Modeling Seizure Data

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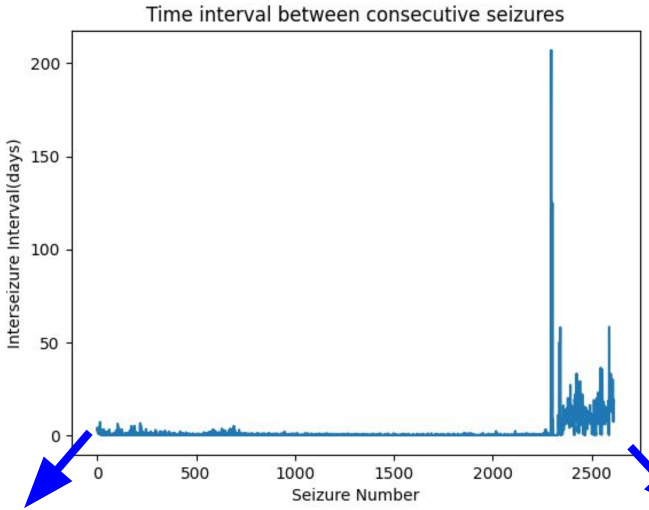
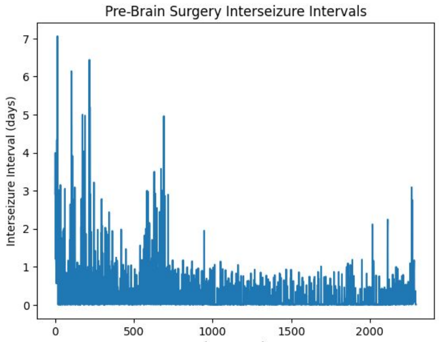
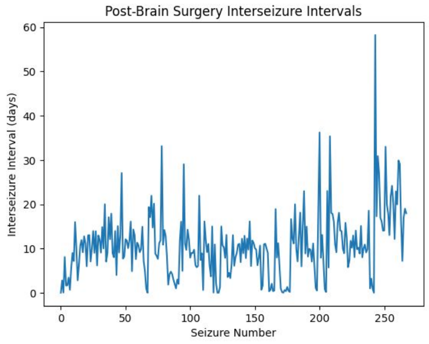
Background



Seizure Diaries

- Commonly assumed to be i.i.d
- Anecdotal evidence suggests otherwise
- Confounds abound
  - Treatment
  - Brain development over time
  - Stimuli
  - Etiology





Characterising the Data

Random Shuffle- Past Results

Null Hypothesis tested:

The data is generated from a IID distribution (no time dependent structure)

Discriminating Statistic- Mutual Information :

$$H(X_t) + H(X_{t+\tau}) - H(X_t, X_{t+\tau})$$

Conclusion: both pre and post-surgery datasets are quite statistically significantly unlikely to have been generated by IID processes

Methodology:

- Create n surrogates by scrambling the order of the data, destroying any time dependence
- Find the mean and variance of mutual information between time lagged surrogate time series
- Perform t test on the mutual information of the original time series, accept or reject null hypothesis

RESULTS:

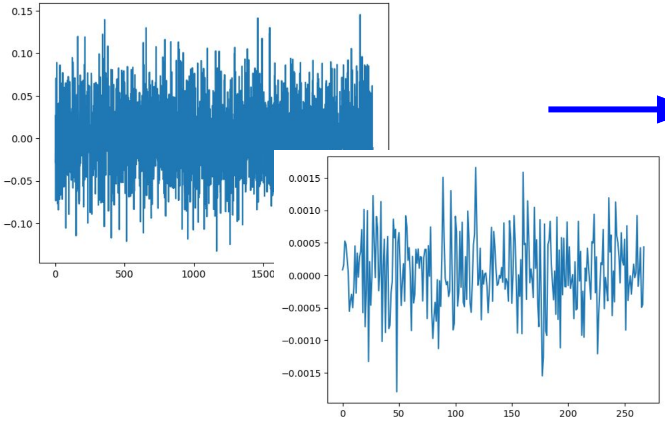
	MI_{actual}	$\mu_{surrogate}$	$\sigma^2_{surrogate}$	z score	p-value
Before Surgery	0.013	0.053	0.000007	14.354	0.0
After Surgery	0.146	0.305	0.002	3.391	0.0003

Random Phases

Null Hypothesis Tested:

The time dependency in the data is explained exclusively by the autocorrelation function.

Surrogate Data:



Methodology:

- Generate *n* surrogates of ISI_1 and ISI_2 by Fourier Transform. Surrogates preserve autocorrelation but randomize phases.
- Find the mean and variance of the mutual informations generated for all *n* surrogates
- By CLT, compare this mean and variance with the mutual information for the actual data to check for statistical significance

Results:

	MI_{actual}	$\mu_{surrogate}$	$\sigma^2_{surrogate}$	z score	p-value
Before Surgery	0.0528	0.0412	0.008	1.509	0.131
After Surgery	0.3053	0.304	0.063	0.028	0.978

FORECASTING

Classical Time Series Forecasting methods: Hazard Function Modeling

<u>HAZARD FUNCTION (λ):</u>
The PDF when the CDF is zero.

Probability of Hazard Function Matching Data

ALGORITHM

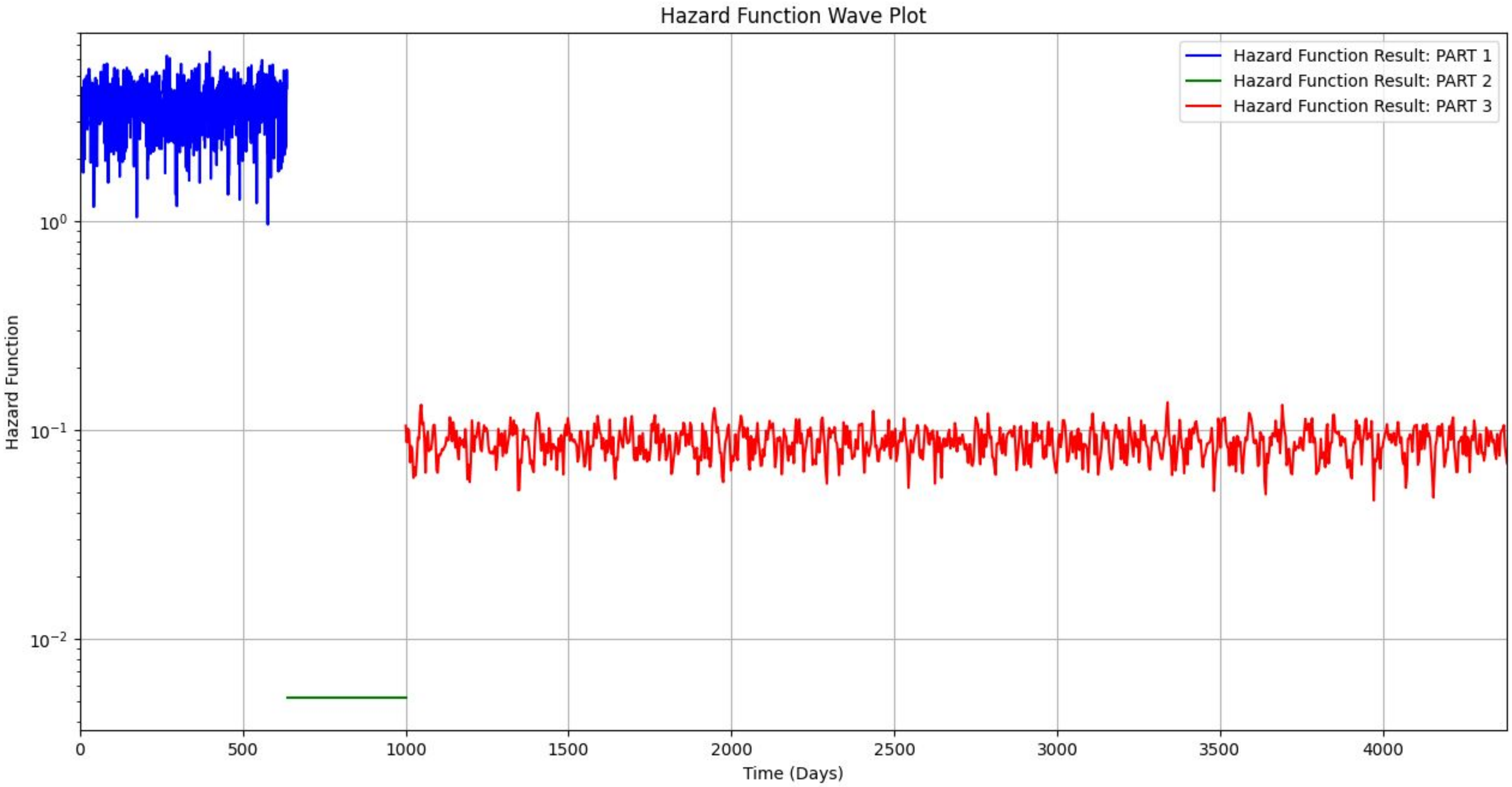
Sum eight waves with different preset parameters to create the hazard function, and then use machine learning to change those parameters until the probability of matching the data is maximized.

- Technically, **any hazard function can match any data of event timecodes**
- However:
  - We can measure **the probability** of a hazard function matching a dataset
    - Always infinitesimal
  - Divide by *dt* to create a nonzero proportionality scale
- Final step is to find the optimal hazard function – aka the highest fit probability

$$\prod_{k \in T[1:]} \lambda(t_k)\, e^{-\int_{t_{k-1}}^{t_k} \lambda(\tau) d\tau}$$

$$\lambda(t) = \frac{F'(t)}{1 - F(t)}$$

$$\frac{\prod_{k \in T} \lambda(t_k)}{e^{\int_a^b \lambda(\tau)\, d\tau}}$$



Final Approach Visual Results: ALL (Log Plot)

Hazard Function Interpretation

MEAN AND STANDARD DEVIATIONS OF HAZARD FUNCTIONS

- Before Surgery (Span: 635 days)
  - Mean: 3.583 per day
  - Standard Deviation: 0.8957 per day
- Directly After Surgery (Span: 365 days)
  - Mean: 0.005222 per day
- Well After Surgery (Span: 3382 days)
  - Mean: 0.08776 per day
  - Standard Deviation: 0.01407 per day

PERIODICITY OF HAZARD FUNCTIONS

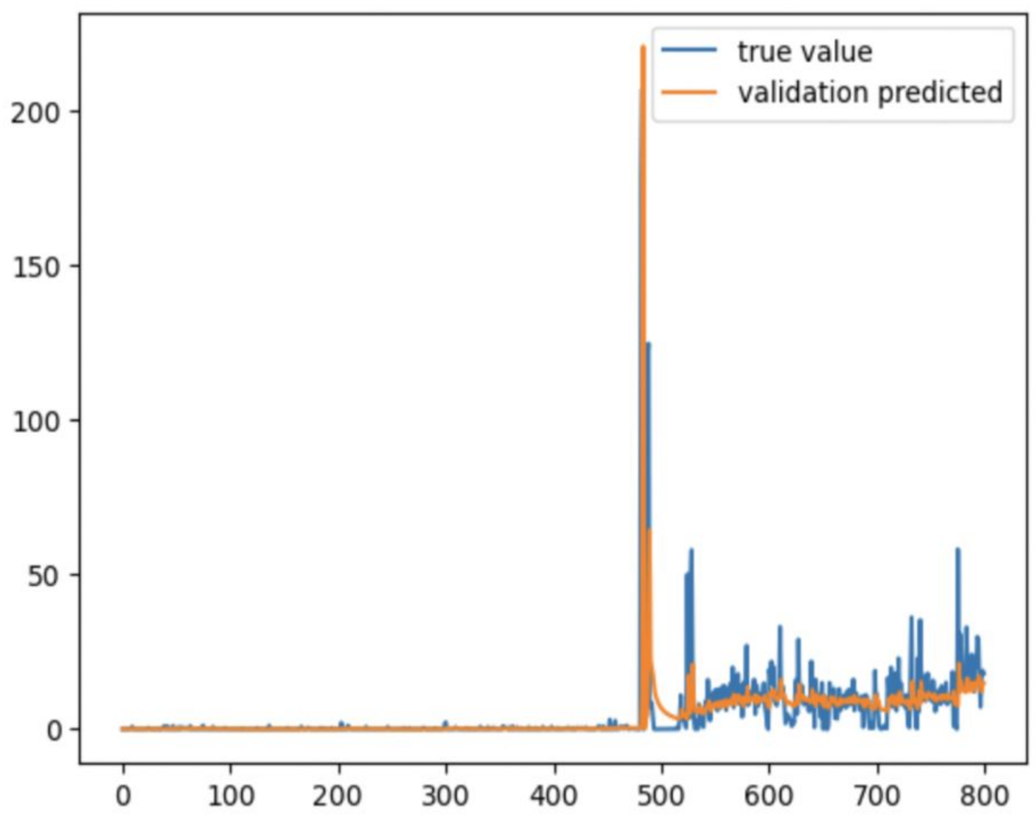
- Before Surgery
  - ~15 full waves per 635 days
    - Wave Period ≈ 42 days
    - Wave Frequency ≈ 8.62 per year
  - “Amplitude” (But Really Standard Deviation)
    - High “Bound”
      - ~4.48 seizures per day
    - Low “Bound”
      - ~2.69 seizures per day
- Directly After Surgery
  - ➔ *Not Enough Data* ←
- Well After Surgery
  - Less variance leads to higher uncertainty for wave patterns

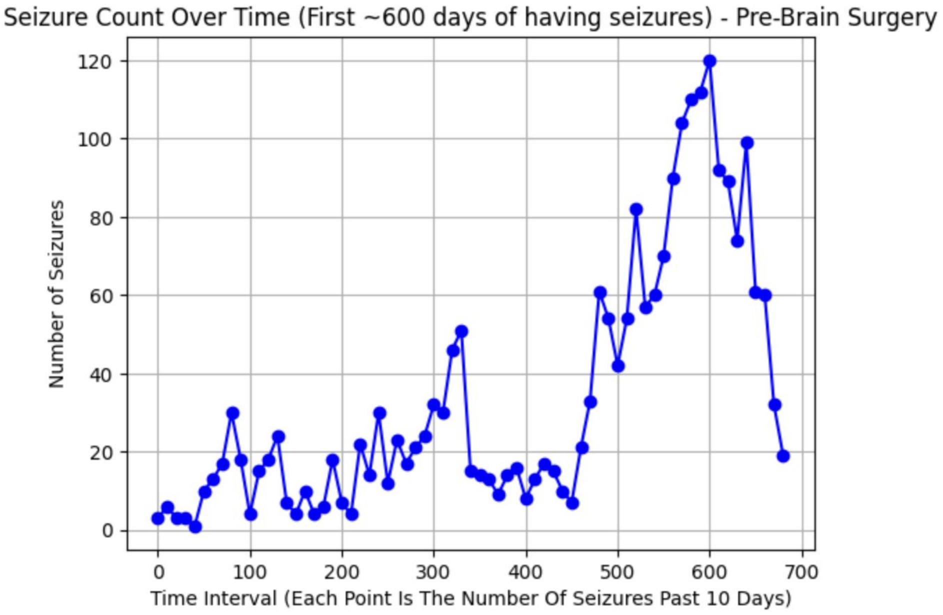
Classical Time Series Forecasting methods: ARIMA and Fourier Methods

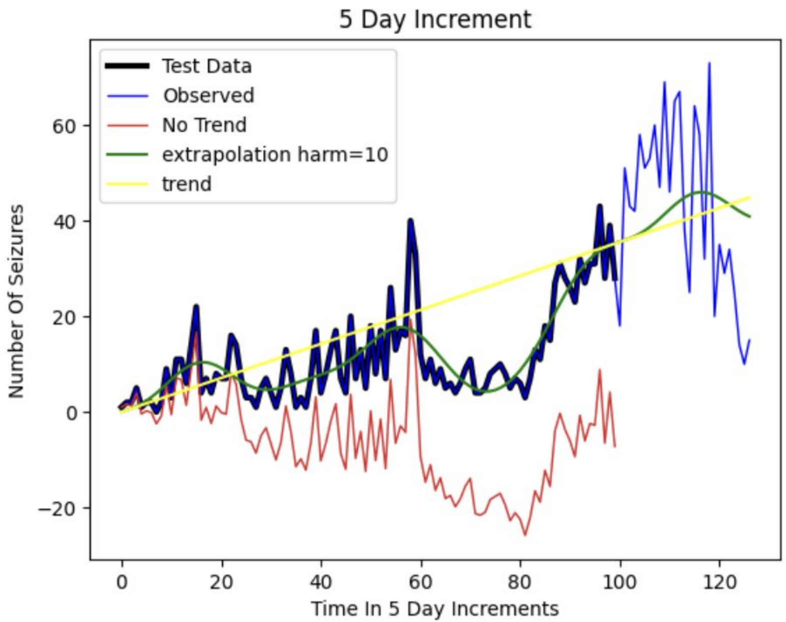
ARIMA model

Pros: ARIMA can handle a wide range of time series data.
It is relatively easy to understand and implement.
Cons:ARIMA requires stationary data, which can be difficult to achieve in practice.
It can be challenging to determine the optimal parameters for the model.
Fix ARIMA with parameters(1,1,1) by minimizing AIC(Akaike information criterion)
By predicting only next seizure and refitting model with the true value

Result







Pro

- Obvious trend
- Possible seasonality

Con

- Limited testing
- Limited understanding of fourier transform

Machine Learning Approaches: Feedforward vs. LSTM

Pre-Processing techniques

Why pre-process?

- Pre-processing can create patterns from a seemingly random dataset-allowing for better predictions using machine learning.

Processed data through different functions on pre- and post-surgery data:

- Differences between data points
- Taking the cosine of each point
- Taking the sine of each point
- Combination between above methods

New modified data is plugged into the Feed Forward neural network

Process of pre-processing

The error and variance explained is calculated using the difference between predicted and observed values

Goal:

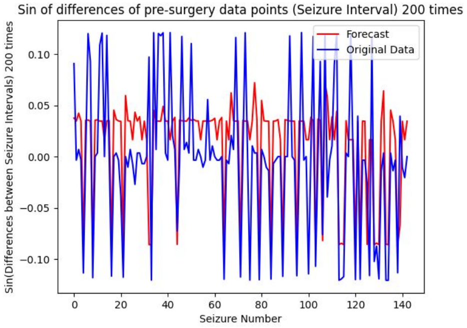
- Obtain low error
- Obtain high variance-best is value of 1 or 100%

Data results for some alterations to the data

Method of alteration of data	Error	Variance Explained
Difference between data points Pre-surgery	[0.14028879]	[0.0574297]
Difference between data points Post-surgery	[167.81034534]	[0.08865209]
Sin of data points pre-surgery	[0.05910263]	[-0.01272133]
Sin of data points post-surgery	[0.54061466]	[-2.91507527]
Cos of data points pre-surgery	[0.01502062]	[-0.22021205]
Cos of data points post-surgery	[0.73507212]	[-0.80966097]
Sin of two times the data point pre-surgery	[0.01834313]	[-0.04512105]
Sin of two times the data point post-surgery	[0.46963754]	[0.06791863]
Sin of four times the data point pre-surgery	[0.10920532]	[0.02678372]
Cos of the differences pre surgery	[0.03696392]	[0.05566345]
Sin of the differences pre surgery	[0.07138248]	[0.33136832]

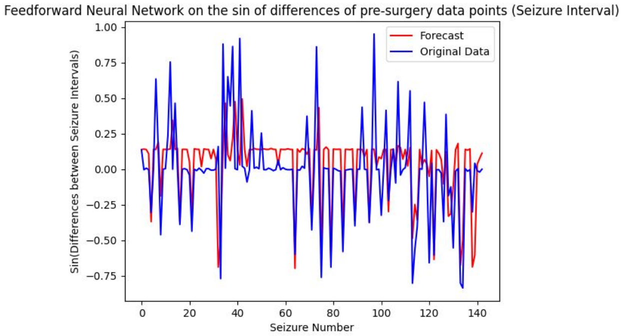
Decent Variance values

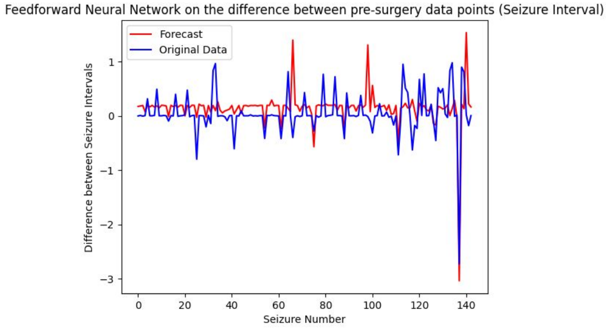
Experiment graph (for fun)



Values: [0.00284121] [0.41833852]

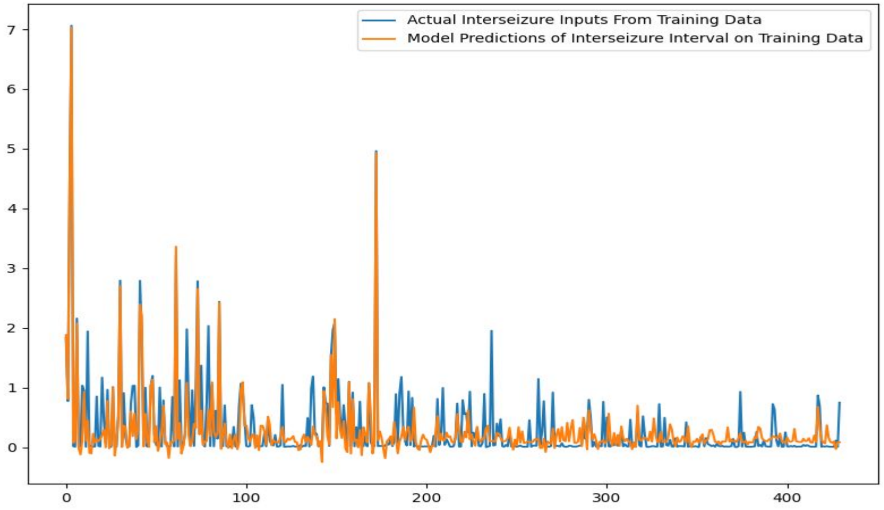
Best two graphs out of the methods tried

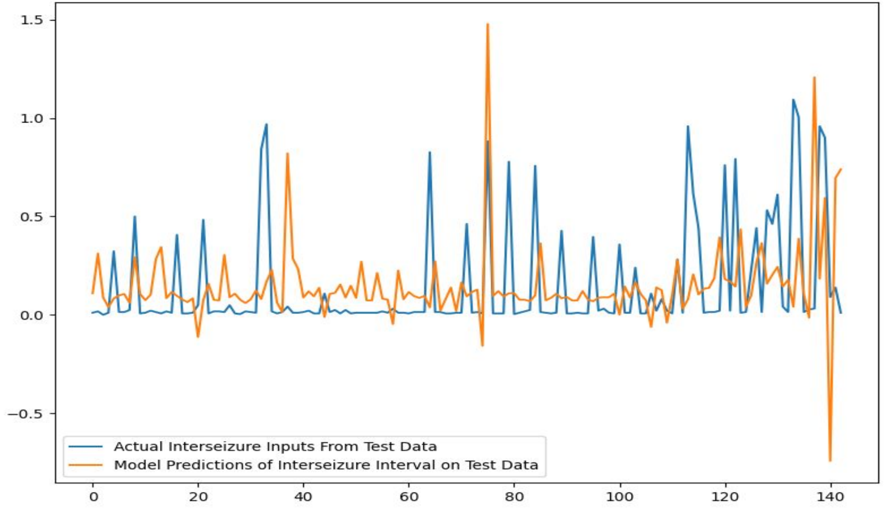




ML Modeling Attempts

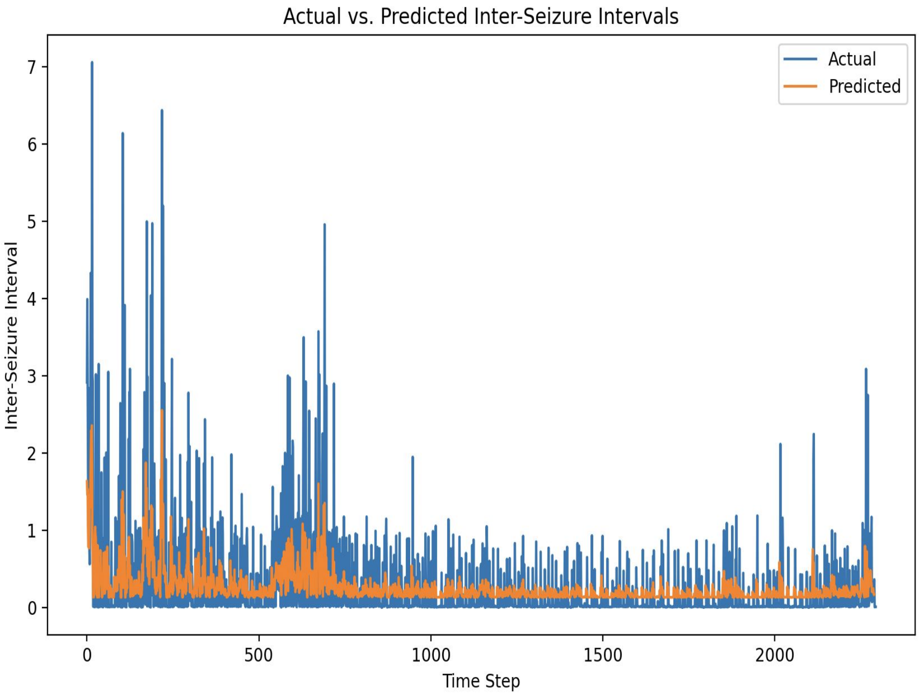
- LSTM
  - Too powerful of a model for the data, overfitted to the noise which bore out in poor performance in cross validated data
  - Some recurrent structure was detected which led us to opt for a LSTM model
  - 51% variance explained suggests some promise but the model needs to be finely tuned and scaled down



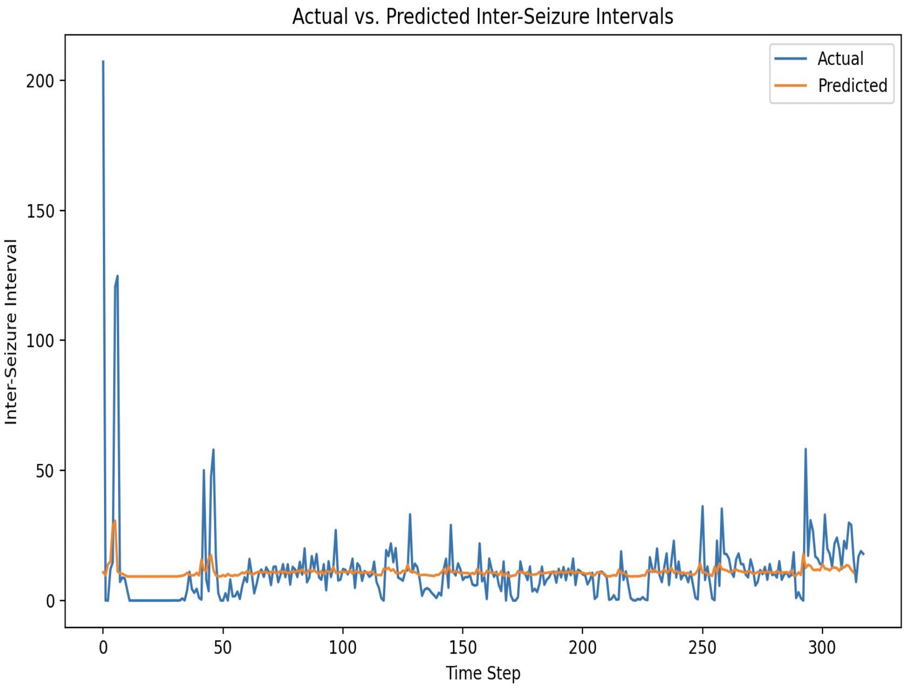


LSTM - CNN

Pre-surgery: -0.0998 (Variance Explained)

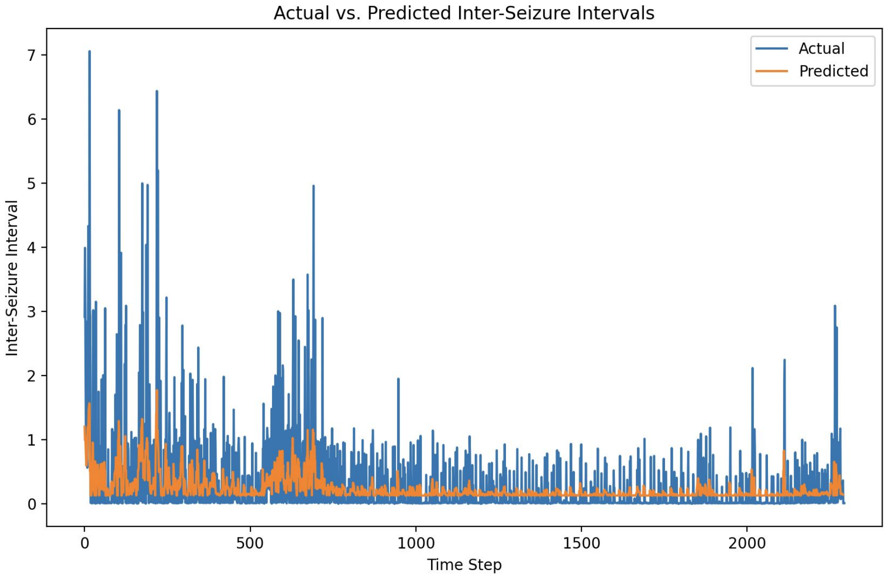


Post-surgery: -0.0234 (Variance Explained)

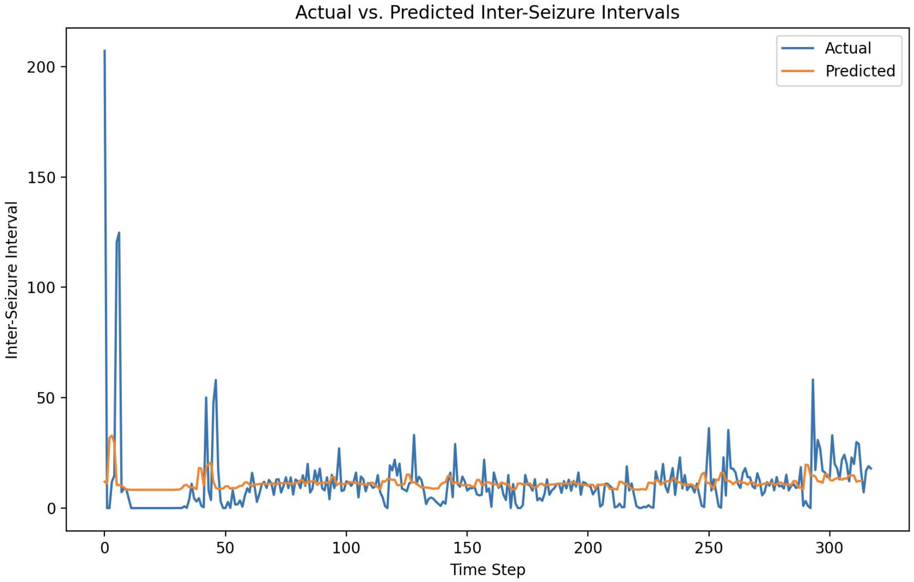


CNN - LSTM

Pre-surgery: -0.116 (Variance Explained)



Post-surgery: -0.00648 (Variance Explained)



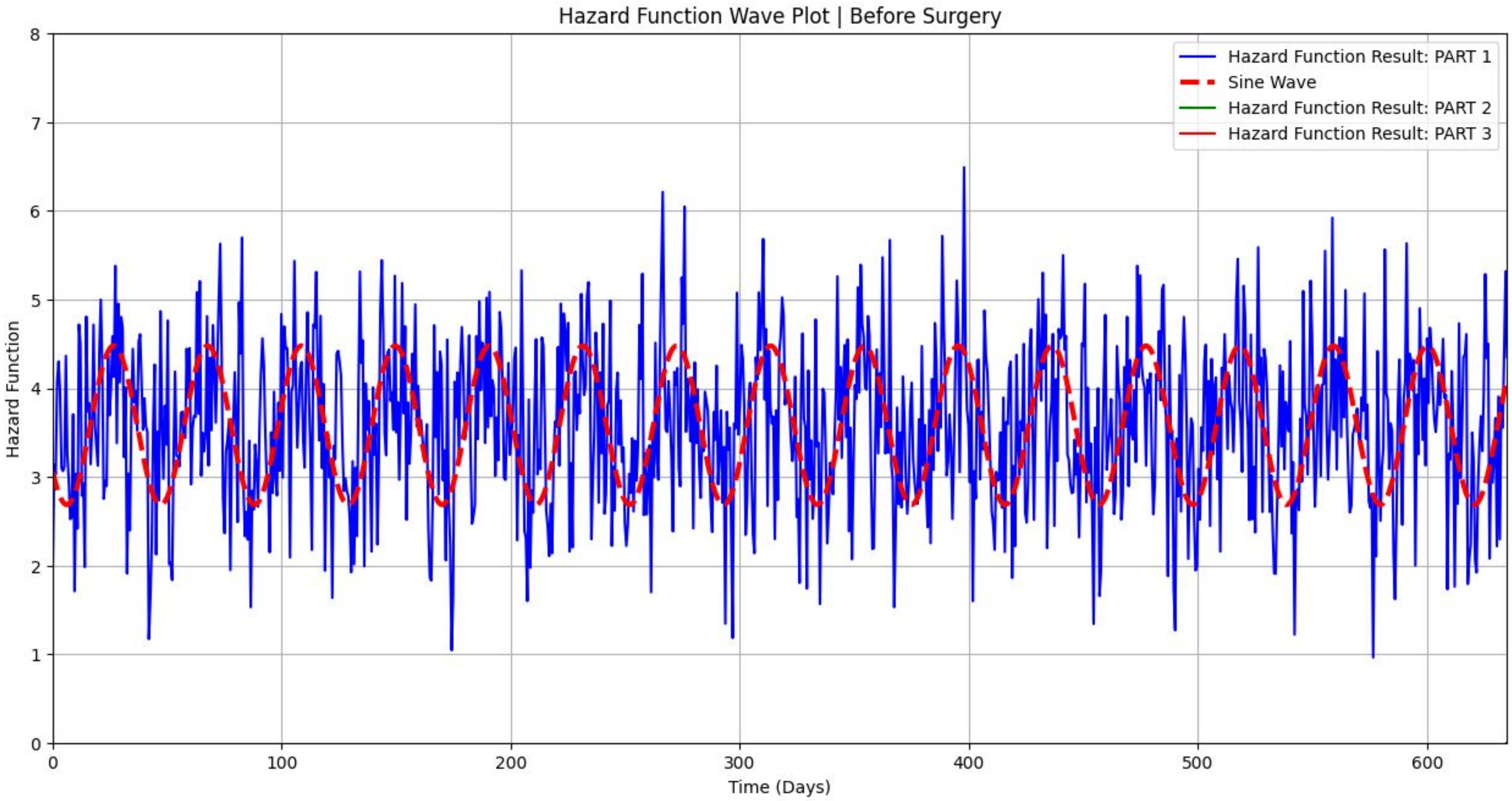
Future Directions

- Enhance data collection
  - Facilitate robust analysis and reduce potential biases
- Compare time dependent features
  - Aim to study different epilepsy (idiopathic) types
- Generalize machine learning model
  - Develop model to accurately predict future seizures
- Examine data on a widespread scale
  - Validate consistency with linear stationary Gaussian process

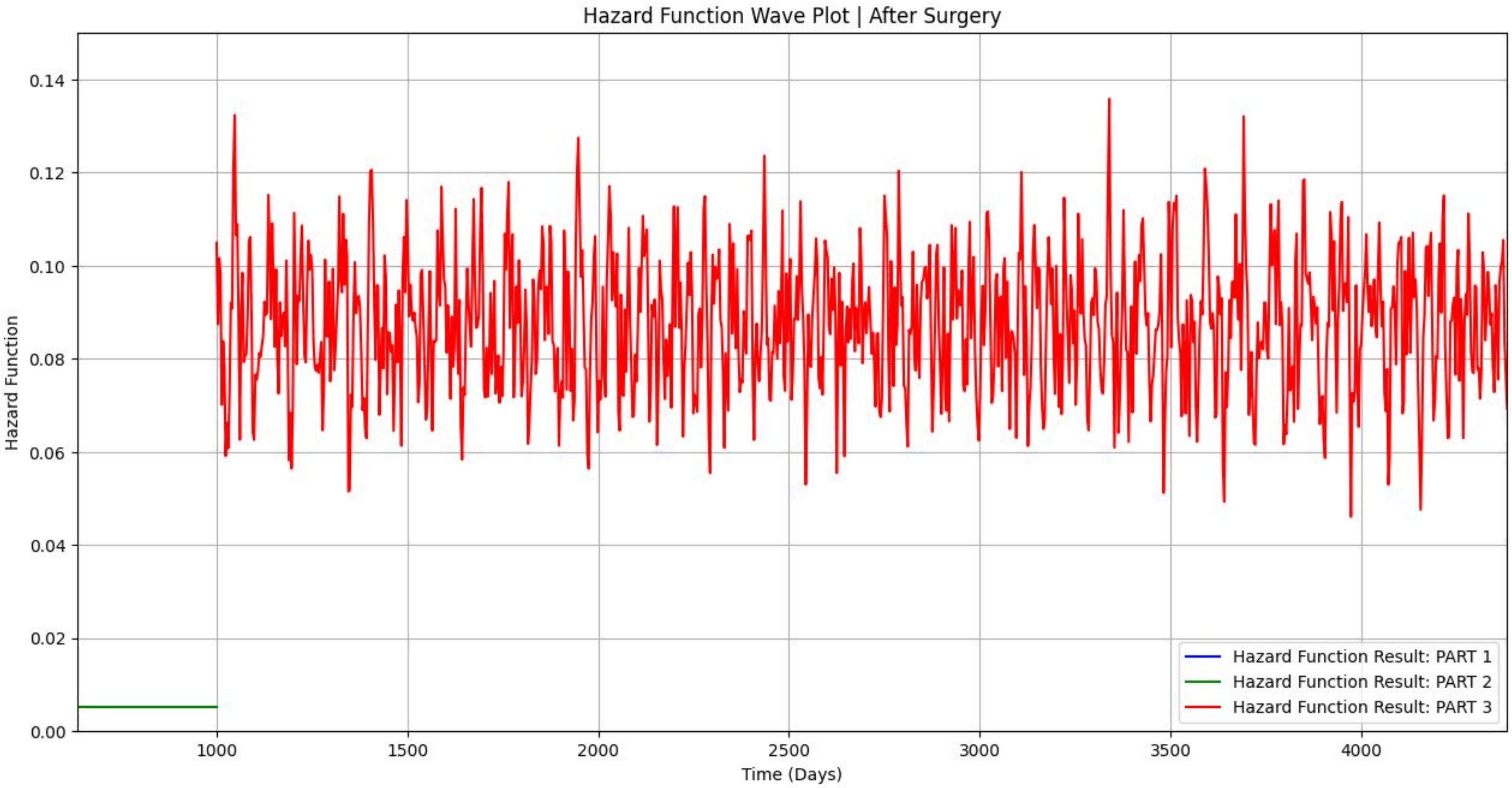
Conclusions

- Pre- and post- brain surgery time series had different degrees of time dependence
  - Neither time series is iid
  - Time dependence in post-op data quite consistent with that of a linear stationary Gaussian process (such as an ARMA model). Less forecastable than pre-op data
  - Pre-op data responds much better to preprocessing methods across the board, particularly sins of differences
- Hazard function analysis detects differences between pre- and post-op data
  - Seizure risk decreased by days after brain surgery
- Classical time series forecasting methods seem to outperform machine learning methods
  - ARIMA model with one autoregressive parameter, one difference to stationarity, and one lagged forecast error modelled seizure counts. ARIMA model cannot be extrapolated much for future prediction
  - LSTMs exhibited tendency to overfit the data

Thank you!



Final Approach Visual Results: PRE-SURGERY



Final Approach Visual Results: POST-SURGERY