# Introduction to Generalized Linear Models

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Generalized Linear Models (GLMs)

Specific Types of GLMs

Count Response Example in R

# **Motivation**

# **Regression Models**

Regression is a statistical technique for modeling the relationship between explanatory variable(s) and response variable(s).



Regression allows us to model relationships adjusted for other factors!

#### Notation:

 $Y_i$ : Response for *i*-th observation  $X_{ij}$ : *j*-th explanatory variable for *i*-th observation

#### Linear Regression Model:

$$Y_i = \beta_0 + \beta_1 X_{i1} + \ldots + \beta_p X_{ip} + \epsilon_i, \quad \epsilon_i \sim N(0, \sigma^2), \quad i = 1, \ldots, n$$

#### **Alternative Notation:**

$$Y_i = \boldsymbol{x}_i^\top \boldsymbol{\beta} + \boldsymbol{\epsilon}_i, \ \ \boldsymbol{x}_i^\top = (1, X_{i1}, \dots, X_{ip}), \ \ \boldsymbol{\beta} = (\beta_0, \beta_1, \dots, \beta_p)^\top$$

Systematic Component:

$$E[Y_i \mid \boldsymbol{x}_i] = \mu_i = \boldsymbol{x}_i^\top \boldsymbol{\beta}$$

We will sometimes use  $E[Y_i]$  as shorthand for  $E[Y_i | \mathbf{x}_i]$ .

**Random Component:** At each level of the predictor, variation in the response is characterized as  $N(0, \sigma^2)$ 

Independence Between Observations

# What if $Y_i$ is Binary?

Histogram of a Binary Variable



**Binary Variable** 

If  $Y_i$  is binary, then

 $Y_i \sim \text{Bernoulli}(\pi_i), \ \pi_i = \pi(\mathbf{x}_i) = P(Y_i = 1 \mid \mathbf{x}_i)$ 

Normality Assumption is violated!

Additionally,

$$E[Y_i] = \pi_i$$
  
 
$$V(Y_i) = \pi_i (1 - \pi_i) = E[Y_i] \{1 - E[Y_i]\}$$

Constant variance assumption is violated!

Predictions from the resulting linear regression model,  $\hat{Y}_i = \mathbf{x}_i^{\top} \hat{\beta}$ , are not restricted to be between 0 and 1.

**Idea:** Model a function of  $E[Y_i]$  rather than  $E[Y_i]$  directly.

#### Need a more general framework for non-normal outcome data:

- Continuous, non-normal response
  - Time-to-event data
- Binary response
  - Disease vs No Disease
- Nominal categorical response
  - Blood type, US state
- Ordinal categorical response
  - Likert scale data
- Count response
  - White blood cell count, number of insurance claims

# Generalized Linear Models (GLMs)

Generalization here refers to the fact that we are:

- Removing the normality requirement
- Relaxing the constant variance assumption
- Allowing for a function of  $E[Y_i]$  to be linear in the parameters

GLMs are based on the exponential family of distributions.

A distribution is in the exponential family of distributions if:

$$f(Y_i; \theta_i, \phi) = \exp\left\{\frac{t(Y_i)\theta_i - b(\theta_i)}{a(\phi)} + c(Y_i, \phi)\right\}$$

#### Notes:

- $\theta_i$ : parameter of interest, relates to the mean function  $E[Y_i | x_i]$
- $\phi$ : Dispersion parameter, relates to the variance
- $t(\cdot)$ ,  $a(\cdot)$ ,  $b(\cdot)$ , and  $c(\cdot, \cdot)$  are functions
- If t(Y<sub>i</sub>) = Y<sub>i</sub>, then the family is in canonical form and θ<sub>i</sub> is called the canonical (natural) parameter.

We can use maximum likelihood theory to show that:

$$E[Y_i] = \frac{d}{d\theta_i} b(\theta_i) = b'(\theta_i)$$
$$V(Y_i) = \frac{d^2}{d\theta_i^2} b(\theta_i) a(\phi) = b''(\theta_i) a(\phi)$$

Notice that  $E[Y_i]$  depends only on the natural parameter, while  $V(Y_i)$  depends on both the natural parameter and the dispersion parameter.

$$f(Y_i) = \frac{1}{\sqrt{2\pi\sigma^2}} \exp\left\{-\frac{1}{2\sigma^2}(Y_i - \mu_i)^2\right\}$$

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=  $\exp\left\{\frac{2Y_i\mu_i - Y_i^2 - \mu_i^2}{2\sigma^2} - \log(2\pi\sigma^2)\right\}$   
=  $\exp\left\{\frac{Y_i\mu_i - \mu_i^2/2}{\sigma^2} - \frac{Y_i^2}{2\sigma^2} - \log(2\pi\sigma^2)\right\}$ 

# Example: Normal Response (with known $\sigma^2$ )

Suppose that  $Y_i \sim N(\mu_i, \sigma^2)$ , as in linear regression. Then,

$$f(Y_i) = \exp\left\{\frac{Y_i\mu_i - \mu_i^2/2}{\sigma^2} - \frac{Y_i^2}{2\sigma^2} - \log(2\pi\sigma^2)\right\}$$

The normal distribution is a member of the canonical exponential family:

$$t(Y_i) = Y_i$$
  

$$\theta_i = \mu_i$$
  

$$b(\theta_i) = \mu_i^2/2$$
  

$$a(\phi) = \sigma^2$$
  

$$c(Y_i, \phi) = -\frac{Y_i^2}{2\sigma^2} - \log(2\pi\sigma^2)$$

Mean and Variance:  $E[Y_i] = b'(\theta_i) = \mu_i$  and  $V(Y_i) = b''(\theta_i)a(\phi) = \sigma^2$ 

## **Example:** Poisson Response

Suppose that  $Y_i \sim \mathsf{Poisson}(\lambda_i)$ , where  $Y_i \in \{0\} \cup \mathbb{Z}^+$ 

$$f(Y_i) = \frac{e^{-\lambda_i}\lambda_i^{Y_i}}{Y_i!}$$

## **Example:** Poisson Response

Suppose that  $Y_i \sim \mathsf{Poisson}(\lambda_i)$ , where  $Y_i \in \{0\} \cup \mathbb{Z}^+$ 

$$f(Y_i) = \frac{e^{-\lambda_i} \lambda_i^{Y_i}}{Y_i!}$$
  
= exp  $\left\{ Y_i \log(\lambda_i) - \lambda_i - \log(Y_i!) \right\}$ 

#### **Example: Poisson Response**

Suppose that  $Y_i \sim \text{Poisson}(\lambda_i)$ , where  $Y_i \in \{0\} \cup \mathbb{Z}^+$ 

$$f(Y_i) = \frac{e^{-\lambda_i} \lambda_i^{Y_i}}{Y_i!}$$
  
= exp  $\left\{ Y_i \log(\lambda_i) - \lambda_i - \log(Y_i!) \right\}$ 

The Poisson distribution is a member of the canonical exponential family:

$$t(Y_i) = Y_i$$
  
 $heta_i = \log(\lambda_i)$   
 $b( heta_i) = \lambda_i = e^{ heta_i}$   
 $a(\phi) = 1$   
 $c(Y_i, \phi) = -\log(Y_i!)$ 

**Mean and Variance:**  $E[Y_i] = b'(\theta_i) = \lambda_i$  and  $V(Y_i) = b''(\theta_i)a(\phi) = \lambda_i$ 

$$f(Y_i) = \pi_i^{Y_i} (1 - \pi_i)^{1 - Y_i}, \ Y_i \in \{0, 1\}$$

#### Questions:

• Is the Bernoulli distribution a member of the canonical exponential family? If yes, what is  $E[Y_i]$  and  $V(Y_i)$ ?

**Canonical Exponential Family:** 

$$f(Y_i; \theta_i, \phi) = \exp\left\{\frac{Y_i\theta_i - b(\theta_i)}{a(\phi)} + c(Y_i, \phi)\right\}$$
$$E[Y_i] = b'(\theta_i), \quad V(Y_i) = b''(\theta_i)a(\phi)$$

$$f(Y_i) = \pi_i^{Y_i} (1 - \pi_i)^{1 - Y_i}$$

$$f(Y_i) = \pi_i^{Y_i} (1 - \pi_i)^{1 - Y_i}$$
  
= exp  $\left\{ Y_i \log(\pi_i) + (1 - Y_i) \log(1 - \pi_i) \right\}$ 

$$\begin{split} f(Y_i) &= \pi_i^{Y_i} (1 - \pi_i)^{1 - Y_i} \\ &= \exp\left\{Y_i \log(\pi_i) + (1 - Y_i) \log(1 - \pi_i)\right\} \\ &= \exp\left\{Y_i \log\left(\frac{\pi_i}{1 - \pi_i}\right) + \log(1 - \pi_i)\right\} \end{split}$$

## Solution: Binary Response

Suppose that  $Y_i \sim \text{Bernoulli}(\pi_i)$ . Then,

$$f(Y_i) = \exp\left\{Y_i \log\left(\frac{\pi_i}{1-\pi_i}\right) + \log(1-\pi_i)\right\}$$

Bernoulli distribution is a member of the canonical exponential family:

$$t(Y_i) = Y_i$$
  

$$\theta_i = \log\left(\frac{\pi_i}{1 - \pi_i}\right) \implies \pi_i = \frac{e^{\theta_i}}{1 + e^{\theta_i}}$$
  

$$b(\theta_i) = -\log(1 - \pi_i) = \log(1 + e^{\theta_i})$$
  

$$a(\phi) = 1$$
  

$$c(Y_i, \phi) = 0$$

 $E[Y_i] = b'(\theta_i) = e^{\theta_i}/(1+e^{\theta_i}), \quad V(Y_i) = b''(\theta_i)a(\phi) = e^{\theta_i}/(1+e^{\theta_i})^2$ 

Generalization here refers to the fact that we are:

- Removing the normality requirement  $\checkmark$
- Relaxing the constant variance assumption  $\checkmark$
- Allowing for a function of  $E[Y_i]$  to be linear in the parameters ?

**Generalized Linear Model:** 

$$g(\mu_i) = \mathbf{x}_i^\top \boldsymbol{\beta}, \ \mu_i = E[Y_i]$$

#### Details:

- $g(\cdot)$  is called the link function, connects  $\mu_i$  and  $x_i$
- $g(\cdot)$  is required to be monotone and differentiable
- $g(\cdot)$  is called the canonical link if  $\eta_i = \theta_i$ , where  $\eta_i = \mathbf{x}_i^\top \boldsymbol{\beta}$
- Linearity assumption now applies to  $g(\mu_i), g(\mu_i) \in (-\infty,\infty)$
- Still assume that  $Y_1, \ldots, Y_n$  are independent

#### Normal Response:

$$\theta_i = \mu_i, \ \eta_i = \mathbf{x}_i^\top \boldsymbol{\beta} \implies \mu_i = \mathbf{x}_i^\top \boldsymbol{\beta}, \ \boldsymbol{E}[Y_i] = \mu_i$$

#### Bernoulli Response:

$$\theta_i = \log\left(\frac{\pi_i}{1-\pi_i}\right), \ \eta_i = \mathbf{x}_i^\top \boldsymbol{\beta} \implies \log\left(\frac{\pi_i}{1-\pi_i}\right) = \mathbf{x}_i^\top \boldsymbol{\beta}, \ E[Y_i] = \pi_i$$

**Poisson Response:** 

$$\theta_i = \log(\lambda_i), \ \eta_i = \mathbf{x}_i^\top \boldsymbol{\beta} \implies \log(\lambda_i) = \mathbf{x}_i^\top \boldsymbol{\beta}, \ E[Y_i] = \lambda_i$$

Canonical links mostly lead to mathematical/algorithmic simplifications, but are not intrinsically better to use than non-canonical links.

The link function is often chosen based on (not an exhaustive list):

- Type of response variable
- The desired interpretability of parameters in your model
- Model fit
- Whether the model specification makes conceptual sense

My recommendation is to default to the canonical link, and only use non-canonical links if there is an explicit rationale.

• **Random Component:** Assume that  $Y_1, \ldots, Y_n$  come from a distribution within the exponential family of distributions:

$$f(Y_i; \theta_i, \phi) = \exp\left\{\frac{Y_i \theta_i - b(\theta_i)}{a(\phi)} + c(Y_i, \phi)\right\}$$

- Systematic Component (Linear Predictor):  $\eta_i = \mathbf{x}_i^\top \boldsymbol{\beta}$
- Link Function:  $\eta_i = g(\mu_i) \implies \mu_i = g^{-1}(\eta_i)$

# **Specific Types of GLMs**

#### Linear Regression Model:

- Assumes a normally distributed response
- Generally good for symmetric responses
- Response takes values in  $(-\infty,\infty)$

#### Gamma Regression Model:

- Assumes a gamma distributed response
- Less common, but applicable for right-skewed responses
- Response takes values in  $(0,\infty)$

**Note:** Alternatively, we can log-transform a right-skewed, positive response variable and use the linear regression framework.

# Bernoulli Responses

#### Logistic Regression (Canonical Link):

$$\operatorname{logit}(\pi_i) = \operatorname{log}\left(\frac{\pi_i}{1-\pi_i}\right) = \mathbf{x}_i^\top \boldsymbol{\beta}, \pi_i = P(Y_i = 1 \mid \mathbf{x}_i)$$

Use as the default link function for binary responses.

#### **Probit Regression:**

 $\Phi^{-1}(\pi_i) = \mathbf{x}_i^\top \boldsymbol{\beta}, \ \Phi(\cdot)$  is the standard normal CDF

Use when you can think of your binary response as being obtained by thresholding a normally distributed latent variable.

#### Complementary log-log (cloglog) Regression:

$$\log\{-\log(1-\pi_i)\} = \mathbf{x}_i^\top \boldsymbol{\beta}$$

Use when you can think of your binary response as quantifying whether a count response is nonzero, with the count being Poisson distributed.

http://bayesium.com/which-link-function-logit-probit-or-cloglog/

Generalized Logit Model (Nominal):

$$\log\left(\frac{\pi_{ij}}{\pi_{i0}}\right) = \mathbf{x}_i^\top \boldsymbol{\beta}_j, \ j = 1, \dots, J$$

$$\pi_{ij} = P(Y_i = j \mid \boldsymbol{x}_i) = \frac{\{\exp(\boldsymbol{x}_i^\top \boldsymbol{\beta}_j)\}}{1 + \sum_{k=1}^J \exp(\boldsymbol{x}_i^\top \boldsymbol{\beta}_k)}, \ \pi_{i0} = 1 - \sum_{k=1}^J \pi_{ik}$$

Can also use this model for ordinal data.

Cumulative Logit Model (Ordinal):

$$\log\left(\frac{P(Y_i \leq j)}{P(Y_i > j)}\right) = \mathbf{x}_i^\top \boldsymbol{\beta}_j, \ j = 0, \dots, J-1$$

Poisson Regression (Likelihood):

$$\log(\lambda_i) = \mathbf{x}_i^\top \boldsymbol{\beta}, \ E[Y_i] = V(Y_i) = \lambda_i$$

 $\lambda_i$  controls the rate at which events happen.

Poisson Regression (Quasi-Likelihood):

$$\log(\lambda_i) = \mathbf{x}_i^\top \boldsymbol{\beta}$$

 $a(\phi) = \phi$  instead of  $a(\phi) = 1 \implies E[Y_i] = \lambda_i, \ Var[Y_i] = \phi \lambda_i$ 

- Used to correct for overdispersion  $(V(Y_i) > E[Y_i])$
- Estimation of  $\beta$  is unchanged from regular Poisson regression
- Standard errors corresponding to  $\widehat{\beta}$  are generally larger when outcome is truly overdispersed

#### Offset:

 $\log(\lambda_i) = \log(T_i) + \mathbf{x}_i^\top \boldsymbol{\beta}, \ T_i = \text{time over which counts were obtained}$ 

# Count Response Example in R

#### Study Details (Thall and Vail, 1990):

- n = 59 participants with epilepsy.
- Randomized to Progabide  $(n_t = 31)$  or placebo  $(n_p = 28)$ .
- Number of seizures were recorded during an 8-week baseline period.
- Seizure counts were recorded for 4 successive 2-week periods.

#### Primary Research Question:

• Is Progabide use associated with fewer numbers of seizures in epileptic individuals during the final two week period of follow-up?

# Data Example: Seizure Counts for Epileptic Individuals

#Read in data and load necessary Libraries
library(MASS)
library(gplot2)
library(grid)
library(grid)
library(gridExtra)
data("epil") #Type ?epil to see dataset details
epil.follow.up.4 <- epil %% filter(period == 4)</pre>

#### Variables in Dataset:

- y: seizure count for the corresponding two week period
- trt: treatment, either placebo or Progabide
- base: seizure count in the 8-week baseline period
- age: individual's age in years
- V4: binary (0, 1) indicator variable for the 4th period
- subject: subject identifier, 1 to 59
- period: indicator of the two-week time period (1, 2, 3 or 4)
- Ibase: log-counts for the baseline period, centered to have mean zero
- lage: log-age, centered to have mean zero

We will use a Poisson regression model, since we have a count response.

Random Component:

 $Y_i \sim Poisson(\lambda_i)$ 

#### Systematic Component and Link Function:

$$\log(\lambda_i) = \beta_0 + \beta_t trt_i + \beta_a age_i + \beta_b base_i$$

Note that we do not need to be concerned with an offset term, because the follow-up time is the exact same for all individuals!

# **Descriptive Statistics**

#### **#Data Exploration**

```
h1 <- ggplot(data = epil.follow.up.4, aes(x = age)) +
geom_histogram(binwidth = 3, fill = "lightseagreen", color = "black") + theme_bw()
h2 <- ggplot(data = epil.follow.up.4, aes(x = base)) +
geom_histogram(binwidth = 10, fill = "lightseagreen", color = "black") + theme_bw()</pre>
```

```
grid.arrange(h1, h2, nrow = 1, ncol = 2)
```



Need to log-transform the baseline number of seizures!

#Crude Overdispersion Check
c(mean(epil.follow.up.4\$y), var(epil.follow.up.4\$y))

Note that the empirical variance  $(93.1) \gg \text{empirical mean} (7.3)!$ 

This suggests that we will need to account for overdispersion.

#### Random Component:

$$f(Y_i; \lambda_i, \phi) = \exp\left\{\frac{Y_i \log(\lambda_i) - \lambda_i}{\phi} - \log(Y_i!)\right\}$$

Note that we have added overdispersion parameter  $\phi$ .

#### Systematic Component and Link Function:

$$\log(\lambda_i) = \beta_0 + \beta_t trt_i + \beta_a age_i + \beta_b lbase_i$$

Note that we are now adjusting for *Ibase* instead of *base*.

## Not Accounting for Overdispersion

```
#Regular Poisson Regression
poisson.reg.full <- glm(y ~ factor(trt) + age + lbase, family = "poisson", data = epil.follow.up.4)
summary(poisson.reg.full)</pre>
```

```
##
## Call:
## glm(formula = y ~ factor(trt) + age + lbase, family = "poisson",
      data = epil.follow.up.4)
##
##
## Deviance Residuals:
##
      Min
               10 Median
                                 30
                                         Max
## -3.5962 -1.1318 0.1552 0.8062 3.6635
##
## Coefficients:
                      Estimate Std. Error z value Pr(>|z|)
##
## (Intercept)
                      1.37181 0.26731 5.132 2.87e-07 ***
## factor(trt)progabide -0.15726 0.10144 -1.550 0.121
                       0.01100 0.00823 1.337 0.181
## age
## lbase
                    1.17365 0.06819 17.211 < 2e-16 ***
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for poisson family taken to be 1)
##
      Null deviance: 476.25 on 58 degrees of freedom
##
## Residual deviance: 145.98 on 55 degrees of freedom
## AIC: 341.74
##
## Number of Fisher Scoring iterations: 5
```

# Accounting for Overdispersion

```
#With Correction for Overdispersion
```

poisson.reg.full <- glm(y ~ factor(trt) + age + lbase, family = "quasipoisson", data = epil.follow.up.4)
summary(poisson.reg.full)</pre>

```
##
## Call:
## glm(formula = y ~ factor(trt) + age + lbase, family = "auasipoisson".
      data = epil.follow.up.4)
##
##
## Deviance Residuals:
      Min
                10 Median
##
                                 30
                                         Max
## -3.5962 -1.1318 0.1552 0.8062 3.6635
##
## Coefficients:
##
                      Estimate Std. Error t value Pr(>|t|)
## (Intercept)
                      1.37181 0.42241 3.248 0.00199 **
## factor(trt)progabide -0.15726 0.16030 -0.981 0.33087
                      0.01100 0.01301 0.846 0.40116
## age
## lbase
                      1.17365 0.10776 10.892 2.4e-15 ***
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for quasipoisson family taken to be 2.497075)
##
##
      Null deviance: 476.25 on 58 degrees of freedom
## Residual deviance: 145.98 on 55 degrees of freedom
## ATC: NA
##
## Number of Fisher Scoring iterations: 5
```

**Treatment Effect Estimate:** 

$$\widehat{\beta}_t = -0.157$$

Mathematical Meaning of Treatment Effect:

$$\log(E[Y_i \mid trt_i = 1]) - \log(E[Y_i \mid trt_i = 0]) = \beta_t$$

**Interpretation:** Progabide lowers the log of the expected number of seizures by 0.157 when compared with the placebo, adjusted for age and the number of baseline seizures.

Not a very intuitive interpretation!

# Interpretation of Progabide Coefficient

Rate Ratio:

$$e^{\widehat{\beta}_t} = 0.854$$

#### Mathematical Meaning of Rate Ratio:

$$\frac{E[Y_i \mid trt_i = 1]}{E[Y_i \mid trt_i = 0]} = e^{\beta_t}$$

#### Interpretations:

(i) A person using Progabide is expected to have 85.4% of the number of seizures as they would using the placebo, adjusted for age and the number of baseline seizures.

(ii) A person using Progabide is expected to have 14.6% fewer seizures than they would using the placebo, adjusted for age and the number of baseline seizures.

#### General Formula for GLM Predictions:

$$\widehat{Y}_i = g^{-1}(\boldsymbol{x}_i^\top \widehat{\beta})$$

#### The predicted value for the first participant is:

$$Y_1 = 3, \quad \widehat{Y}_1 = \exp(\widehat{\beta}_0 + \widehat{\beta}_t \times 0 + \widehat{\beta}_a \times 31 + \widehat{\beta}_b \times -0.7563538) = 2.28$$

#Predicted number of seizures in the final two-week follow-up period value for the first participant
pred.obs <- epil.follow.up.4[1,]
eta.1.hat <- predict.glm(poisson.reg.full, newdata = pred.obs)
Y.1.hat <- exp(eta.1.hat)
Y.1 <- pred.obs\$y</pre>

```
#Get 95% Confidence Interval for Treatment
ci95.beta <- confint(poisson.reg.full)
ci95.beta.t <- ci95.beta[row.names(ci95.beta) == "factor(trt)progabide",]
ci95.rr <- exp(ci95.beta.t)
ci95.rr
```

**Interpretation:** The probability that the true rate ratio is between 0.62 and 1.17 is 0.95.

Many other inferential techniques you can employ with GLMs!

- GLMs are useful for modeling many different types of responses
- Requires Specification of:
  - A random component from the exponential family
  - Systematic component
  - Link function
- Many of the concepts that apply to multivariable linear regression continue to apply when using GLMs.

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P. F. Thall and S. C. Vail. Some covariance models for longitudinal count data with over-dispersion. *Biometrics*, 46(3):657–671, 1990.