Evaluation of Epilepsy Surgery Using Bayesian Multinomial Regression

Kacy Danielle Kane
kacykane3113@yahoo.com

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ABSTRACT

EVALUATION OF EPILEPSY SURGERY USING BAYESIAN MULTINOMIAL REGRESSION

Kacy D. Kane, M.S.
Division of Statistics
Northern Illinois University, 2019
Duchwan Ryu, Director

We are exploring the effectiveness of brain surgeries that are supposed to eliminate or reduce the frequency of seizures in young Epilepsy patients. The long-term effectiveness of brain surgeries is evaluated by ordinal categories and brings longitudinal categorical responses. Using a Bayesian multinomial regression model we examine the responses by the lobe of brain and other covariates as well as time. To overcome computational difficulties we utilize latent variables for multinominal responses and compare the results with frequentists methods.
EVALUATION OF EPILEPSY SURGERY USING BAYESIAN
MULTINOMIAL REGRESSION

BY

KACY D. KANE
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A THESIS SUBMITTED TO THE GRADUATE SCHOOL
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FOR THE DEGREE
MASTER OF SCIENCE

DIVISION OF STATISTICS

Thesis Director:
Duchwan Ryu
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CHAPTER 1
INTRODUCTION

1.1 Epilepsy

Epilepsy is a disorder classified as an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychological, and social consequences of the condition (Fisher et al., 2005). An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity (Fisher et al., 2005). Epilepsy is not only the physical symptoms that come from the epileptic seizures, but also the mental ones. These symptoms can be loss of consciousness, changes in emotional state, loss of memory, or behavioural changes to name a few (Fisher et al., 2005). Seizures only need to have one symptom, physical or other, be be considered a seizure. To be considered an epileptic seizure, the brain needs to be altered in a manner that would lead to a predisposition to having additional seizures (Fisher et al., 2005).

Some of the non-physical symptoms could lead to changes in the patients lives. Such changes are restriction of driving privileges, disability pension, education, and workplace safety to name a few (Fisher et al., 2005). These life altering outcomes of having epileptic seizures are a reason that finding a cure to this condition is so important. It would help the people who have epilepsy eventually be able to find a normal life Fisher et al. (2005).

Because not enough is known about the brain, we are unable to complete a surgery that would eliminate the predisposition to having an epileptic seizure. However, doctors are able to identify the part of the brain that the epileptic seizure originates from and to complete
the lobectomy. This surgery will be discussed further later in chapter 1, however, the idea is removing the portion of the brain that the seizure initiates in may eliminate the seizures in the patient.

There are a limited number of treatments to eliminate epileptic seizures. One option other than the lobectomy surgery is medication. There are problems associated with the medication such as dizziness, blurred vision, headache, nausea, depression, and a rash, to name a few (Marson et al., 2005). Using medication is relatively effective at eliminating the seizures in patients. According to the Cleveland Clinic, about two-thirds to three-quarters of patients will become seizure free through the use of medication (Cleveland Clinic, 2019a). However, for the remaining one-quarter to one-third of patients medication fails to help them. When this occurs, ”this type of epilepsy is called medically refractory or intractable epilepsy” and may be able to be treated through having a surgery (Cleveland Clinic, 2019a).

There is not only one option for a type of surgery that a patient can get if medication fails. They can get a Lobectomy (considered in this analysis), Lesionectomy, Hemispherectomy, Corpus Callostomy, or Neuropace RNS System (Cleveland Clinic, 2019b). Each surgical option has side effects for the patients and some options have multiple surgery options. For example, a Hemispherectomy surgery could be a functional hemispherectomy where a portion of the brain is removed and the fibers that connect this portion of the brain to the other hemisphere are disconnected, anatomic hemispherectomy where an entire hemisphere is removed from the patient (leaving certain brain structures such as the thalamus), and a peri-insular hemispherectomy which disconnects certain fiber changing the network of the brain and its ability to communicate (Cleveland Clinic, 2019b).
1.2 What is a Lobectomy?

Surgeries aren’t always effective at eliminating epilepsy in patients. The results of an ineffective surgery can be tremendous due to the price-tag of the surgery and the hope that the seizures would end for the patient. In many cases this surgery, or any surgery, is a final option for the parents and the patient to help with the epileptic seizures. Because of this, it is important to have a model that is good at representing the data and contains assumptions that can be verified or has fewer assumptions that need to be made. This would hopefully lead to a better longitudinal categorical data analysis method for future experiments on seizure medications and other longitudinal analysis done in the future. However, in this report we are trying to create a more flexible and less computationally cumbersome model for our data analysis.

The brain is broken into two hemispheres, the left and the right, and each hemisphere has four lobes that have different functions. The left hemisphere, depicted in Figure 1.1, are the frontal lobe, occipital lobe, parietal lobe, and the temporal lobe. Because these lobes in the brain have different functions, there are portions that can not be removed during a surgery. For instance, the occipital lobe is the lobe responsible for processing vision. The portion of the occipital lobe that does the processing would not be able to be removed, therefore, if the seizures initiates in this portion of the brain, the surgeon would have to remove only part of the problem area.

Removing only part of the portion that the seizure originates from would not be an effective surgery. Therefore, the lobe that the surgery is taking place for the patient we believe would be considered a significant factor in determining whether the result of the surgery will be effective.
Figure 1.1 depicts a brain colored based on the lobe. We are looking at the left hemisphere of the brain in the image. The image on the right, Figure 1.2, shows one type of temporal lobectomy that could be done to aid epilepsy patients (Wiebe et al., 2001). Again, note that we have data for the frontal, occipital, and temporal lobes in the brain. We do not have any data for the parietal lobe surgeries.

A lobectomy is a type of surgery where the lobe of an organ is removed. The reason that a patient is having a lobectomy could be a tumor, cancer, or, as in our case, epileptic seizures. In the case of the epileptic seizure the brain is having a portion of one of their lobes removed. Doctors are able to find the portion of the brain that should be removed through brain scans while the patient is having a seizure to pinpoint the location of the brain that the seizure is initiating from. This allows the doctors to remove the portion of the brain where the seizure is starting, and hopefully, eliminate future seizures for the patient. This does not always work in the case of epilepsy as epilepsy is defined above as an "enduring predisposition to generate epileptic seizures" (Fisher et al., 2005). Therefore, the seizures could initiate from a new location in the brain after the current trouble section is removed.
Additionally, this particular surgery is performed in younger patients. This could cause problems later on for the patient if an important portion of the brain in removed before the brain is finished developing. For this reason there are certain treatment methods that can only be used if the patient is over a certain age or if less invasive methods did not work for the patient. For instance the Neuropace RNS System is only for patients over the age of 18.

### 1.3 Longitudinal Categorical Data Analysis

Epilepsy surgeries lead to longitudinal categorical data and we may use Frequentist or Bayesian approached to analyze it. There are problems in analysis of longitudinal data analysis that exist in both the Frequentist and the Bayesian methods of analyzing this type of data. One such problem is the tendency for missing data when the experimental or observational period is over months, or in some cases, years (Yu, 2016). A frequentist method used for this type of analysis is the Kaplan-Meier estimator which assumes non-informative censoring. The problem with this assumption is explained later on. Another method for analyzing longitudinal data is Cox Regression which assumes the hazard rates for any two people are proportional over time. However, with this assumption (unlike with other assumptions made) you are able to test and see if the assumption is met through a graph. The final frequentist method we are going to consider here is Mann-Whitney U test for non-parametric values. This has four main assumptions and one requires the missing at random assumption to hold for the missing values which could be incorrect. Lastly, there is the maximum likelihood method for inference also needs the longitudinal data to be MAR, (Liu, 2016).

In the Bayesian Longitudinal Categorical Data Analysis there are some problems that we come across. There are assumptions that are made that we are unable to check based
on the data which, if incorrect, could be problematic with regards to the final conclusions of the model. For instance, "when commercial software such as SAS or Stata is used to analyze incomplete longitudinal data using a random effects model, the missing at random (MAR) assumption is being used; when the Kaplan-Meier estimator is used to summarize a survival curve from censored event times, non-informative censoring is being assumed" (Daniels and Hogan, 2008). Non-informative censoring could be an incorrect assumptions for many reasons. One such reason could be a treatment is not working so the subjects switched to another one and drop out of the study. This would make the non-informative condition fail. Additionally, this would make the missing at random condition fail as well. Finally, in the Bayesian method, because of the complex posterior distribution, we could have a longer computing time than the traditional Frequentist method.

To reduce the computing time for the Bayesian method we are utilizing the latent variables in our models. By doing this, we are hoping that our models run at a speed that is closer to that of the Frequentist method and will also give us the ability to create confidence intervals using the Bayesian method rather than the frequentist method. The result would hopefully be a faster, less complex, Bayesian model with the ability to represent the confidence intervals more effectively.

1.4 Considerations of Collected Data

To ensure the analysis is accurate, we need to ensure that the data is consistently defined. We have added a variable for the lobe that the surgery takes place and have variables for the age the patient first experienced a seizure, current age, date of surgery, gender, race, their engel value at one, three, five, and ten years post-surgery, and many other variables in this data set, of which, only some were used. For this analysis we were given three different
data sets that related to surgeries in different lobes of the brain. For instance, we had a
dataset that only had patients that had a surgery in their frontal lobe. This meant defining a
separate variable within SAS that states where the surgery took place for the patient, called
the location indicator or location in the output.

After completing this step we needed to ensure that these variables are consistently
defined within the different datasets for the different surgery types. For race we defined
black as 1, white as 2, and other as 3. Additionally, we redefined the gender variable so male
was defined as 1 and females as 2. We redefined the check-in variables as one variable called
year and 1, 3, 5, and 10 represent the time passed since the surgery. Finally, LocationF,
LocationO, and LocationT stand for the surgery taking place in the frontal, occipital, and
temporal lobes, respectively. After redefining the variables mentioned above we had to
reformat the data to make the analysis easier to use later. We transposed the data to have
the year values be vertical instead of horizontal to allow us to run regression on this for the
models section of this paper in Chapter 3. Finally, we merged all the datasets into one so
every lobe location surgery was in one dataset with all our corrections.

The variables that we are using in the analysis are gender, sex, age the seizures started,
surgery location, and engel value at each visit (1, 3, 5, and 10 years post operation). Why
we chose these variables, and how, will be explained in the next chapter. While age is an
important variable in determining the effectiveness of this surgery (it is know to be less
effective in older and younger patients based on previous research (Kim et al., 2010)) the
age data was not available for all surgery locations so it is not included in the analysis.
Additionally, based on our preliminary analysis in section 2.2, age is not significant using
the multinomial probability model for the frontal lobe patients at a significance level of
$\alpha = 0.05$. 
CHAPTER 2
PRELIMINARY DATA ANALYSIS

2.1 Descriptive Statistics

Below we have a graphical summary of the data based on their starting engel value one-year after the surgery, three-years after surgery, five-years after surgery, and ten-years after surgery. As you can see in Figure 2.3 at least one of the patients has their engel value decline from year 1 to 3, colored blue. There are many reasons that this decrease in engel value could have occurred. For instance, the patient could have considered the surgery to be ineffective so he or she decided to start medication that helped reduce or eliminate his or her seizures. Since we have no further information beyond the data, we can only speculate. Additionally, the graphs also show patients that started with low engel values, as shown in Figure 2.1, and increased to the an engel value of 4, as shown by the green dashed line. Again, this could be due to many factors that we could only speculate about, so we will ignore it for the purposes of this analysis.

Figure 2.1 shows that we have some patients have missing data points for some of the check-ins. For example, consider the yellow line in Figure 2.1 where the patient went from engel 1 during the first visit to engel 3 the second visit. Note that after this visit the patient does not have any additional data points. There, are many reasons that we could be missing this data point such as the patient moved, started going to a different doctor, or the patient just decided to stop going for check-ins. We are going to consider missing data points in Chapter 5 of this report, however, right now they will be ignored.
We have a total of 191 patients in this study. These patients make up a total of 536 data points of which 170 are in the frontal lobe, 116 are in the occipital lobe, and 250 are in the temporal lobe. We have more data points than patients because each patient has the option of having an observation for their year 1, 3, 5, and 10 check-ins. This means that each patient could have as many as 4 observational points. For the occipital lobe, we have no data points with a 10 year check-in, therefore, we are not going to consider that lobe for year 10. There are a lot of missing data in this dataset, which we will discuss later in Chapter 5 during the case study.
We have the highest percentage of engel 1 identifications in the temporal lobe with 78.4% showing as engel 1 out of the 250 data observations. The lowest is the frontal lobe with 42.9% showing as engel 1. The lowest percentage classified as engel 4, the worst classification, is the temporal lobe (3.2%), and the highest is the frontal lobe (17.7%). Therefore, we can speculate that lobectomies in frontal lobes showed the worst performance and lobectomies in temporal lobes showed the best performance.

2.2 Pilot Study

For our multinomial probability model we are using an ordinal data set. Therefore, our data has an order and as mentioned in Section 1.4 we have engel 1 being the best case for the patient and engel 4 being the worse case. Additionally, our patients are considered independent because we are ignoring the doctor effect since one doctor completed all the surgeries.

The variables we focused on, based on our analysis in the Bayesian and Frequentist models, are considered significant. Therefore, our model will include the gender, race, location, and engel values as variables. For gender we have female as the dummy variable, race we have other as the dummy variable, and location we have occipital lobe as the dummy variable. Based on this, we ran our regression which is introduced in Chapter 3.

To decide which variables, mentioned above, will be included in our dataset we ran a non-mixed multinomial model for the frontal lobe to see which variables are considered significant. Based on the output in Table 2.1 we have variables year, sex, race, and age the seizures began as being considered significant. Therefore, we will use these variables in our Bayesian and Frequentist models later on in our analysis. If all variables are significant, they will be included in our final Bayesian Model as well. As we can also see, in Table 2.1,
variables for the age at time of operation and the average duration of the seizures in minutes are not considered significant using $\alpha = 0.05$.

Table 2.1: Significant Variables Test

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>Standard Error</th>
<th>Chi-Squared</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept1</td>
<td>0.531</td>
<td>0.2779</td>
<td>3.65</td>
<td>0.056</td>
</tr>
<tr>
<td>Intercept2</td>
<td>1.3983</td>
<td>0.2818</td>
<td>24.62</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Intercept3</td>
<td>2.3764</td>
<td>0.2942</td>
<td>65.24</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>year</td>
<td>-0.227</td>
<td>0.0257</td>
<td>78.14</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Sex</td>
<td>-0.3606</td>
<td>0.1611</td>
<td>5.01</td>
<td>0.0252</td>
</tr>
<tr>
<td>Race</td>
<td>0.6045</td>
<td>0.1994</td>
<td>9.19</td>
<td>0.0024</td>
</tr>
<tr>
<td>AgeAtOp</td>
<td>0.035</td>
<td>0.0194</td>
<td>3.23</td>
<td>0.0723</td>
</tr>
<tr>
<td>AgeOnsetM</td>
<td>-0.0001</td>
<td>0</td>
<td>11.74</td>
<td>0.0006</td>
</tr>
<tr>
<td>DurationM</td>
<td>-0.003</td>
<td>0.0017</td>
<td>3.08</td>
<td>0.0794</td>
</tr>
</tbody>
</table>

The model, depicted in Figure 2.1, was used to determine which variables will be used in our merged dataset regression, that includes the location indicator, in Chapter 3. However, our final model for both the Bayesian and Frequentist models will include only the significant variables from the merged Frequentist multinomial probability model.

Now that we have defined and chosen our significant terms, we are going to obtain the multinomial probability models for both the Bayesian and Frequentist approaches. Once we have done that, we will compare the two models and analyze the results. First, we are going to introduce our models and explain the terms included in our models.
CHAPTER 3
MODELS

3.1 Model for the Multinomial Data

We consider a multinomial response with cumulative logistic regression model. Let \( y_{ic} \) denote the categorical response from the \( i \)th subject in the \( c \)th category among \( C \) orderable categories, and let \( x_i \) denote the corresponding covariates. Further, we utilize latent variables for the convenience of the computation. Let \( Z_{ic} \) denote the latent variable corresponding cumulative logit of the \( i \)th subject of the \( c \)th category. Then the model can be described below:

\[
y_{ic} \overset{\text{ind}}{\sim} \text{Multinomial}(\theta_{i1}, \ldots, \theta_{iC}), \quad \text{for} \quad \sum_{c=1}^{C} \theta_{ic} = 1,
\]

\[
Z_{ic} = \log \left( \frac{P_{ic}}{1 - P_{ic}} \right) + U_i = x_i \beta_c + U_i, \quad \text{for} \ c \in \{1, \ldots, C\},
\]

where \( P_{ic} \) is the cumulative probability of being in category \( c \) that is \( P_{ic} = \sum_{k=1}^{c} \theta_{ik}, \beta_c \) is the vector of regression coefficients, and \( U_i \) are Gaussian random effect with zero mean and variance \( \sigma_u^2 \). We ran both the glimmix and genmod models for our dataset based on the variables that we decided to include in Chapter 2. Based on the model output we chose to use the glimmix model for the comparison and analysis to the Bayesian of this dataset as the model appeared to fit the data better.

Table 3.1 is the cumulative genmod and glimmix models, labeled “Frequentist Models All Variables.” Since this model is cumulative that means that to find the engel 2 value you
need to find the cumulative for engel 2 and subtract off the cumulative engel 1 in this model. That will give you the model for the engel 2 excluding engel 1. This will be discussed further in Chapter 4.

We have assigned the occipital lobe as the dummy variable for this, meaning that the other lobes (frontal and temporal) are being compared to the occipital lobe. Therefore, if you would like to find the model for the occipital lobe you set the variable equal to 0 for the other two. Similarly, engel 4 is the dummy variable for the intercepts of the engel values. This means that the variable "intercept1" in the table below is the intercept for engel 1, "intercept2" is the intercept for engel 2 and so on.

We consider the following covariates for the model:

\[
\begin{align*}
\text{LocationF} & = \begin{cases} 
1, & \text{frontal lobe surgery} \\
0, & \text{otherwise}
\end{cases} \\
\text{LocationT} & = \begin{cases} 
1, & \text{temporal lobe surgery} \\
0, & \text{otherwise}
\end{cases} \\
\text{Sex} & = \begin{cases} 
1, & \text{Patient is male} \\
0, & \text{otherwise}
\end{cases} \\
\text{RaceW} & = \begin{cases} 
1, & \text{patient is White} \\
0, & \text{otherwise}
\end{cases} \\
\text{RaceB} & = \begin{cases} 
1, & \text{patient is Black} \\
0, & \text{otherwise}
\end{cases}
\end{align*}
\]

Hence, LocationF is the location adjustment to the model for the frontal lobe surgery, and LocationT is the location adjustment for the temporal lobe. The variable SexM means that the patient is male. In this case female is the dummy variable. For race, other is the dummy variable we defined for this dataset. The variable year represents is the number of years since the surgery took place for the patient.
Using the values from Table 3.1 will help us calculate our cumulative probabilities for our patients to have a particular engel value based on our explanatory variables. These values will be used in graphs later to compare the Bayesian and Frequentist models. Table 3.1 shows estimated effects and the corresponding $p$-values.

From Table 3.1, regarding significance of covariates, we have included all covariates except for the age at time of onset at $\alpha < 0.05$ level of significance. That includes year post surgery, the patients ethnicity and gender, and the location of surgery. Table 3.2 summarizes the estimated effects and their $p$-values for the model with only significant covariates. We will consider only the significant covariates in our Bayesian model in Section 3.2.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Not Mixed</th>
<th>P-Value</th>
<th>Mixed</th>
<th>P-Value</th>
</tr>
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<tr>
<td>Intercept1</td>
<td>4.5672(1.0274)</td>
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<td>4.4152(1.0266)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
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<td>&lt; 0.0001</td>
<td>5.1379(1.0279)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Intercept3</td>
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<td>&lt; 0.0001</td>
<td>6.1812(1.0303)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>year</td>
<td>-0.1622(0.0182)</td>
<td>&lt; 0.0001</td>
<td>-0.1346(0.01781)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>SexM</td>
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<td>0.0001</td>
<td>-0.476(0.1039)</td>
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<tr>
<td>RaceB</td>
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<td>0.0035</td>
<td>-3.2278(1.0268)</td>
<td>0.0017</td>
</tr>
<tr>
<td>RaceW</td>
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<td>0.0011</td>
<td>-3.3766(1.0192)</td>
<td>0.0009</td>
</tr>
<tr>
<td>LocationF</td>
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<td>-0.6009(0.1597)</td>
<td>0.0002</td>
</tr>
<tr>
<td>LocationT</td>
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<td>1.0529(0.1629)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>AgeOnsetM</td>
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<td>-0.00056(0.00111)</td>
<td>0.6128</td>
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Table 3.2: Frequentist Models

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<th>Estimate(SE)</th>
<th>Pr &gt; ChiSq</th>
<th>Estimate(SE)</th>
<th>Pr &gt; ChiSq</th>
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<tr>
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<td>4.4987(1.0255)</td>
<td>&lt; 0.0001</td>
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<tr>
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<td>5.2379(1.0268)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
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<td>&lt; 0.0001</td>
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<tr>
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<td>&lt; 0.0001</td>
<td>-0.1413(0.01752)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
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<td>&lt; 0.0001</td>
<td>-0.5464(0.1021)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>RaceB</td>
<td>-3.0002(1.0261)</td>
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<td>0.0016</td>
</tr>
<tr>
<td>RaceW</td>
<td>-3.3676(1.0182)</td>
<td>0.0035</td>
<td>-3.4040(1.0189)</td>
<td>0.0009</td>
</tr>
<tr>
<td>LocationF</td>
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<td>&lt; 0.0001</td>
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<tr>
<td>LocationT</td>
<td>0.8016(0.1453)</td>
<td>&lt; 0.0001</td>
<td>1.0335(0.1470)</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

3.2 Bayesian Models

For our Bayesian model we use latent variables and prior descriptions to help get approximations. This method may allow for greater flexibility in the model which, theoretically, can lead to better predictions of likelihoods for our data. In the model, depicted by Equation 3.1, we have unknown parameters $\beta_c$ and $\sigma^2_u$. Using the Bayesian approach, we assign prior description for the parameters. It is well known there is no conjugate prior for regression coefficients under multinomial regression. However, using the random effect, we have conjugate normal prior for the regression coefficients. In addition, we assign a conjugate
inverse Gamma prior for $\sigma_u^2$. We consider a multinomial response with cumulative logistic regression model. Let $y_{ic}$, $x_i$, and $Z_{ic}$ be defined as it was for Equation 3.1.

$$y_{ic} \overset{\text{ind}}{\sim} \text{Multinomial}(\theta_{i1}, \ldots, \theta_{iC}), \text{ where } \sum_{c=1}^{C} \theta_{ic} = 1$$

$$Z_{ic} = \log \left( \frac{P_{ic}}{1 - P_{ic}} \right) + U_i = x_i \beta_c + U_i, \ c \in 1, \ldots, c \quad (3.2)$$

where $P_{ic}$ is the cumulative probability distribution of category $c$ that is $P_{ic} = \sum_{k=1}^{c} \theta_{ik}$, $\beta_c$ is the vector of regression coefficients, and $U_i$ are Gaussian random effect with mean zero and variance $\sigma_u^2$.

We consider conjugate prior distributions for all parameters. However, it is well known there is no conjugate priors for regression coefficients. Hence, we utilize the latent variables to take the advantage of data augmentation (Neal and Kypraios, 2015) and assign Gaussian prior on regression coefficient and use the slice sampling list prior distributions Let $Z$ denote a vector of latent variables.

$$\beta_c \sim N(0, \sigma_b^2 \mathbf{I}),$$

$$Z \sim N(\mathbf{X}\beta_c, \sigma_u^2),$$

$$\sigma_u^2 \sim IG(A, B).$$

where $A$ and $B$ are hyperparameters from the prior description
From the likelihood and the prior descriptions, we have the following posterior descriptions of parameters and latent variables:

\[
p(\beta_c|\cdot) \propto \exp \left[ -\frac{1}{2} (\beta_c - V^{-1}M)^T V (\beta_c - V^{-1}M) \right]
\]

\[
p(\sigma^2|\cdot) = IG[A^*, B^*]
\]

\[
p(Z_i|\cdot) \propto \left( \frac{e^{Z_iy_i}}{1 + e^{Z_i}} \right) e^{-\frac{1}{2\sigma^2} (z_i - f(x_i))^2}
\]

where \( A^* = \frac{n}{2} + A \), \( B^* = \frac{RSS}{2} + B \), \( V = \frac{X^T X}{\sigma^2} + \frac{I}{\sigma^2} \), and \( M = \frac{X^T Z}{\sigma^2} \).

Using Gibbs sampling (Geman and Geman, 1984) we generate Markov Chain Monte Carlo (MCMC) samples of all unknown parameters. From MCMC samples we obtain the credible intervals of coefficients of covariates and investigate their inclusion of zero to determine significant covariates. Based on the above information we have obtained confidence intervals for the variables included in our model. The intercept, sex, year, race, and location frontal compared to occipital are all considered significant. However, the temporal lobe when compared to the occipital lobe included 0 in the 95% confidence interval so it is not considered significant for this Bayesian model. The 95% confidence intervals are given in a table in the appendix labeled “Tables and Graphs.”

Typically, using the Bayesian model would require additional computing time for the model to run. Utilizing the latent variables will hopefully give us a model run time closer to the frequentist models and allow us to calculate confidence intervals using the Bayesian method. Utilizing the latent variables in this model will hopefully help us to simplify our final model. This would potentially lead to a model that is more quick to run. Latent variables can simplify our model because they provide an alternative to calculating the posterior distribution which, for our model, would get quite complex. Simplifying our model is what
we are hoping will obtain a faster result in the end that is closer to the Frequentist models run time.

Now that we have our models for both the Bayesian and the Frequentist approaches, we can find the probabilities for the patients. Once we have the probabilities, defined in Chapter 4, we can graph them and compare our Mixed Bayesian model to the Mixed Frequentist model. After we have compared our models, we will complete a case study of the data to comment on the missing values in our data set and mention some characteristics we noticed in the patients.
CHAPTER 4

ANALYSIS OF EPILEPSY DATA

4.1 Probability models

In Chapter 3 we explained our models and why we chose them. Our models have location, race, and gender included as explanatory variables and engel value as our response. Let \( p(k) \) be defined as the cumulative probability for the \( k \)th engel value where \( k = 1, 2, 3, \) and \( 4. \) Based on this information, we have the following probability model:

\[
p(k) = \frac{1}{1 + e^{-y}}
\]

where \( y = \beta_{0k} + \beta_{1k}X_{1k} + \beta_{2k}X_{2k} + \beta_{3k}X_{3k} + \beta_{4k}X_{4k} + \beta_{5k}X_{5k} + \beta_{6k}X_{6k} \) with \( \beta_{0k} \) begin the intercept for the \( k \)th engel value, \( \beta_{1k} \) being the estimate for year, \( \beta_{2k} \) being the estimate for a male patient, \( \beta_{3k} \) being the estimate for a white patient, \( \beta_{4k} \) being the estimate for a black patient, \( \beta_{5k} \) being the estimate for a frontal lobe surgery, and \( \beta_{6k} \) being the estimate for a temporal lobe surgery. The dummy variable for gender is female, for ethnicity is other, and for location is occipital. For the Frequentist model we are going to define the cumulative multinomial probability model as \( p_f(k) \) and for Bayesian we are going to define it as \( p_b(k) \).
The probability models we need are going to be discrete models to compare the probability of individual engel value probabilities. Let $p_l(k)$ be the discrete multinomial probability model for the $k$th engel value where $k = 1, 2, 3, \text{ and } 4$. This model is defined as below:

$$p_l(k) = \frac{1}{1 + e^{-y_k}}, \text{ for } k = 1$$

$$p_l(k) = \frac{1}{1 + e^{-y_k}} - \frac{1}{1 + e^{-y_{k-1}}}, \text{ for } k = 2 \text{ and } 3$$

$$p_l(k) = 1 - \frac{1}{1 + e^{-y_{k-1}}}, \text{ for } k = 4$$

(4.2)

where $y_k = \beta_{0k} + \beta_{1k}X_{1k} + \beta_{2k}X_{2k} + \beta_{3k}X_{3k} + \beta_{4k}X_{4k} + \beta_{5k}X_{5k} + \beta_{6k}X_{6k}$ with $\beta_{0k}$ begin the intercept for the $k$th engel value, $\beta_{1k}$ being the estimate for year, $\beta_{2k}$ being the estimate for a male patient, $\beta_{3k}$ being the estimate for a white patient, $\beta_{4k}$ being the estimate for a black patient, $\beta_{5k}$ being the estimate for a frontal lobe surgery, $\beta_{6k}$ being the estimate for a temporal lobe surgery, and $y_k$ being the non-cumulative multinomial probability model for the $k$th engel value. The dummy variable for gender is female, for ethnicity is other, and for location is occipital. For the Frequentist model we are going to define the discrete multinomial probability model as $p_{fl}(k)$ and for Bayesian we are going to define it as $p_{bl}(k)$.

### 4.1.1 Frequentist Model

Using Equations 4.1 and 4.2, we get the multinomial probability models graphed below as Figure 4.1. The x-axis is the patient based on their ID number and on the y-axis we have the engel probability. Blue is the line for the probability of being in engel 1, red is the line for the probability of being engel 2, green is for engel 3, and orange is for engel 4. As we can see the frontal lobe, notated on the top of Figure 4.1, has the lowest probability of being in engel 1 when compared to occipital and temporal. Based on this information the
frontal lobe appears to be the surgery location least likely to result a favorable outcome in our Frequentist model.

![Graphs of Frequentist Estimated Categorical Probabilities by Locations](image)

Figure 4.1: Frequentist Estimated Categorical Probabilities by Locations

Also note that the occipital and temporal lobes appear to have similar outcomes, however, the model shows that the temporal lobe is significant when compared to the occipital lobe.
This must mean that there is something that we cannot see by looking only at the graphs of the data, in terms of this variables level of significance.

4.1.2 Bayesian Model

Next, we are looking at the Bayesian models with the same variables from before. Figures 4.2 through 4.5 show the “spaghetti plots” for our dataset. We have race, gender, and location as variables in our models. For gender we have male and female, for race we have white, black, and other, and for location we have frontal, occipital, and temporal lobes. Therefore, we have a total number of $2 \times 3 \times 3 = 18$ total probabilities, or lines, that can be in our spaghetti plots at each engel value.
As we can see in Figures 4.2 through 4.5, some of the lines in the graphs end before year 10. There are many reasons that this could be the case one such case may be the face that the occipital lobe does not have a year 10 observation for any of the patients. Therefore, the lines would end at year 5 for these patients which account for 6 of the 18 lines in the plots above. As we see in Figure 4.2 above there are some patients that stopped coming to their doctors appointments after the first year, denoted by the dots. This could also be due to a number of reasons which we will not speculate about.

Now, note that engel 4, Figure 4.5, appears to have more clustering in the higher probabilities and the lower probabilities but not much in the middle of the graph. This, when compared to Figure 4.2 tells us a lot about the surgery. Mainly, that engel 4 has a high or low probability of occurrence for all years, which could mean that if you are not at engel 4 after year 1 visit, you may never obtain that classification. Based on the information in Chapter 3, your highest probability of being in the engel 4 classification would be if you had the surgery in the frontal lobe.
The Bayesian models are shown in Figure 4.6 below. Similarly to the frequentist models the x-axis is the patient based on their ID number and on the y-axis we have the engel probability, and blue is the line for the probability of being in engel 1, red is for engel 2, green is for engel 3, and orange is for engel 4. As we can see, the frontal lobe appears to have the worst outcome again for the data. In this case the probability of being engel 4 after surgery seems to be the highest for most patients based on our model. Additionally, the temporal lobe of the Bayesian model appears to have higher volatility than that of the temporal lobe for the Frequentist model.

4.1.3 Comparison of Bayesian and Frequentist Methods

Now that we have looked at the models separately, we are going to compare our Bayesian and Frequentist models. In figures 4.7 through 4.10 the blue line denotes the Bayesian model and the red line denotes the Frequentist model. For engel 1, Figure 4.7, we can see that they are similar. However, the Bayesian approach does appear to show a little more movement than that of the Frequentist model. This is consistent with the idea that the Bayesian approach is more flexible.

There are two engel values that show a difference in the models that we are using. Mainly engel 2, Figure 4.8, and engel 3, Figure 4.9. In the middle portion of engel 2, corresponding to the temporal lobe, the probabilities show significant differences in their behavior. The Bayesian model shows a significantly higher probability of the patient having engel 2 results than that of the frequentist model. Also, engel 3 shows a significant difference in the probability of being in engel 3 than the frequentist model does. As we can see, the Bayesian approach shows a basically 0 probability of some of the patients having engel 3 where the Frequentist approach shows much higher probabilities.
Figure 4.6: Bayesian Estimated Categorical Probabilities by Locations
Figure 4.7: Engel 1

Figure 4.8: Engel 2

Figure 4.9: Engel 3

Figure 4.10: Engel 4
Based on Figures 4.7 through 4.10, our Bayesian model appears to represent the data with more variability due to the increased flexibility introduced by the latent variables for our posterior distribution. Now that we have compared our two models we are going to complete a case study followed by our conclusions about the models.

4.2 Case Study

The data was collected by Dr. Yong Park at Augusta University Health in the Pediatric Neurology Department in Augusta, GA. He collected the data over many years from his patients and has given Dr. Ryu and I permission to use this data in our analysis. Because of the time period the data is being collected over, missing values are expected. Some reasons that the missing values could have occurred are the patient moved, switched doctors, decided to not go to follow up appointments, or died. We assumed the missing values were missing randomly in this data set and not because of a common characteristic among the results of the patients. This allowed us to complete our analysis.

Because of the nature of our dataset we have some missing values. For instance, for the occipital lobe we do not have any data for year 10 after surgery. This is important as it means we cannot make any predictions regarding the patients 10 year post surgery outcome for the occipital lobe where we can for the other lobes. Additionally, our probabilities may have been changed if we had these values so comparison to other lobes could be problematic unless we excluded the year 10 variable from all patients and re-ran the regression. This could have been why the Bayesian model showed occipital lobe compared to temporal lobe to be insignificant at $\alpha = 0.05$.

We have a lot of missing values in our dataset. For 3 year post surgery the missing values are less than 10% for each of the locations. When we are 5 years post surgery we
have similar but higher missing data percentages at 30.3% for the frontal lobe, 33.3% for the occipital lobe, and 34.4% for the temporal lobe. Finally, when we get to the 10 year post surgery check-in we have 62.5% of our data missing for the frontal lobe and 80% missing for the temporal lobe. This is a very significant amount of data missing for our analysis. For gender, the total percentage that is male is 57.4% and the remaining 42.5% is female. Based on lobe location, the percentages are similar with 63.5%, 52.6%, and 55.6% being male for the frontal, occipital, and temporal lobes, respectively. Finally, for race 18.8% of patients are black, 78.5% or patients are white, and 2.6% of patients are listed as an other race.

In chapter 1 we discussed about how some of the brain is laid out, what a lobectomy is, longitudinal categorical analysis, and changes made to the original dataset. Chapter 2 we talked about the descriptive statistics and completed a pilot study of the variables to see which ones should be in our Frequentist model. Chapter 3 discussed the Frequentist and Bayesian multinomial models that were used for this analysis. Finally, chapter 4 discussed the discrete probability models used, showed graphical representations of these discrete probabilities, compared the two models, and completed a case study to discuss missing variables and characteristics of the sample. Based on our results, we can see that the Bayesian Model could allow for greater flexibility which may lead to a better fit of the data. However, additional testing with multiple datasets would be required to confirm.
REFERENCES

Cleveland Clinic (2019a), “Cleveland Clinic Children Epilepsy Guide Treatments.”


APPENDIX A

SIGNIFICANCE VARIABLE CHECK FOR BAYESIAN
<table>
<thead>
<tr>
<th>Parameter</th>
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</tr>
<tr>
<td>Intercept Engel 2</td>
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</tr>
<tr>
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<td>0.2437205</td>
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APPENDIX B

SAS AND R CODE
B.1 SAS Code

/*************************************************************/
/* */
/* PULLING IN DATA */
/* */
/*************************************************************/

/*FRONTAL LOBE Transpose*/
Proc import out=FLE
datafile="H:\Thesis\Final FLE Done.csv"
DBMS=CSV replace;
Getnames=yes;
datarow=2;
run;
quit;

data new;
set fle;
new = input(AgeOnsetM, 8.);
drop AgeOnsetM;
rename new= AgeOnsetM;
run;

data fle1; format year1 year3 year5 year10 best13.0;
set new;
year1 = _1_yr;
year3 = _3_yr;
year5 = _5yr;
year10 = _10yr;
drop _1_yr _3_yr _5yr _10yr;
if patient_id = . then delete;
run;

proc sort data=fle1;
by patient_id;
run;
data flelong;
array engels{4} year1 year3 year5 year10;
set fle1; by patient_id;
do i=1 to 4;
engel = engels{i};
if i=1 then year = 1;
if i=2 then year = 3;
if i=3 then year = 5;
if i=4 then year = 10;
output;
end;

drop year1 year3 year5 year10 i;
if engel = . then delete;
keep patient_id AgeOnsetM race year engel sex;
run;
data flelong2;
set flelong;
if engel = . then delete;
location = 'FLE';
if engel > 4 then engel = 4;
run;

/*TEMPORAL LOBE Transpose*/
Proc import out=TLE
datafile="H:\Thesis\Final TLE Done.csv"
DBMS=CSV replace;
Getnames=yes;
datarow=2;
run;
quit;

data TLE1; format year1 year3 year5 year10 best13.0;
set TLE;
year1 = _1_yr;
year3 = _3_yr;
year5 = _5yr;
year10 = _10yr;
drop _1_yr _3_yr _5yr _10yr;
if patient_id = . then delete;
run;
proc sort data=tle1;
   by patient_id;
run;

data tlelong;
array engels{4} year1 year3 year5 year10;
set tle1;
   by patient_id;
   do i=1 to 4;
      engel = engels{i};
      if i=1 then year = 1;
      if i=2 then year = 3;
      if i=3 then year = 5;
      if i=4 then year = 10;
      output;
   end;
   drop year1 year3 year5 year10 i;
   if engel = . then delete;
keep patient_id AgeOnsetM year race engel sex;
run;

data tlelong2;
set tlelong;
   if engel = . then delete;
   location = 'TLE';
   if engel > 4 then engel = 4;
run;

/*OCCIPITAL LOBE Transpose*/
Proc import out=OLE
datafile="H:\Thesis\Final OLE Done.csv"
DBMS=CSV replace;
Getnames=yes;
datarow=2;
run;
quit;

data ole1; format year1 year3 year5 best13.0;
set ole;
year1 = _1_yr;
year3 = _3_yr;
year5 = _5yr;
drop _1_yr _3_yr _5yr;
if patient_id = . then delete;
run;

proc sort data=ole1;
by patient_id;
run;

data olelong;
array engels{3} year1 year3 year5;
set ole1;
by patient_id;
do i=1 to 3;
engel = engels{i};
if i=1 then year = 1;
if i=2 then year = 3;
if i=3 then year = 5;
output;
end;
drop year1 year3 year5 i;
if engel = . then delete;
keep patient_id AgeOnsetM year engel race sex;
run;
data olelong2;
set olelong;
if engel = . then delete;
location = 'OLE';
if engel > 4 then engel = 4;
run;

/*Merges the three data sets for this project*/
data MergeLobe;
merge olelong2 flelong2 tlelong2;
by location;
run;

/*Data representation*/
proc sgplot data=mergelobe;
    series x=year y=engel / group=patient_id lineattrs=(thickness=2);
run;

proc sort data=mergelobe;
by patient_id year;
run;

data mergelobe1;
retain group 0;
set mergelobe;
by patient_id;
if first.patient_id then do;
    if year = 1 then do;
        if engel=1 then group = 1;
        if engel=2 then group = 2;
        if engel=3 then group = 3;
        if engel=4 then group = 4;
    end;
    if year = 3 then do;
        if engel=1 then group = 5;
end;
if engel=2 then group = 6;
if engel=3 then group = 7;
if engel=4 then group = 8;
end;

if year = 5 then do;
if engel=1 then group = 9;
if engel=2 then group = 10;
if engel=3 then group = 11;
if engel=4 then group = 12;
end;

if year = 10 then do;
if engel=1 then group = 13;
if engel=2 then group = 14;
if engel=3 then group = 15;
if engel=4 then group = 16;
end;
end;
run;

proc univariate data=mergelobe1;
var group;
run;
quit;
ods graphics / reset attrpriority=color;
title 'Engel 1 Start';
proc sgplot data=mergelobe1(where=(group=1));
series x=year y=engel / group=patient_id lineattrs=(thickness=2);
run;
ods graphics / reset attrpriority=color;
title 'Engel 2 Start';
proc sgplot data=mergelobe1(where=(group=2));
   series x=year y=engel / group=patient_id lineattrs=(thickness=2);
run;
ods graphics / reset attrpriority=color;
title 'Engel 3 Start';
proc sgplot data=mergelobe1(where=(group=3));
   series x=year y=engel / group=patient_id lineattrs=(thickness=2);
run;
ods graphics / reset attrpriority=color;
title 'Engel 4 Start';
proc sgplot data=mergelobe1(where=(group=4));
   series x=year y=engel / group=patient_id lineattrs=(thickness=2);
run;

**************************************************************************
/*
/* FREQUENTIST MODELS
/*
**************************************************************************

/GENMOD Model for the prior information gathering*/
proc genmod data = mergelobe1 rorder=data;
freq year;
class location (ref = 'OLE') sex race;
model engel = year sex race location ageonsetm / dist=multinomial
  link=cumlogit type1;
estimate 'LogOR12' location 1 -1 0/ exp;
estimate 'LogOR13' location 1 0 -1 / exp;
estimate 'LogOR23' location 0 1 -1 / exp;
run;

/*GLIMMIX Model for the prior information gathering*/
proc glimmix data=mergelobe1 method=quad(qpoints=21) noclprint;
freq year;
class location (ref = 'OLE') sex race;
model engel = year sex race location ageonsetm /dist=multinomial
  link=cumlogit solution;
ods output SolutionR=ranomeff;
output out=pred pred(blup)=yhat pred(noblup)=myhat pred(blup ilink)=Phat;
run;

/*********************************************************************************/
/*
  Variable Selection
*/
/*********************************************************************************/
Proc import out=FLE11
datafile="H:\Thesis\Final FLE VarSel.csv"
DBMS=CSV replace;
Getnames=yes;
datarow=2;
run;
quit;

data fle12; format year1 year3 year5 year10 best13.0;
set fle11;
year1 = _1_yr;
year3 = _3_yr;
year5 = _5yr;
year10 = _10yr;
drop _1_yr _3_yr _5yr _10yr;
if patient_id = . then delete;
run;

proc sort data=fle12;
by patient_id;
run;

data flelong1;
array engels{4} year1 year3 year5 year10;
set fle12;
by patient_id;
    do i=1 to 4;
        engel = engels{i};
        if i=1 then year = 1;
        if i=2 then year = 3;
        if i=3 then year = 5;
        if i=4 then year = 10;
        output;
    end;
    drop year1 year3 year5 year10 i;
    if engel = . then delete;
    drop VAR13 VAR14 VAR15 VAR16 OpDate DOB;
run;
data flelong21;
    set flelong1;
    if engel = . then delete;
    location = 'FLE';
    if engel > 4 then engel = 4;
run;

proc genmod data = flelong21 rorder=data;
    freq year;
    class sex race;
    model engel = year sex race AgeAtOp AgeOnsetM DurationM / dist=multinomial
        link=cumlogit type1;
run;
# Pulling in Datasets

```r
library(readr)

Data <- read.csv("Northern Illinois University/Thesis/Data/R Data.csv")

attach(Data)

# y is 0 if not 1 is engel is 1 then y is 1

y1 <- (engel == 1)+0
y2 <- ((engel == 1)|(engel == 2))+0
y3 <- ((engel == 1)|(engel == 2)|(engel == 3))+0
y <- cbind(y1, y2, y3)

# y <- (y - min(y))/(max(y) - min(y))

dimy<-dim(y)

n <- dimy[1]

SexInd <- (Sex=='1')+0
RaceInd1 <- (Race=='1')+0
RaceInd2 <- (Race=='2')+0
LocInd1 <- (location=='FLE')+0
LocInd2 <- (location=='TLE')+0

X = cbind(rep(1,n),year, SexInd, RaceInd1, RaceInd2, LocInd1, LocInd2)

y1<-y[!is.na(apply(X,1,mean)),]
```
X1<-X[!is.na(apply(X,1,mean)),]

n1 <- length(y1[,1])

XtX = t(X1)%*%X1

#mvtnorm library MASS
#install.packages("MASS")
require(MASS)
library(MASS)

# Use M-H to generate a vector of latent variables z
genZ <- function(y,fx,sigu2,oldz){
  n <- length(y)
sigu <- sqrt(2*sigu2)
candz <- rnorm(n,0,sigu)+oldz # candidate are from N(oldz,2*sigu2)

  # log of the transition probability for
  # (exp(z*y))/(1+exp(z))*exp(-(z-fx)^2/(2*sigu2))
  logalp <- (candz*y-log(1+exp(candz))-(candz-fx)^2/(2*sigu2)) -
             (oldz*y-log(1+exp(oldz))-(oldz-fx)^2/(2*sigu2))
  logU <- log(runif(n,0,1))

  z <- oldz
  z[logU<logalp] <- candz[logU<logalp]
  return(z)
\#With Constraint

```
genZC <- function(y, fx, sigu2, oldz, zc) {
  n <- length(y)
  sigu <- sqrt(2 * sigu2)
  candz <- rnorm(n, 0, sigu) + oldz # candidate are from N(oldz, 2 * sigu2)

  # log of the transition probability for
  # (exp(z*y))/(1+exp(z))*exp(-(z-fx)^2/(2*sigu2))
  logalp <- (candz * y - log(1 + exp(candz)) - (candz - fx)^2 / (2 * sigu2)) -
            (oldz * y - log(1 + exp(oldz)) - (oldz - fx)^2 / (2 * sigu2))
  logU <- log(runif(n, 0, 1))

  z <- oldz
  z[(logU < logalp) & (candz > zc)] <- candz[(logU < logalp) & (candz > zc)]
  return(z)
}
```

plot(X[, 2], y[, 1])
#lines(X[, 2], phat, col="red")

# initialization
z = rep(0, n)

# set hyperparameters
# for sigu2
A = 1
B = 1
# for b0 and b1
m0 = 0
s0 = 1
m1 = 0
s1 = 1
sigu21 = 1
sigu22 = 1
sigu23 = 1
sigu2 = 1
sib2 = 100

# iteration
burn = 10000
nsamp = 1000
niter = burn+nsamp

# initialize MCMC sample repository
b01all = rep(0,nsamp)
b11all = rep(0,nsamp)
b21all = rep(0,nsamp)
b31all = rep(0,nsamp)
b41all = rep(0,nsamp)
51all = rep(0, nsamp)
52all = rep(0, nsamp)
53all = rep(0, nsamp)
54all = rep(0, nsamp)
55all = rep(0, nsamp)
56all = rep(0, nsamp)
02all = rep(0, nsamp)
03all = rep(0, nsamp)
04all = rep(0, nsamp)
05all = rep(0, nsamp)
06all = rep(0, nsamp)
12all = rep(0, nsamp)
13all = rep(0, nsamp)
14all = rep(0, nsamp)
15all = rep(0, nsamp)
16all = rep(0, nsamp)
22all = rep(0, nsamp)
23all = rep(0, nsamp)
24all = rep(0, nsamp)
25all = rep(0, nsamp)
26all = rep(0, nsamp)
32all = rep(0, nsamp)
33all = rep(0, nsamp)
34all = rep(0, nsamp)
35all = rep(0, nsamp)
36all = rep(0, nsamp)
42all = rep(0, nsamp)
43all = rep(0, nsamp)
44all = rep(0, nsamp)
45all = rep(0, nsamp)
46all = rep(0, nsamp)
52all = rep(0, nsamp)
53all = rep(0, nsamp)
54all = rep(0, nsamp)
55all = rep(0, nsamp)
56all = rep(0, nsamp)
62all = rep(0, nsamp)
63all = rep(0, nsamp)
64all = rep(0, nsamp)
65all = rep(0, nsamp)
66all = rep(0, nsamp)

z1 = rep(0, n1)
z2 = rep(0, n1)
z3 = rep(0, n1)
k <- 1
bet1 <- rep(0, 7)
bet2 <- rep(0, 7)
bet3 <- rep(0, 7)
for (k in 1:niter){
  #This is for engel 1 vs other
    fx1 = X1%*%bet1
    z1 <- genZ(y1[,1],fx1,sigu21,z1)
    Xtz1 <- t(X1)%*%z1

    V = XtX/sigu2 + diag(rep(1,7))/sigb2
    M = Xtz1/sigu2
    Vinv = solve(V) #V inverse
    bet1 = mvrnorm(1,Vinv%*%M, Vinv) #beta

    AstarS = n1/2 + As
    resid = z1 - X1%*%bet1
    BstarS = t(resid)%*%resid/2 + Bs
    rsigu2 = rgamma(1, AstarS, scale = 1/BstarS)
    sigu21 = 1/rsigu2

    #This is for engel 1&2 vs other
    fx2 = X1%*%bet2
    z2 <- genZC(y1[,2],fx2,sigu22,z2,z1)
    Xtz2 <- t(X1)%*%z2
\[ V = \frac{X^T X}{\sigma_{u^2}} + \frac{\text{diag}(\text{rep}(1,7))}{\sigma_{b^2}} \]

\[ M = \frac{X^T z_2}{\sigma_{u^2}} \]

\[ V^{-1} = \text{solve}(V) \# V \text{ inverse} \]

\[ \beta_2 = \text{mvrnorm}(1, V^{-1} \times M, V^{-1}) \# \beta \]

\[ A_{\text{starS}} = \frac{n_1}{2} + A_s \]

\[ \text{resid} = z_2 - X_1 \% \* \% \beta_2 \]

\[ B_{\text{starS}} = t(\text{resid}) \% \* \% \text{resid}/2 + B_s \]

\[ \sigma_{u^2} = \text{rgamma}(1, A_{\text{starS}}, \text{scale} = 1/B_{\text{starS}}) \]

\[ \sigma_{u^2} = 1/\sigma_{u^2} \]

\#This is for engel 1&2&3 vs other

\[ \text{fx}_3 = X_1 \% \* \% \beta_3 \]

\[ z_3 \leftarrow \text{genZC}(y_1[,3], \text{fx}_3, \sigma_{u^2}, z_3, z_2) \]

\[ X_{t z_3} \leftarrow t(X_1) \% \* \% z_3 \]

\[ V = \frac{X^T X}{\sigma_{u^2}} + \frac{\text{diag}(\text{rep}(1,7))}{\sigma_{b^2}} \]

\[ M = \frac{X^T z_3}{\sigma_{u^2}} \]

\[ V^{-1} = \text{solve}(V) \# V \text{ inverse} \]

\[ \beta_3 = \text{mvrnorm}(1, V^{-1} \times M, V^{-1}) \# \beta \]

\[ A_{\text{starS}} = \frac{n_1}{2} + A_s \]

\[ \text{resid} = z_3 - X_1 \% \* \% \beta_3 \]

\[ B_{\text{starS}} = t(\text{resid}) \% \* \% \text{resid}/2 + B_s \]

\[ \sigma_{u^2} = \text{rgamma}(1, A_{\text{starS}}, \text{scale} = 1/B_{\text{starS}}) \]
sigu23 = 1/rsigu2

if (k>burn){
    kk = k-burn
    b01all[kk] = bet1[1]
    b11all[kk] = bet1[2]
    b21all[kk] = bet1[2]
    b31all[kk] = bet1[3]
    b41all[kk] = bet1[4]
    b51all[kk] = bet1[5]
    b61all[kk] = bet1[6]
    sigu21all[kk] = sigu21

    b02all[kk] = bet2[1]
    b12all[kk] = bet2[2]
    b22all[kk] = bet2[2]
    b32all[kk] = bet2[3]
    b42all[kk] = bet2[4]
    b52all[kk] = bet2[5]
    b62all[kk] = bet2[6]
    sigu22all[kk] = sigu22

    b03all[kk] = bet3[1]
    b13all[kk] = bet3[2]
    b23all[kk] = bet3[2]
    b33all[kk] = bet3[3]
b43all[kk] = bet3[4]
b53all[kk] = bet3[5]
b63all[kk] = bet3[6]
sigu23all[kk] = sigu23
}
}

######################################################
# Bayes Est.  #
######################################################

b01hat <- mean(b01all)
b11hat <- mean(b11all)
b21hat <- mean(b21all)
b31hat <- mean(b31all)
b41hat <- mean(b41all)
b51hat <- mean(b51all)
b61hat <- mean(b61all)

b02hat <- mean(b02all)
b12hat <- mean(b12all)
b22hat <- mean(b22all)
b32hat <- mean(b32all)
b42hat <- mean(b42all)
b52hat <- mean(b52all)
b62hat <- mean(b62all)
b03hat <- mean(b03all)
b13hat <- mean(b13all)
b23hat <- mean(b23all)
b33hat <- mean(b33all)
b43hat <- mean(b43all)
b53hat <- mean(b53all)
b63hat <- mean(b63all)

#######################################################
# Sig Est.     #
#######################################################
quantile(b01all, c(0.025,0.975)) #sig
quantile(b11all, c(0.025,0.975)) #sig
quantile(b21all, c(0.025,0.975)) #sig
quantile(b31all, c(0.025,0.975)) #sig
quantile(b41all, c(0.025,0.975)) #sig
quantile(b51all, c(0.025,0.975)) #sig
quantile(b61all, c(0.025,0.975)) #not sig
quantile(b02all, c(0.025,0.975)) #sig
quantile(b12all, c(0.025,0.975)) #sig
quantile(b22all, c(0.025,0.975)) #sig
quantile(b32all, c(0.025, 0.975)) # sig
quantile(b42all, c(0.025, 0.975)) # sig
quantile(b52all, c(0.025, 0.975)) # sig
quantile(b62all, c(0.025, 0.975)) # not sig
quantile(b03all, c(0.025, 0.975)) # sig
quantile(b13all, c(0.025, 0.975)) # sig
quantile(b23all, c(0.025, 0.975)) # sig
quantile(b33all, c(0.025, 0.975)) # sig
quantile(b43all, c(0.025, 0.975)) # sig
quantile(b53all, c(0.025, 0.975)) # sig
quantile(b63all, c(0.025, 0.975)) # not sig

# Cumulative Probability Calculations#

# cumulative prob of c1 do the cp1 for all the other probabilities
b1ind <- rbind(b01all, b11all, b21all, b31all, b41all, b51all, b61all)
cp1 <- matrix(rep(0,1000*536), ncol=536)
for(k in 1:1000) {
cp1[k,] <- 1/(1+exp(-X%*%b1ind[,k]))
}

pc1 <- apply(cp1,2,mean)
pc1[pc1 < 0] = 0
#Not cumulative prob of c2 marginal probability

b2ind <- rbind(b02all, b12all, b22all, b32all, b42all, b52all, b62all)
cp2 <- matrix(rep(0,1000*536),ncol=536)
for(k in 1:1000) {
cp2[k,] <- 1/(1+exp(-X%*%b2ind[,k]))
}

pc2 <- apply(cp2,2,mean)
p2 <- pc2 - pc1
p2[p2 < 0] = 0

#Not cumulative prob of c3

b3ind <- rbind(b03all, b13all, b23all, b33all, b43all, b53all, b63all)
cp3 <- matrix(rep(0,1000*536),ncol=536)
for(k in 1:1000) {
cp3[k,] <- 1/(1+exp(-X%*%b3ind[,k]))
}

pc3 <- apply(cp3,2,mean)
p3 <- pc3 - pc2
p3[p3 < 0] = 0

#Not cumulative prob of c4

p4 <- 1 - pc3
p4[p4 < 0] = 0

# Changing Graphs #

#engel 1
d11 <- as.matrix(pc1[1:170])
d21 <- as.matrix(pc1[171:420])
d31 <- as.matrix(pc1[421:536])
#engel 2
d12 <- as.matrix(p2[1:170])
d22 <- as.matrix(p2[171:420])
d32 <- as.matrix(p2[421:536])
#engel 3
d13 <- as.matrix(p3[1:170])
d23 <- as.matrix(p3[171:420])
d33 <- as.matrix(p3[421:536])
#engel 4
d14 <- as.matrix(p4[1:170])
d24 <- as.matrix(p4[171:420])
d34 <- as.matrix(p4[421:536])
# Spaghetti Plots #

# engel 1 plot
upi <- unique(Data[,2])
plot(c(0,10), c(0,1), main = "Engel 1", xlab = "Time",
     + ylab = "Probability", type = "n")
for (k in 1:191){
t1 <- Data[Data[,2] == upi[k],8]
den1 <- pc1[Data[,2] == upi[k]]
if(length(t1)<=1){
    points(t1, den1, col = rgb(k/191,0.0,1-(k/191)))
}
lines(t1, den1, col = rgb(k/191,0.0,1-(k/191)))
}

# engel 2 plot
upi <- unique(Data[,2])
plot(c(0,10), c(0,0.45), main = "Engel 2", xlab = "Time",
     + ylab = "Probability", type = "n")
for (k in 1:191){
t1 <- Data[Data[,2] == upi[k],8]
den1 <- p2[Data[,2] == upi[k]]
if(length(t1)<=1){
    points(t1, den1, col = rgb(k/191,0.0,1-(k/191)))
}
lines(t1, den1, col = rgb(k/191,0.0,1-(k/191)))
# engel 3 plot
upi <- unique(Data[,2])
plot(c(0,10), c(0,0.25), main = "Engel 3", xlab = "Time",
     + ylab = "Probability", type = "n")
for (k in 1:191){
t1 <- Data[Data[,2] == upi[k],8]
den1 <- p3[Data[,2] == upi[k]]
if(length(t1)<=1){
  points(t1, den1, col = rgb(k/191,0.0,1-(k/191)))
}
lines(t1, den1, col = rgb(k/191,0.0,1-(k/191)))
}

# engel 4 plot
upi <- unique(Data[,2])
plot(c(0,10), c(0,1), main = "Engel 4", xlab = "Time",
     + ylab = "Probability", type = "n")
for (k in 1:191){
t1 <- Data[Data[,2] == upi[k],8]
den1 <- p4[Data[,2] == upi[k]]
if(length(t1)<=1){
  points(t1, den1, col = rgb(k/191,0.0,1-(k/191)))
}
lines(t1, den1, col = rgb(k/191,0.0,1-(k/191)))
par(mfrow = c(2,2))

plot(d11, type = "b", main = "Frontal Lobe", xlab = "Observation", 
    + ylab = "Probability", ylim = c(0,1), col = "blue", pch = 3)
lines(d12, type = "b", col = "red", pch = 1)
lines(d13, type = "b", col = "green", pch = 2)
lines(d14, type = "b", col = "orange", pch = 4)
plot(d21, type = "b", main = "Temporal Lobe", xlab = "Observation", 
    + ylab = "Probability", ylim = c(0,1), col = "blue", pch = 3)
lines(d22, type = "b", col = "red", pch = 1)
lines(d23, type = "b", col = "green", pch = 2)
lines(d24, type = "b", col = "orange", pch = 4)
plot(d31, type = "b", main = "Occipital Lobe", xlab = "Observation", 
    + ylab = "Probability", ylim = c(0,1), col = "blue", pch = 3)
lines(d32, type = "b", col = "red", pch = 1)
lines(d33, type = "b", col = "green", pch = 2)
lines(d34, type = "b", col = "orange", pch = 4)

#legend("right", 0, 1, legend=c("Engel 1", "Engel 2", "Engel 3", "Engel 4"), 
   + col=c("blue", "red", "green", "orange"), lwd=1, cex=1.0)
# Separate Graphs

```r
par(mfrow = c(2,2))

plot(pc1, type = "b", main="Engel Value 1", xlab = "Observation",
     + ylab = "Probability", ylim = c(0,1), col = "blue", pch = 3)
plot(p2, type = "b", main="Engel Value 2", xlab = "Observation",
     + ylab = "Probability", ylim = c(0,1), col = "red", pch = 1)
plot(p3, type = "b", main="Engel Value 3", xlab = "Observation",
     + ylab = "Probability", ylim = c(0,1), col = "green", pch = 2)
plot(p4, type = "b", main="Engel Value 4", xlab = "Observation",
     + ylab = "Probability", ylim = c(0,1), col = "orange", pch = 4)
```

# Separate Lobes Graphs#

### Frontal Lobe

```r
par(mfrow = c(2,2))

plot(d11, type = "b", xlab = "Observation", ylab = "Probability",
     + ylim = c(0,1), col = "blue", pch = 3)
plot(d12, type = "b", xlab = "Observation", ylab = "Probability",
     + ylim = c(0,1), col = "red", pch = 1)
plot(d13, type = "b", xlab = "Observation", ylab = "Probability",
     + ylim = c(0,1), col = "green", pch = 2)
plot(d14, type = "b", xlab = "Observation", ylab = "Probability",
     + ylim = c(0,1), col = "orange", pch = 4)
```
+ ylim = c(0,1), col = "orange", pch = 4)

#Temporal Lobe
par(mfrow = c(2,2))
plot(d21, type = "b", xlab = "Observation", ylab = "Probability",
    + ylim = c(0,1), col = "blue", pch = 3)
plot(d22, type = "b", xlab = "Observation", ylab = "Probability",
    + ylim = c(0,1), col = "red", pch = 1)
plot(d23, type = "b", xlab = "Observation", ylab = "Probability",
    + ylim = c(0,1), col = "green", pch = 2)
plot(d24, type = "b", xlab = "Observation", ylab = "Probability",
    + ylim = c(0,1), col = "orange", pch = 4)

#Occipital Lobe
par(mfrow = c(2,2))
plot(d31, type = "b", xlab = "Observation", ylab = "Probability",
    + ylim = c(0,1), col = "blue", pch = 3)
plot(d32, type = "b", xlab = "Observation", ylab = "Probability",
    + ylim = c(0,1), col = "red", pch = 1)
plot(d33, type = "b", xlab = "Observation", ylab = "Probability",
    + ylim = c(0,1), col = "green", pch = 2)
plot(d34, type = "b", xlab = "Observation", ylab = "Probability",
    + ylim = c(0,1), col = "orange", pch = 4)
# Frequentist Models

```r
f1hat <- rbind(4.6651, -0.1666, -0.4482, -3.0002, -3.3676, -0.8418, 0.8016)
f2hat <- rbind(5.4046, -0.1666, -0.4482, -3.0002, -3.3676, -0.8418, 0.8016)
f3hat <- rbind(6.4486, -0.1666, -0.4482, -3.0002, -3.3676, -0.8418, 0.8016)
```

# Glimix

```r
gm1hat <- rbind(4.4987, -0.1413, -0.5464, -3.2485, -3.4040, -0.6588, 1.0335)
gm2hat <- rbind(5.2379, -0.1413, -0.5464, -3.2485, -3.4040, -0.6588, 1.0335)
gm3hat <- rbind(6.2472, -0.1413, -0.5464, -3.2485, -3.4040, -0.6588, 1.0335)
```

# cumulative prob of c1

```r
pf1 <- 1/(1+exp(-X%*%gm1hat))
```

# Not cumulative prob of c2

```r
pf2 <- 1/(1+exp(-X%*%gm2hat))
prob2 <- pf2 - pf1
```
# Not cumulative prob of c3
pf3 <- 1/(1+exp(-X%*%gm3hat))
prob3 <- pf3 - pf2

# Not cumulative prob of c4
prob4 <- 1 - pf3

# Spaghetti Plots

# engel 1 plot
upi <- unique(Data[,2])
plot(c(0,10), c(0,1), main = "Engel 1", xlab = "Time",
     + ylab = "Probability", type = "n")
for (k in 1:191){
t1 <- Data[Data[,2] == upi[k],8]
den1 <- pf1[Data[,2] == upi[k]]
if(length(t1)<=1){
    points(t1, den1, col = rgb(k/191,0.0,1-(k/191)))
} 
lines(t1, den1, col = rgb(k/191,0.0,1-(k/191)))
}

# engel 2 plot
upi <- unique(Data[,2])
plot(c(0,10), c(0,0.2), main = "Engel 2", xlab = "Time",
     + ylab = "Probability", type = "n")
for (k in 1:191){
t1 <- Data[Data[,2] == upi[k],8]
den1 <- pf1[Data[,2] == upi[k]]
if(length(t1)<=1){
    points(t1, den1, col = rgb(k/191,0.0,1-(k/191)))
} 
lines(t1, den1, col = rgb(k/191,0.0,1-(k/191)))
}
for (k in 1:191) {
  t1 <- Data[Data[,2] == upi[k],8]
  den1 <- prob2[Data[,2] == upi[k]]
  if(length(t1)<=1) {
    points(t1, den1, col = rgb(k/191,0.0,1-(k/191)))
  }
  lines(t1, den1, col = rgb(k/191,0.0,1-(k/191)))
}

# engel 3 plot
upi <- unique(Data[,2])
plot(c(0,10), c(0,0.3), main = "Engel 3", xlab = "Time",
     + ylab = "Probability", type = "n")
for (k in 1:191) {
  t1 <- Data[Data[,2] == upi[k],8]
  den1 <- prob3[Data[,2] == upi[k]]
  if(length(t1)<=1) {
    points(t1, den1, col = rgb(k/191,0.0,1-(k/191)))
  }
  lines(t1, den1, col = rgb(k/191,0.0,1-(k/191)))
}

# engel 4 plot
upi <- unique(Data[,2])
plot(c(0,10), c(0,0.5), main = "Engel 4", xlab = "Time",
     + ylab = "Probability", type = "n")
for (k in 1:191) {
  t1 <- Data[,2] == upi[k,8]
  den1 <- prob4[Data[,2] == upi[k]]
  if (length(t1) <= 1) {
    points(t1, den1, col = rgb(k/191, 0.0, 1-(k/191)))
  }
  lines(t1, den1, col = rgb(k/191, 0.0, 1-(k/191)))
}

########################
# Break out lobe   #
########################
#Frontal
pf1f <- pf1[1:170,1]
prob2f <- prob2[1:170,1]
prob3f <- prob3[1:170,1]
prob4f <- prob4[1:170,1]
#Temporal
pf1o <- pf1[171:420,1]
prob2o <- prob2[171:420,1]
prob3o <- prob3[171:420,1]
prob4o <- prob4[171:420,1]
#Occipital
pf1t <- pf1[421:536,1]
prob2t <- prob2[421:536,1]
prob3t <- prob3[421:536,1]
prob4t <- prob4[421:536,1]

# Complete the plots#

par(mfrow = c(3,1))

#Frontal Lobe
plot(pf1f, type = "b", main = "Frontal Lobe", ylim = c(0.0, 1.0),
     + xlab = "Observation", ylab = "Probability", col = "blue", pch = 3)
lines(prob2f, type = "b", col = "red", pch = 1)
lines(prob3f, type = "b", col = "green", pch = 2)
lines(prob4f, type = "b", col = "orange", pch = 4)

#Temporal Lobe
plot(pf1o, type = "b", main = "Temporal Lobe", ylim = c(0.0, 1.0),
     + xlab = "Observation", ylab = "Probability", col = "blue", pch = 3)
lines(prob2o, type = "b", col = "red", pch = 1)
lines(prob3o, type = "b", col = "green", pch = 2)
lines(prob4o, type = "b", col = "orange", pch = 4)

#Occipital Lobe
plot(pf1o, type = "b", main = "Occipital Lobe", ylim = c(0.0, 1.0),
lines(prob2t, type = "b", col = "red", pch = 1)
lines(prob3t, type = "b", col = "green", pch = 2)
lines(prob4t, type = "b", col = "orange", pch = 4)

# Separate Graphs  
par(mfrow = c(2,2))
plot(pf1, type = "b", main="Engel Value 1", xlab = "Observation",
     + ylab = "Probability", ylim = c(0,1), col = "blue", pch = 3)
plot(prob2, type = "b", main="Engel Value 2", xlab = "Observation",
     + ylab = "Probability", ylim = c(0,1), col = "red", pch = 1)
plot(prob3, type = "b", main="Engel Value 3", xlab = "Observation",
     + ylab = "Probability", ylim = c(0,1), col = "green", pch = 2)
plot(prob4, type = "b", main="Engel Value 4", xlab = "Observation",
     + ylab = "Probability", ylim = c(0,1), col = "orange", pch = 4)

# Compare Graphs  
#Engel 1
plot(pc1, type = "l", main="Engel 1", xlab = "Observation",
     + ylab = "Probability", ylim = c(0,1), col = "blue")
lines(pf1, type = "l", col = "red")
legend("bottomright", 0, 1, legend=c("Bayesian", "Frequentist"),
        + col=c("blue", "red"), lty=1, cex=0.8)

#Engel 2
plot(p2, type = "l", main="Engel 2", xlab = "Observation",
        + ylab = "Probability", ylim = c(0,0.5), col = "blue")
lines(prob2, type = "l", col = "red")
legend("topright", 0, 1, legend=c("Bayesian", "Frequentist"),
        + col=c("blue", "red"), lty=1, cex=0.8)

#Engel 3
plot(p3, type = "l", main="Engel 3", xlab = "Observation",
        + ylab = "Probability", ylim = c(0,0.3), col = "blue")
lines(prob3, type = "l", col = "red")
legend("topright", 0, 1, legend=c("Bayesian", "Frequentist"),
        + col=c("blue", "red"), lty=1, cex=0.8)

#Engel 4
plot(p4, type = "l", main="Engel 4", xlab = "Observation",
        + ylab = "Probability", ylim = c(0,1.0), col = "blue")
lines(prob4, type = "l", col = "red")
legend("topright", 0, 1, legend=c("Bayesian", "Frequentist"),
        + col=c("blue", "red"), lty=1, cex=0.8)