure frequency information
- Seizures can be logged as they happen
- Data can be backed up easily
- Entries are time stamped
- Reminders can be scheduled

Disadvantages

- Patients are estimated to fail to report between 40% and 60% of seizures.
- Nocturnal seizures can occur frequently in a patient and are hard to log.
- Parental report for absences is especially poor (≥5%), due to its subtle presentation.

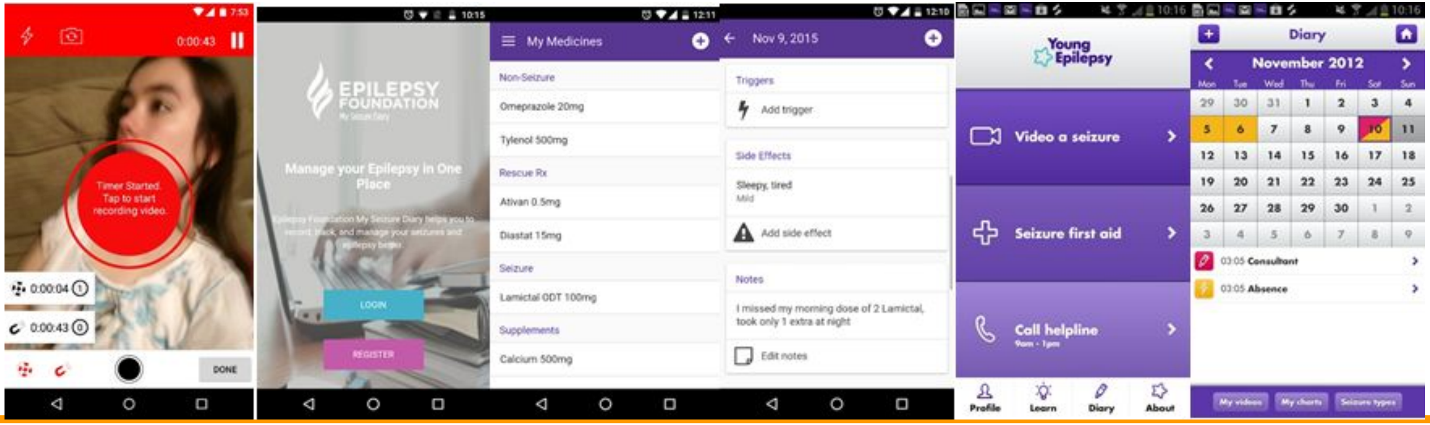
Seizure Tracking Apps

SeizureTracker

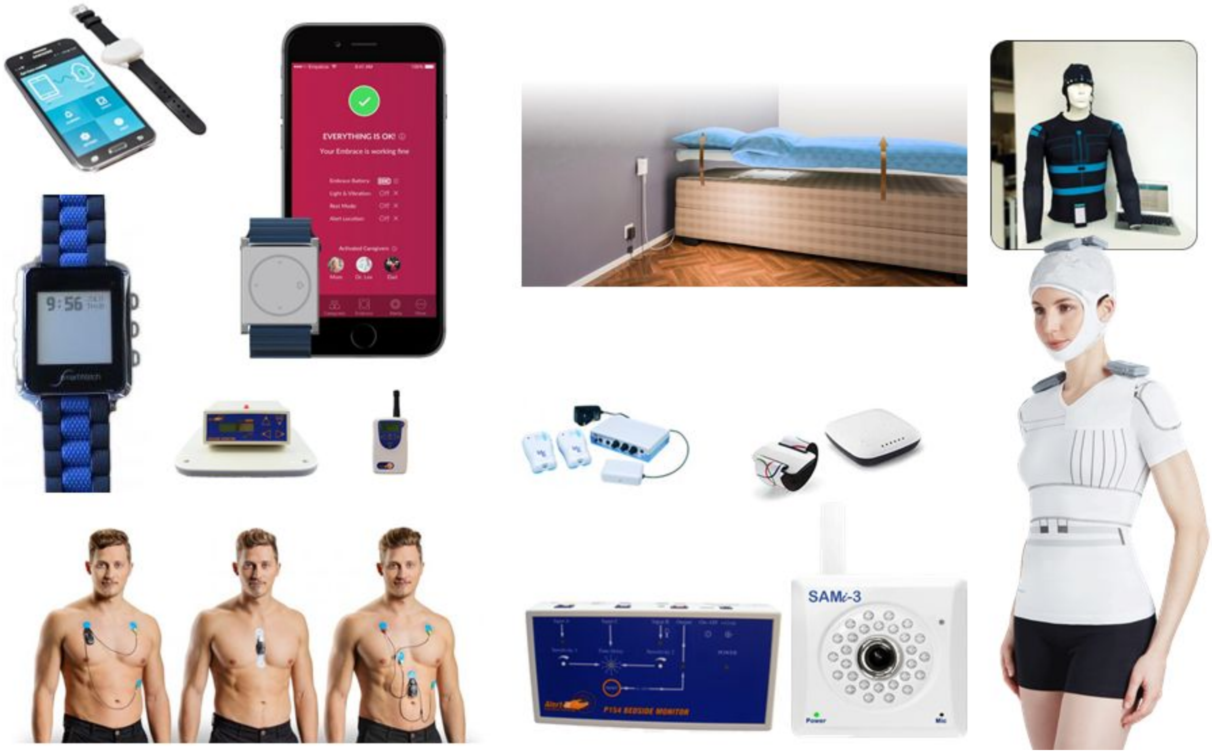
(www.seizuretracker.com)

My Seizure Diary *(www.epilepsy.com/seizurediary)*

Young Epilepsy App *(http://www.youngepilepsy.org.uk)*



Currently Available/Upcoming Seizure Detection Systems



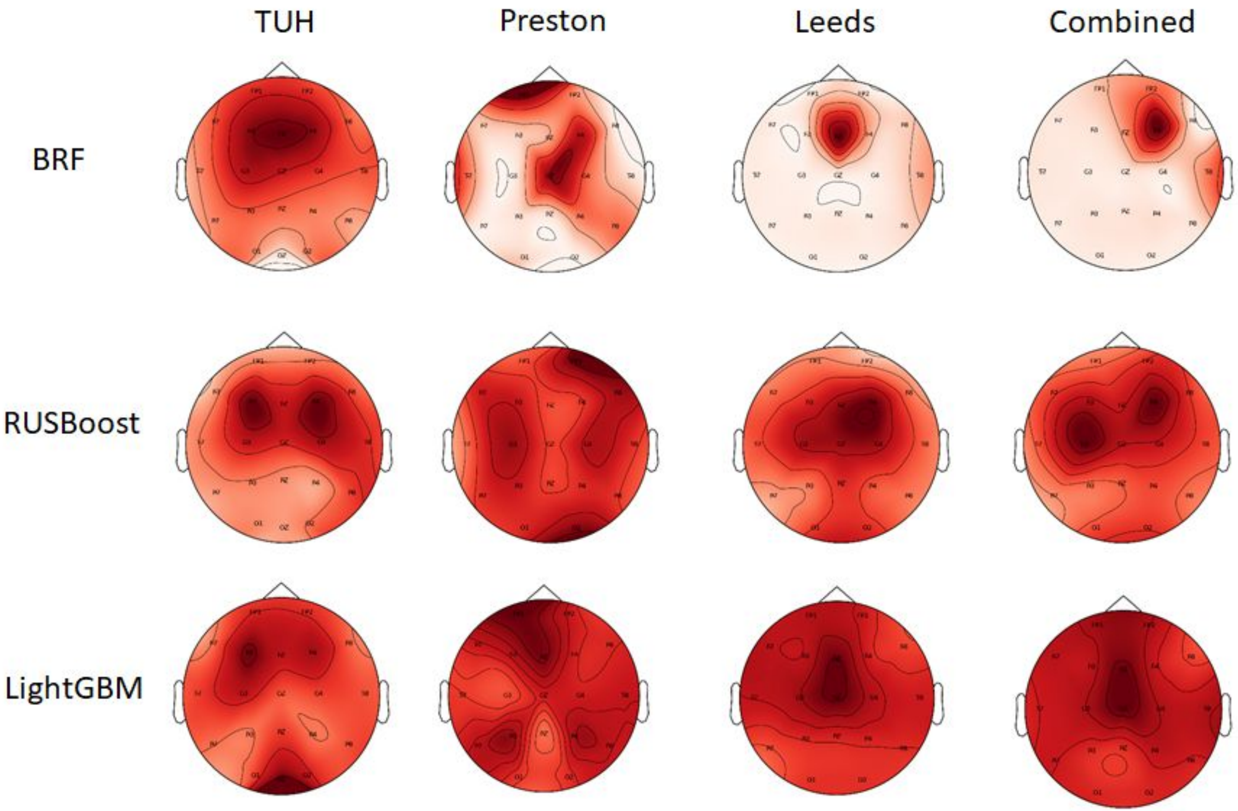
Automated/Semi-Automated Opportunities

Personalisation?

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.

Training



Automated/Semi-Automated Opportunities

A user-friendly system, could aid clinical decision making and lead to future discoveries in brain functioning.

Seizures are unlikely to be marked as a binary decision, requiring systems that enable a combination of **expert and automated workflows** to highlight differences between different seizure types and benign features.

Such systems should be clear regarding the decision process, such as…

- ...highlighting where potential seizures are in records,
- ...the certainty regarding the diagnostic label,
- ...what specific features of highlighted segmented were important for labelling.

Automated/Semi-Automated Opportunities

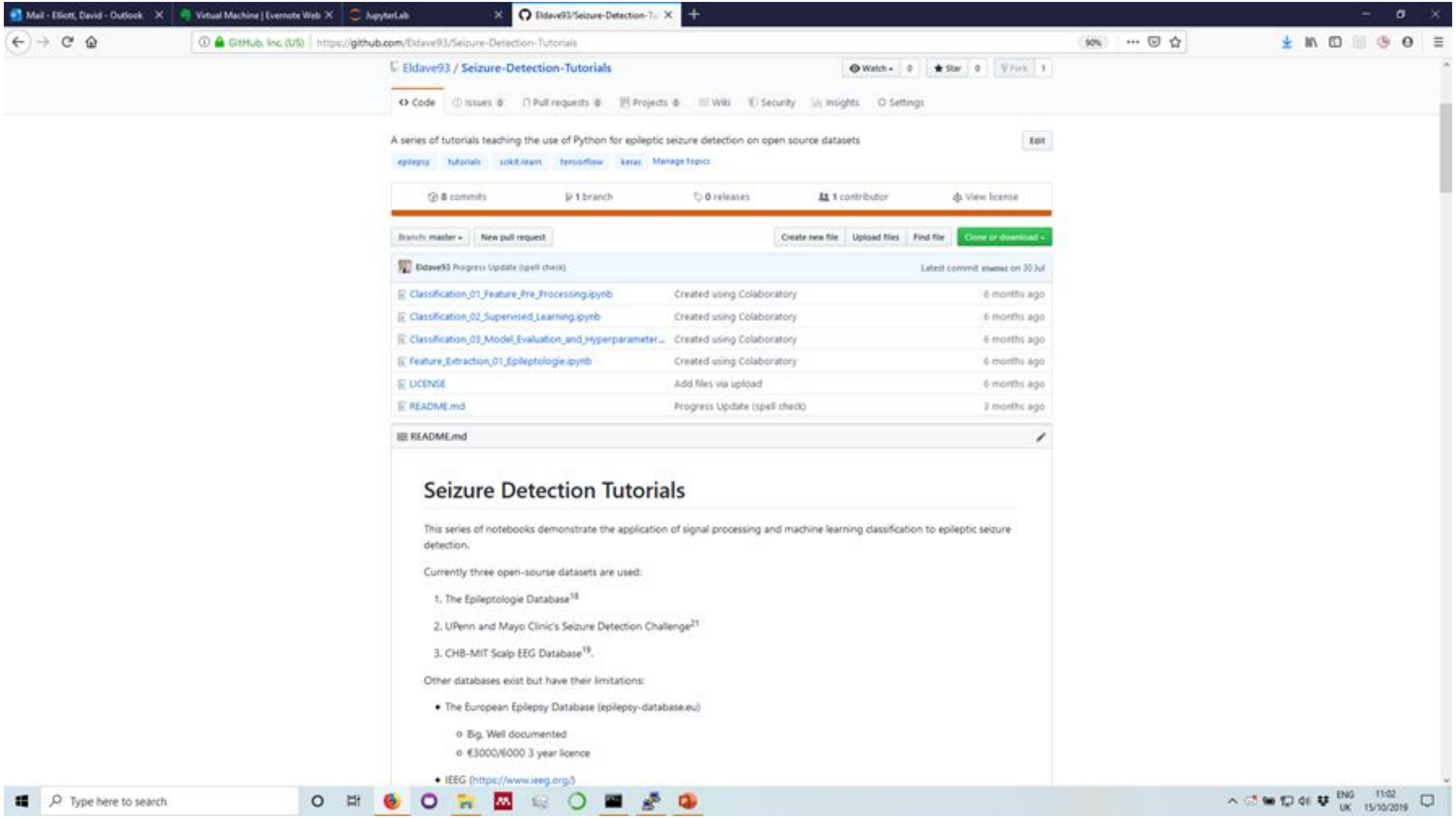
Clear potential monetary, performance, and productivity savings

- Currently likely a preference for computationally-efficient ML techniques (Thompson et al., 2020).
- Estimates of freed up time from automation range from 11% to 57% for different job roles, at a total estimated value of £12.5 billion a year for the NHS and £6 billion for social care (Darzi, 2018).

A “single payer" system (e.g. NHS) has the advantage of providing a complete, deep, and broad dataset which helps ML training.

- UK also has world-leading big data and artificial intelligence research.

GitHub


Eldave93 / Seizure-Detection-Tutorials
Code
Issues 0
Pull requests 0
Projects 0
Wiki
Security
Insights
Settings
A series of tutorials teaching the use of Python for epileptic seizure detection on open source datasets
Edit
epilepsy
tutorials
scikit-learn
tensorflow
keras
Manage topics
8 commits
1 branch
0 releases
1 contributor
View license
Branch: master
New pull request
Create new file
Upload files
Find file
Clone or download
Eldave93 Progress Update (spell check)
Classification_01_Feature_Pre_Processing.ipynb
Created using Colaboratory
6 months ago
Classification_02_Supervised_Learning.ipynb
Created using Colaboratory
6 months ago
Classification_03_Model_Evaluation_and_Hyperparameter...
Created using Colaboratory
6 months ago
Feature_Extraction_01_Epileptologie.ipynb
Created using Colaboratory
6 months ago
LICENSE
Add files via upload
6 months ago
README.md
Progress Update (spell check)
3 months ago
README.md
Seizure Detection Tutorials
This series of notebooks demonstrate the application of signal processing and machine learning classification to epileptic seizure detection.
Currently three open-sourse datasets are used:
1. The Epileptologie Database
2. UPenn and Mayo Clinic's Seizure Detection Challenge
3. CHB-MIT Scalp EEG Database
Other databases exist but have their limitations:
The European Epilepsy Database (epilepsy-database.eu)
Big, Well documented
€3000/6000 3 year licence
IEEG (https://www.ieeg.org/)
Type here to search

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)*