Statistical Methods for Reliability Data from Designed Experiments

Laura J. Freeman

Dissertation submitted to the Faculty of the

Virginia Polytechnic Institute and State University

in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

in

Statistics

G. Geoffrey Vining, Chair

Jeffrey B. Birch

Pang Du

Yili Hong

Scott M. Kowalski

May 6, 2010

Blacksburg, Virginia

Keywords: Design of Experiments, Lifetime Data, Nonlinear Mixed Models, Random Effect, Weibull Distribution, Weighted Least Squares

Statistical Methods for Reliability Data from Designed Experiments

Laura J. Freeman

(ABSTRACT)

Product reliability is an important characteristic for all manufacturers, engineers and consumers. Industrial statisticians have been planning experiments for years to improve product quality and reliability. However, rarely do experts in the field of reliability have expertise in design of experiments (DOE) and the implications that experimental protocol have on data analysis. Additionally, statisticians who focus on DOE rarely work with reliability data. As a result, analysis methods for lifetime data for experimental designs that are more complex than a completely randomized design are extremely limited. This dissertation provides two new analysis methods for reliability data from life tests. We focus on data from a sub-sampling experimental design. The new analysis methods are illustrated on a popular reliability data set, which contains sub-sampling. Monte Carlo simulation studies evaluate the capabilities of the new modeling methods. Additionally, Monte Carlo simulation studies highlight the principles of experimental design in a reliability context. The dissertation provides multiple methods for statistical inference for the new analysis methods. Finally, implications for the reliability field are discussed, especially in future applications of the new analysis methods.

Dedication

To my brother, Peter John Morgan.

Acknowledgments

I wish to express my thanks and appreciation to my advisor, Dr. G. Geoffrey Vining for his guidance, support, and encouragement throughout my graduate studies. In addition, I would like to thank the other members of my committee, Dr. Jeffrey B. Birch, Dr. Pang Du, Dr. Yili Hong, and Dr. Scott M. Kowalski. I would also like to thank my family for their support throughout my life, without them this would have never been possible. Thank you Mom, Dad, Danny, Peter and Emily. You all have served as a pillar of strength for me throughout my graduate experience. I also would like to thank my husband, James Freeman, for his love and support, and teaching me to enjoy the journey. I also want to thank all of the members of the Graduate Student Assembly that I have worked with during graduate school. Without friends and colleagues like the members of the Graduate Student Assembly, graduate school would not have been nearly as rewarding and enjoyable. Thank you to all the friends who have supported me along the way. I am truly blessed to have so many loving and supportive friends.

Contents

List of Figures

List of Tables

Chapter 1

Introduction

Failure time data are commonly found in many fields ranging from engineering to medicine. The Weibull distribution is a popular for modeling lifetime data because of its flexibility. In engineering applications, the Weibull distribution can be used to model the failure of everything from simple parts, like a sheet of metal undergoing fatigue testing, to complex systems, like aircraft engines. The distribution's flexibility allows it to model many different types of failure.

An issue that plagues lifetime data is that it is often expensive and time consuming to collect. Engineers are constantly seeking ways to improve product reliability. Therefore, collecting data on the failure times of finalized products can take a long period of time. This often results in expensive testing procedures and small samples sizes for lifetime experiments. In an attempt to combat expensive testing procedures, often designs that are not completely

randomized and independent are used. These designs can have complicated experimental error structures which need to be properly modeled.

Response Surface Methodology (RSM) is a set of statistical methodologies that are commonly utilized to plan and analyze experiments in an industrial setting. The methodologies of RSM are very attractive in such a setting because they focus on the optimization of a process using small sample sizes. RSM also incorporates the natural sequential nature of experimentation so that engineers can use information from a first round screening experiment to assist in designing the next round of experiments. Many researchers have looked at implementing complex experimental error structures into RSM which may provide some guidance on how to handle these complicated experimental error structures for failure time data. However, the methodologies for RSM, are derived under normal theory; so, they do not provide a ready solution for the analysis of lifetime data, which are intrinsically non-normal.

The current research in lifetime data analysis utilizes several different distributions to model failure times and predict future failures. Popular distributions among statisticians include the lognormal, exponential, and the gamma distributions because they are members of the exponential family. However, engineering literature reveals that engineers tend to prefer the Weibull distribution and the smallest extreme value (SEV) distribution for modeling lifetime data. This preference is understandable because the Weibull distribution's flexibility allows it to model multiple failure mechanisms.

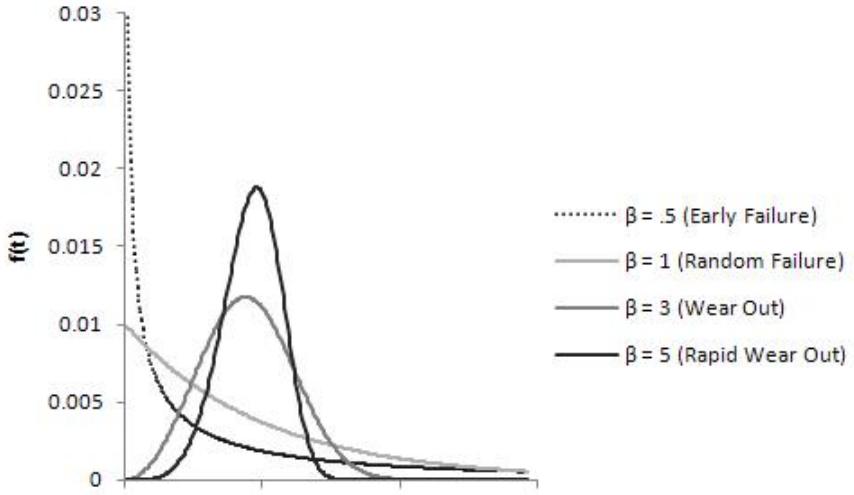
1.1 Weibull Distribution

A common parametrization of the Weibull distribution is:

$$f(t, \beta, \eta) = \frac{\beta}{\eta}\left(\frac{t}{\eta}\right)^{\beta-1} e^{-\left(\frac{t}{\eta}\right)^{\beta}} \tag{1.1}$$

where $\beta > 0$ is the shape parameter and $\eta > 0$ is the scale parameter, and t is the observed failure time. Different values of the shape parameter model several different failure modes, as illustrated in Figure 1.1.

Figure 1.1: Probability Distribution Function of the Weibull Distribution ($\eta = 100$)



Products may follow the early failure distribution, $\beta < 1$, if there is a design flaw in the product or a manufacturing defect. Products that follow the early failure distribution are referred to as having infant mortality. Carbon fiber strands are an engineering example of a product that succumbs to an infant mortality failure mechanism. Carbon fiber strands are used by NASA to encase the outside of composite over-wrapped pressure vessels (COPV).

Space vehicles use COPVs to maintain pressure and therefore the repercussions of a COPV failing in use would be catastrophic. To ensure that the strands encasing the COPVs will not fail, engineers perform tensile strength tests on the carbon fiber strands. In these tests, they observe that either the strands fail very quickly or they last forever. This is a classic example of a product that has an infant mortality failure mechanism.

Products that do not fail early may eventually fail due to wear out. The Weibull distribution models wear out with $\beta > 1$. An example of a product that succumbs to wear out is and aircraft engine. The design specifications on aircraft engines are extremely rigorous which prevents engines from failing early. Eventually, however, parts of the engine tend to break down due to regular use and the engine fails. The magnitude of the shape parameter reflects how quickly these engines fail.

Random failures are modeled under the Weibull distribution using $\beta = 1$. Random failures may be due to external events. Nelson (1990) however notes that random failures are not as common in practice as most product failures occur either because of design defects ($\beta < 1$) of product wear out ($\beta > 1$). The Weibull distribution with $\beta = 1$ is equivalent to the exponential distribution.

The scale parameter, η, which is sometimes referred to as the characteristic life, adds another dimension of flexibility to the Weibull distribution. The scale parameter is called the characteristic life because for any value of β, η is the time by when 63.21% of the population is expected to fail.

The hazard function illustrates how the Weibull distribution models the physics of failure. The hazard function is defined as the instantaneous rate of failure and is:

$$h(t) = \frac{f(t)}{1 - F(t)} \tag{1.2}$$

For the Weibull Distribution the hazard function is:

$$h(t) = \frac{\beta}{\eta}\left(\frac{t}{\eta}\right)^{\beta-1} \tag{1.3}$$

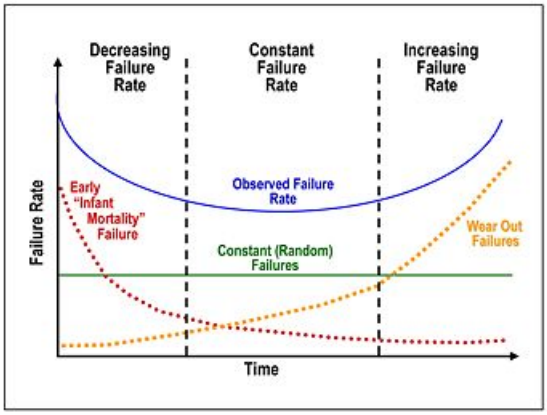
Notice:

- For $\beta < 1$ the hazard function is decreasing (Early Failure/Infant Mortality)
- For $\beta > 1$ the hazard function is increasing (Wear Out)
- For $\beta = 1$ the hazard function, $h(t) = \frac{1}{\eta}$, is constant (Random Failure)

The bathtub hazard function is well known among statisticians and engineers who study failure time data. In fact, the bathtub hazard function is so well known it is illustrated on Wikipedia shown below in Figure 1.2. The bathtub hazard function accounts for infant mortality, random failures during the lifetime of a product and then rapid wear out. It has increasing, constant, and decreasing hazards.

The bathtub hazard function can be expressed as a combination of three Weibull distributions. In many applications of failure time data analysis all three types of failure are present

Figure 1.2: Bathtub Hazard Function (meets fair use requirements)



which makes the bathtub function a great approximation of the failure distribution. The Weibull distribution can model the bathtub hazard function through a linear combination of Weibull distributions as well as all three failure modes independently. This flexibility is why the Weibull distribution is preferred by engineers for modeling lifetime data over the lognormal, exponential and the gamma distributions.

1.2 Response Surface Methodology

Box and Wilson's (1951) seminal work, "On the Experimental Attainment of Optimum Conditions," provided the foundation for RSM, which is a methodology that combines design of experiments (DOE), model fitting using regression methods, and process optimization. Since Box and Wilson's initial paper, RSM has shaped and transformed the way that engineers and statisticians conduct industrial experimentation.

The primary goal of RSM is to utilize Taylor series approximations to find a parametric

model for response prediction over a finite experimental region. RSM uses a sequential experimentation process that lends itself well to industrial applications. In a standard RSM experiment, an experimenter conducts an initial screening experiment to narrow the field of potentially important factors. The experimenter then performs a steepest ascent to find the optimum experimental region. Next, a second-order experiment is run to fully characterize the response surface. This sequential nature allows industrial researchers to take advantage of significant cost savings, especially when little is known about the nature of the response surface.

In recent years many statisticians have noticed the need for methodologies that allow for non-normal responses in an industrial setting. Lifetime data is a common industrial data type especially with the recent push for more reliable products. Myers, Montgomery and Vining (2002) provided a general modeling strategy for analyzing data from response surface designs using a generalized linear models (GLM) framework first developed by Nelder and Wedderburn (1972). Lewis, Montgomery and Myers (2001) , Hamada and Nelder (1997), and Myers and Montgomery (1997) provide examples of quality improving experiments where the response of interest is non-normal. The current work incorporating GLM with RSM focuses the analysis and optimization portions of RSM. A major shortcoming to GLM methodologies is that they are limited to distributions that are in the exponential family, i.e. the normal, Poisson, binomial, gamma and exponential. The exponential family does not include the Weibull distribution or the smallest extreme value distribution.

Clearly, the goals of RSM are inline with the needs of industrial research. The small samples

sizes of RSM designs provide a cost effective solution for lifetime data experiments where testing subjects to failure can be time consuming and costly. The sequential nature of RSM, which has proven itself successful in an industrial setting, may prove to be especially useful in lifetime testing where the physics of failure is not well understood. First order designs provide a method for narrowing down the number of significant factors and help determine the optimum experimental region.

The next section of this dissertation provides a comprehensive literature review of work pertinent to the research which follows. The literature review outlines the current research and methodologies for lifetime data analysis focusing on parametric analysis using the Weibull distribution. We discuss the existing work on using GLMs to analyze data obtained from response surface designs in greater detail. Additionally, we summarize work in generalized linear mixed models (GLMM), which incorporate a random effect into the GLM analysis. The insights gained from GLMM analysis are invaluable to the method developed in Chapter 4 of the dissertation. Finally, the literature review provides a discussion on response surface designs and the current state of design of experiments for lifetime data experiments.

Chapter 3 of the dissertation provides a simple new analysis method that takes into account a more complicated experimental design structure using a two stage analysis. This new analysis can be implemented using current statistical packages with some simple additional calculations. Limitations of this simple approach are presented to motivate Chapter 4.

Chapter 4 provides a second analysis method using nonlinear mixed models (NLMM) methodologies. This method models the experimental design correctly by incorporating a random

effect into the analysis. We discuss the additional complications in the analysis induced by incorporating the random effect. A Monte Carlo simulation study compares the new Weibull NLMM analysis to the currently used independent data analysis for a situation when a completely randomized design is not used.

Chapter 5 focuses on experimental design. We use a Monte Carlo simulation study to evaluate the implication of the principles of experimental design on a simple RSM design, a 2^2 factorial with replication. Additionally, a discussion on statistical testing and inference for the new NLMM analysis methodology is provided.

This dissertation merges lifetime data analysis with principles of experimental design. Throughout the dissertation we focus on modeling the experimental error correctly for lifetime data analyses. In addition to developing two new analysis methods for lifetime data, the dissertation motivates the need for more comprehensive recommendations for designed experiments for lifetime data in the future. The dissertation concludes with a summary of current research and ideas for future research. The novelty of the new analysis methods proposed in this dissertation provide several avenues for future research.

Chapter 2

Literature Review

This literature review consists of three major subsections. The first section presents the current state of lifetime data analysis. The second section looks at the analysis from a different angle. It examines general linear models, linear mixed models and generalized linear model approaches to data analysis. In the third section we look at the current state of design of experiments for both lifetime testing and response surface designs.

The background on lifetime data analysis is presented first in the literature review, despite the fact that it would occur second in an actual experiment because the methodologies of the data analysis must be clearly understood to design an experiment that takes advantage of the analysis methodologies.

2.1 Lifetime Data Analysis

Meeker and Escobar (1998) , Lawless (2003), and Nelson (1990) provide detailed methodologies for the analysis of lifetime data. There are many different methods for modeling lifetime lifetime data. This literature review provides the background for parametric models. Meeker and Escobar provide a brief discussion of nonparametric models and Lawless provides a more comprehensive discussion of nonparametric models. Lawless also provides several semi-parametric techniques for lifetime data analysis. Meeker and Escobar also provide an introduction to Bayesian analysis methodologies for reliability data.

The parametric methods covered in this literature review fall under one of three categories:

1. Parameter estimation and inference for location scale and log-location scale models
2. Coefficient estimation and inference for location scale and log-location scale regression models
3. Coefficient estimation and inference for location scale and log-location scale accelerated life models

In the first subsection, the quantities of interest are the parameters of a particular distribution. In the second and third subsections the quantities of interest are the coefficients in a regression model that relate independent experimental factors to failure times. Location scale and log-location scale models are two general families of distributions that contain the Weibull distribution as well as the normal distribution, the lognormal distribution, the lo-

gistic distribution, the log-logistic distribution, and the smallest extreme value distribution. The range of distributions that they cover makes these distributional families very useful for lifetime data analysis.

This section on lifetime data analysis is primarily based on the work of three textbooks, Nelson (1990), Lawless(2003), and Meeker and Escobar (1998). These authors provide a sound framework for likelihood based methods for reliability analysis. Unless otherwise noted, the analysis approach presented in section 2.1 comes from these textbooks.

2.1.1 Location Scale and Log-Location Scale Models

Meeker and Escobar use location scale and log-location scale distributions to derive their lifetime data analysis methodology. The use of these general distributional forms allows for the derivation of the analysis for many distributions (i.e. normal, lognormal, smallest extreme value, Weibull, logistic and log-logistic) all at once. The location parameter, μ, and the scale parameter, σ, are the two parameters of any location-scale or log-location-scale distribution. Additionally, Meeker and Escobar denote the response vector as $\mathbf{y}$ when the response follows a location scale distribution and as $\mathbf{t}$ when the response follows a log-location scale distribution. This notation will be used throughout this literature review for consistency and clarity. However, instead of using σ for the scale parameter we will use $\beta = \frac{1}{\sigma}$ to avoid any confusion with experimental error, which σ commonly denotes. Lawless also uses a similar log-location-scale approach for deriving his models. Nelson on the other

hand focuses on individual distributions for his derivations. This literature review primarily uses the location scale/log-location scale method for generality; however, if an example is warranted, the Weibull distribution will be used to illustrate the derivations for the example. Fortunately, the different methods that Meeker and Escobar, Lawless, and Nelson use are all equivalent for the Weibull distribution.

Weibull Distribution and Smallest Extreme Value Distribution

The Weibull distribution is a log-location scale distribution. The log-location scale parametrization of the Weibull distribution takes advantage of the relationship between the Weibull distribution and the smallest extreme value (SEV) distribution, if $T \sim Weibull(\beta, \eta)$ and $Y = log(T)$ then $Y \sim SEV(\mu, \beta)$ where $\mu = log(\eta)$. Therefore, the Weibull distribution in log-location scale form is: $T \sim Weibull(\mu, \beta)$ with:

$$f(t, \mu, \beta) = \left(\frac{\beta}{t}\right) \phi_{SEV} \left[\beta \left(log(t) - \mu\right)\right] \tag{2.1}$$

$$F(t, \mu, \beta) = \Phi_{SEV} \left[\beta \left(log(t) - \mu\right)\right] \tag{2.2}$$

where ϕ_{SEV} is the probability distribution function (PDF) for the SEV distribution and Φ_{SEV} is the CDF for the SEV distribution.

The PDF and the CDF as well as other distributional properties of the smallest extreme

value distribution are important because of their relationship to the Weibull distribution. If $Y \sim SEV(\mu, \beta)$, then:

$$f(y, \mu, \beta) = \beta \exp[z - \exp(z)] \tag{2.3}$$

$$F(y, \mu, \sigma) = 1 - \exp[-\exp(z)] \tag{2.4}$$

where $z = \beta(y - \mu)$. The SEV distribution is skewed left with mean: $E(Y) = \mu - \frac{\gamma}{\beta}$ ($\gamma = .5772$, Euler's constant) and variance: $Var(Y) = \frac{\pi^2}{6\beta^2}$. It is important to note we are using μ to refer to the location parameter of distribution not the mean.

Censoring

Censored data are very common in lifetime data analysis. The three types of censoring are right, left, and interval. Right censoring is the most common in reliability data because it occurs when not all of the subjects tested fail. For example, a company that produces aircraft engines wishes to test how reliable they are, and they have 3 months to run an experiment. They run 10 engines at accelerated rates until failure. After 3 months however, only 4 of the 10 aircraft engines have failed. The remaining 6 engines are right censored. Right censored observations can be Type I censored or Type II censored. Type I censoring creates time censored observations. The aircraft engines in the above example are time censored because

after 3 months all engines that are still running are censored. Type II censoring is failure censoring. An example of failure censoring would be if the company decided that they were going to run the engines until 5 of them fail regardless of how long it takes. In practice Type I censoring is more common because of its practical time constraint implications. However, Type II censoring is often used in designed experiments.

Left censoring occurs when subjects enter an experiment at different times or if failures are unobservable for some initial time period. Interval censoring occurs when the exact failure time of a unit is unknown. For example, in the aircraft engine experiment, if the the engines were only inspected once a week during the 3 months then the week interval when an engine fails would be known but not the exact day/hour.

All three types of censored data (right, left and interval) contain information that we do not want to ignore when performing lifetime data analysis. Fortunately, censoring can be taken into account in the likelihood function fairly easily. The ease of incorporating censoring into the likelihood function makes likelihood based methods ideal for analyzing lifetime data.

Parameter Estimation for Location Scale and Log-Location Scale Models

Maximum likelihood methods are generally recommended for calculating parameter estimates for lifetime models. Maximum likelihood methods are statistically optimum for large sample sizes, and they easily allow for non-normal data and censoring, both of which are common in reliability data. In addition to these benefits, likelihood based estimation meth-

ods provide a ready solution for statistical inference based on the information matrix derived from the log-likelihood.

Common location scale distributions in reliability data analysis include the normal distribution, the smallest extreme value distribution, and the logistic distribution. The likelihood function for location scale distributions if there is no censoring present is:

$$L(\mu, \beta; \mathbf{y}) = \prod_{i=1}^{n} f(y_i; \mu, \beta) = \prod_{i=1}^{n} \{\beta\phi [\beta (y_i - \mu)]\} \tag{2.5}$$

If right censoring is present in the data because not all of the units have failed, the likelihood is:

$$L(\mu, \beta; \mathbf{y}) = \mathcal{C} \prod_{i=1}^{n} \{\beta\phi [\beta (y_i - \mu)]\}^{\delta_i} \{1 - \Phi [\beta (y_i - \mu)]\}^{1-\delta_i} \tag{2.6}$$

$$\delta_i = \begin{cases} 1 & \text{if the observation is exact} \\ 0 & \text{if the observation is censored} \end{cases}$$

where $\mathcal{C}$ is a constant which varies based on the censoring type (Type I or Type II). This constant however, does not impact the maximum likelihood estimates and therefore is generally taken as $\mathcal{C} = 1$ for simplicity. These likelihood expressions are general expressions for all location-scale distributions. One must substitute the appropriate PDF and CDF to obtain the likelihood for a specific distribution. For example, for the normal distribution one

would use $\phi = \phi_{Norm}$ (the PDF for the normal distribution) and $\Phi = \Phi_{Norm}$ (the CDF for the normal distribution). The likelihood can easily be adapted to accommodate left censoring or interval censoring by multiplying the likelihood by additional terms if these types of censoring are present. The right censored likelihood is presented here because it is the most common type of censoring in reliability data analysis.

To find the maximum likelihood estimates, the likelihood is then maximized with respect to the model parameters μ and β. Typically, we maximize the log-likelihood function for simplicity of calculations. Numerical methods are used to maximize the likelihood expression with respect to μ and β except in cases where a closed form solution exists. The resulting estimates for μ and β are the maximum likelihood estimates denoted by $\hat{\mu}$ and $\hat{\beta}$.

Maximum Likelihood Method for Log-Location Scale Distributions

Common log-location scale distributions used in reliability data analysis are the lognormal distribution, the Weibull distribution, and the log-logistic distribution. The likelihood function for these distributions if there is no censoring present is:

$$L(\mu, \sigma; \mathbf{t}) = \prod_{i=1}^{n} f(t_i; \mu, \beta) = \prod_{i=1}^{n} \left\{ \frac{\beta}{t_i} \phi \left[\beta \left(\log(t_i) - \mu \right) \right] \right\} \tag{2.7}$$

If right censoring is present in the data because not all of the units have failed, the likelihood is :

$$L(\mu, \sigma; \mathbf{t}) = \mathcal{C} \prod_{i=1}^{n} \left\{ \frac{\beta}{t_i} \phi \left[\beta \left(\log(t_i) - \mu \right) \right] \right\}^{\delta_i} \left\{ 1 - \Phi \left[\beta \left(\log(t_i) - \mu \right) \right] \right\}^{1-\delta_i} \tag{2.8}$$

$$\delta_i = \begin{cases} 1 & \text{if the observation is exact} \\ 0 & \text{if the observation is censored} \end{cases}$$

Again, we can assume $\mathcal{C} = 1$ for simplicity for obtaining maximum likelihood estimates for both Type I and Type II censoring. For the lognormal distribution: $\phi = \phi_{Norm}$ and $\Phi = \Phi_{Norm}$; for the Weibull distribution $\phi = \phi_{SEV}$ and $\Phi = \Phi_{SEV}$; and for the log-logistic distribution $\phi = \phi_{logistic}$ and $\Phi = \Phi_{logistic}$. Again the likelihood function must be maximized with respect to μ and β using numerical methods to obtain the maximum likelihood estimates $\hat{\mu}$ and $\hat{\beta}$ except in cases where closed form solutions exist.

Lawless, presents the reduced form for the the log-likelihood for the Weibull distribution. For this case the log-likelihood reduces to:

$$\ell(\mu, \beta) = r log(\beta) + \sum_{i=1}^{n} \left[\delta_i z_i - exp(z_i) \right] \tag{2.9}$$

where r is the total number of observed failures and $z_i = \beta[log(t_i) - \mu]$.

For the Weibull distribution with right censoring a closed form solution can be found for $\hat{\mu}$, but numerical methods must be used to find the maximum likelihood estimate for β. The closed form solution for $\hat{\mu}$ is (Lawless, 2003, page 219):

$$\hat{\mu} = \frac{1}{\hat{\beta}} \log \left(\frac{1}{r} \sum_{i=1}^{n} e^{\left(\hat{\beta} \log(t_i)\right)} \right) \tag{2.10}$$

Other Estimation Methods

Other estimation methods are available for the parameter estimation. Nelson (1990) provides a descriptions of least squares (LS) estimation methods for complete data. Median rank regression (MRR) is a special case of LS estimation that is detailed in Abernathy (2004). A significant amount of literature exists on different estimation methods for the Weibull distribution, see for example Hossain and Howlader (1996), who compare least squares estimation to maximum likelihood estimation. Somboonsavatee, Nair, and Sen (2007) also compare least squares estimation to maximum likelihood estimation in terms of mean square error.

LS estimation and MRR were very popular in the early lifetime data analysis because of the simplicity of calculations required. More recently however, these other methods are losing momentum due to increased availability of computing power. Nelson, Lawless, and Meeker and Escobar prefer maximum likelihood methods because they can be applied to a wide range of data types. Additionally, they can easily incorporate censored data into the analysis, which is extremely important for lifetime data. Maximum likelihood estimates are also asymptotically optimum and functions of MLEs are also MLE by the invariance property of MLEs. For all of these reasons the focus of this literature review will be on maximum likelihood estimation methods despite the availability of additional estimation methods.

Inference for Location Scale and Log-Location Scale Models

Wald's Method can be used to find confidence intervals on μ and β for the location scale and log-location scale distributions. It is reasonable to assume that μ is asymptotically normal because it is already on the log scale, but because β is a positive parameter, it is common practice to use a log transformation. Therefore, the confidence interval for β is derived using the delta method. The $(1-\alpha)100\%$ confidence intervals for μ and β are respectively:

$$\left[\hat{\mu} - z_{1-\frac{\alpha}{2}} \hat{s.e.}(\hat{\mu}), \quad \hat{\mu} + z_{1-\frac{\alpha}{2}} \hat{s.e.}(\hat{\mu}) \right] \tag{2.11}$$

$$\left[\frac{\hat{\beta}}{w}, \quad w\hat{\beta} \right] \tag{2.12}$$

where, $w = z_{1-\frac{\alpha}{2}} \frac{\hat{s.e.}(\hat{\beta})}{\hat{\beta}}$. The standard error of the estimates come from the inverse of the estimation of the parameter's Fisher's Information matrix. The information matrix for the location scale and log-location scale parameters is:

$$\begin{aligned} \hat{\Sigma} &= \begin{bmatrix} \widehat{Var}(\hat{\mu}) & \widehat{Cov}(\hat{\mu}, \hat{\beta}) \\ \widehat{Cov}(\hat{\beta}, \hat{\mu}) & \widehat{Var}(\hat{\beta}) \end{bmatrix} \\ &= \begin{bmatrix} -\frac{\partial^2 \ell(\mu,\beta)}{\partial \mu^2} & -\frac{\partial^2 \ell(\mu,\beta)}{\partial \mu \partial \beta} \\ -\frac{\partial^2 \ell(\mu,\beta)}{\partial \mu \partial \beta} & -\frac{\partial^2 \ell(\mu,\beta)}{\partial \beta^2} \end{bmatrix}^{-1} \end{aligned} \tag{2.13}$$

where the partial derivatives of the log-likelihood are evaluated at the maximum likelihood estimates $\hat{\mu}$ and $\hat{\beta}$. It is important to note that for the Weibull distribution a significant correlation between the two parameters exists. The standard error of each of the parameters is then given by the square-root of its variance estimate in $\hat{\Sigma}$. Alternative methods for computing confidence intervals given by Meeker and Escobar, Lawless and Nelson include using the likelihood ratio method of computing confidence intervals and Monte-Carlo simulation.

Invariance Property of Maximum Likelihood Estimates

Often in reliability data analysis, the end goal of the analysis is not to predict the distribution parameters but instead to predict some scalar function, $f(\mu, \beta)$, of the distribution parameters. For example, a common function of interest in reliability data analysis is the failure time for the p^{th} percentile. The p^{th} percentile for the two-parameter Weibull distribution is:

$$t_p = \exp\left[\mu + \frac{\Phi_{SEV}^{-1}(p)}{\beta}\right] \tag{2.14}$$

The invariance property of maximum likelihood estimates ensures us that any function of the MLEs is the maximum likelihood estimate for that function. Therefore, the MLE of the p^{th} percentile is:

$$\hat{t}_p = \exp\left[\hat{\mu} + \frac{\Phi_{SEV}^{-1}(p)}{\hat{\beta}}\right] \tag{2.15}$$

The standard error for $\hat{t}_p$ can then be calculated using the multivariate delta method. The multivariate delta method states that if $\hat{f} = f(\hat{\boldsymbol{\theta}})$ then the standard error of $\hat{f}$ is:

$$\hat{\Sigma}_{\hat{f}} = \left[\frac{\partial f(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}}\right]^T \hat{\Sigma}_{\hat{\boldsymbol{\theta}}} \left[\frac{\partial f(\boldsymbol{\theta})}{\partial \boldsymbol{\theta}}\right] \tag{2.16}$$

The invariance property of maximum likelihood estimates is another reason that they are very popular and useful for estimating parameters. From the multivariate delta method we can derive the standard error for $\hat{t}_p$ to be:

$$\widehat{s.e.}_{\hat{t}_p} = \hat{t}_p \left[\widehat{Var}(\hat{\mu}) - 2\frac{\Phi^{-1}_{SEV}(p)}{\beta^2}\widehat{Cov}(\hat{\mu},\hat{\beta}) + \left[\frac{\Phi^{-1}_{SEV}(p)}{\beta^2}\right]^2 \widehat{Var}(\hat{\beta})\right]^{1/2} \tag{2.17}$$

2.1.2 Location Scale and Log-Location Scale Regression Models

The maximum likelihood methods of Section 2.1.1 deal with fitting a particular distribution to failure times. In the previous section, we estimated the distribution's parameters based on failure time data. In this section, we are interested in if these distributional parameters depend on some explanatory variables. Some notation will assist in the following discussion.

- The vector of the failure time distribution parameters will be represented by $\boldsymbol{\theta}$, for location scale and log-location scale distributions $\boldsymbol{\theta} = \begin{pmatrix} \mu \\ \beta \end{pmatrix}$.
- The failure times are denoted by the vector $\mathbf{t}$ for log-location scale models and by the

vector $\mathbf{y}$ for location scale models

- The explanatory variable(s) will be represented by the matrix $\mathbf{X}_{nxp}$, where p is the number of regression model parameters.
- The regression model parameters will be represented by the vector $\boldsymbol{\gamma}_{px1} = (\gamma_0, \gamma_1, ..., \gamma_{p-1})^T$.

In reliability data analysis often the explanatory variable of interest is an accelerating factor. This section deals solely with statistical issues of the failure time regression analysis. Accelerated life tests are discussed in the next section.

Coefficient Estimation for the Simple Linear Regression Model

Meeker and Escobar and Lawless focus on modeling the location parameter, μ, as a function of the regression factors as an appropriate method for translating the effect of the factors in a designed experiment to the failure times. The simplest possible model for translating the factors of a designed experiment to failure times is the simple linear regression model. This section discusses this model for the location scale and log-location scale distributions.

The likelihood function for a sample of n observations with right censoring is:

$$L(\gamma_0, \gamma_1, \beta; \mathbf{y}) = \mathcal{C} \prod_{i=1}^{n} \{\beta\phi[\beta(y_i - \mu_i)]\}^{\delta_i} \{1 - \Phi[\beta(y_i - \mu_i)]\}^{1-\delta_i} \tag{2.18}$$

where $\mu_i = \gamma_0 + \gamma_1 x_i$ and $\delta_i = 1$ for an exact failure and $\delta_i = 0$ for a right censored observation. Choosing Φ determines the shape of the distribution. Note that $\mathcal{C}$ is a constant which varies

based on the censoring type that is generally taken as $\mathcal{C} = 1$ for simplicity because it does not impact the maximum likelihood estimation. Also, notice that this likelihood can be generalized to uncensored data if all $\delta_i = 1$. We maximize the likelihood function with respect to γ_0, γ_1 and β to obtain the MLEs.

The log-location scale regression model for simple linear regression is very similar to the model for the location scale regression. The likelihood function for a sample of n observations with right censoring is:

$$L(\gamma_0, \gamma_1, \beta; \mathbf{t}) = \mathcal{C} \prod_{i=1}^{n} \left\{ \frac{\beta}{t_i} \phi \left[\beta(\log(t_i) - \mu_i) \right] \right\}^{\delta_i} \left\{ 1 - \Phi \left[\beta(\log(t_i) - \mu_i) \right] \right\}^{1-\delta_i} \tag{2.19}$$

where $\mu_i = \gamma_0 + \gamma_1 x_i$ and $\delta_i = 1$ for an exact failure and $\delta_i = 0$ for a right censored observation. The likelihood function is maximized with respect to γ_0, γ_1 and β to obtain the MLEs. Numerical methods must now be used to maximize the likelihood function. For the Weibull distribution a partial closed form solution no longer exists now that the location parameter is a function of experimental factors.

Inference for Simple Linear Regression Model

Wald's method can again be used to calculate confidence intervals on the model parameters. These confidence intervals require the estimation of the parameter's Fisher Information matrix. For the simple linear regression case when $\boldsymbol{\theta} = (\gamma_0, \gamma_1, \beta)^T$ the Information matrix is:

$$\begin{aligned}\hat{\Sigma}_{\hat{\theta}} &= \begin{bmatrix} \widehat{Var}(\hat{\gamma}_0) & \widehat{Cov}(\hat{\gamma}_0,\hat{\gamma}_1) & \widehat{Cov}(\hat{\gamma}_0,\hat{\beta}) \\ \widehat{Cov}(\hat{\gamma}_0,\hat{\gamma}_1) & \widehat{Var}(\hat{\gamma}_1) & \widehat{Cov}(\hat{\gamma}_1,\hat{\beta}) \\ \widehat{Cov}(\hat{\gamma}_0,\hat{\beta}) & \widehat{Cov}(\hat{\gamma}_1,\hat{\beta}) & \widehat{Var}(\hat{\beta}) \end{bmatrix} \\ &= \begin{bmatrix} (-\frac{\partial^2\ell(\gamma_0,\gamma_1,\beta)}{\partial\gamma_0^2} & -\frac{\partial^2\ell(\gamma_0,\gamma_1,\beta)}{\partial\gamma_0\partial\gamma_1} & -\frac{\partial^2\ell(\gamma_0,\gamma_1,\beta)}{\partial\gamma_0\partial\beta} \\ -\frac{\partial^2\ell(\gamma_0,\gamma_1,\beta)}{\partial\gamma_0\partial\gamma_1} & -\frac{\partial^2\ell(\gamma_0,\gamma_1,\beta)}{\partial\gamma_1^2} & -\frac{\partial^2\ell(\gamma_0,\gamma_1,\beta)}{\partial\gamma_1\partial\beta} \\ -\frac{\partial^2\ell(\gamma_0,\gamma_1,\beta)}{\partial\gamma_0\partial\beta} & -\frac{\partial^2\ell(\gamma_0,\gamma_1,\beta)}{\partial\gamma_1\partial\beta} & -\frac{\partial^2\ell(\gamma_0,\gamma_1,\beta)}{\partial\beta^2} \end{bmatrix} \end{aligned} \tag{2.20}$$

where the partial derivatives are evaluated at the MLEs, $\hat{\gamma}_0$, $\hat{\gamma}_1$ and $\hat{\beta}$. The standard error of each of the parameters is the square-root of its variance estimate in $\hat{\Sigma}_{\hat{\boldsymbol{\theta}}}$. These standard errors are then used to construct confidence intervals and statistical tests for $\hat{\gamma}_0$, $\hat{\gamma}_1$ and $\hat{\beta}$. Again, the confidence interval for β is on the log scale.

From $\hat{\Sigma}_{\hat{\boldsymbol{\theta}}}$ the variance for $\hat{\mu}$ and the covariance between $\hat{\mu}$ and $\hat{\beta}$ can be calculated using statistical properties of variance and covariance:

$$\widehat{Var}(\hat{\mu}) = \widehat{Var}(\hat{\gamma}_0) + x_1^2\widehat{Var}(\hat{\gamma}_1) + 2x_1\widehat{Cov}(\hat{\gamma}_0,\hat{\gamma}_1) \tag{2.21}$$

$$\widehat{Cov}(\hat{\mu},\hat{\beta}) = \widehat{Cov}(\hat{\gamma}_0,\hat{\beta}) + x_1\widehat{Cov}(\hat{\gamma}_1,\hat{\beta}) \tag{2.22}$$

Then the delta method can be implemented to calculate standard errors for functions of $\hat{\mu}$

and $\hat{\beta}$ making inference on additional quantities possible. The standard error for $\hat{t}_p$ can now be calculated using Equation 2.17 just as it was before.

Coefficient Estimation for Multiple Regression Model with Nonconstant Variance

The maximum likelihood methods described in the simple linear regression section of this literature review can be extended to more general models. Meeker and Escobar examine models with multiple linear regression links to the location parameter as well as models with nonconstant variance. Matrix notation allows for the discussion of more general models. Let,

$$\mu_i = \mathbf{x}_{[\mu]i}^T \boldsymbol{\gamma}_{[\mu]} \tag{2.23}$$

$$\beta_i = \mathbf{x}_{[\beta]i}^T \boldsymbol{\gamma}_{[\beta]} \tag{2.24}$$

It is important to note for total generality the explanatory variables in the location model can be different from those in the scale model, also the two models can have different dimensions. These quantities are then used in place of μ_i and β_i in the same likelihood as the simple linear regression model likelihood. The resulting function is maximized with respect to each of the model parameters. However, because of complications with maximizing the likelihood function with respect to a large number of parameters, it is common to assume a constant

scale parameter (i.e. β_i does not depend on any regressors). Additionally, this assumption makes sense from an engineering perspective as long as the failure mechanism is not expected to change due to the levels of the explanatory variables.

In addition to estimation becoming more difficult when there are multiple factors that impact both the location and scale parameters, inference becomes tricky as well. The covariance matrix $\hat{\Sigma}_{\hat{\boldsymbol{\theta}}}$ is now a larger matrix calculated in a similar fashion to the covariance matrix for the simple linear regression model. It is easy to see that a large number of predictive variables quickly complicates the analysis and can result in information matrices that may not have inverses. For this reason it is important to have an engineering reason for expanding beyond simple models. Well designed experiments may also be able to assist in appropriate model selection.

2.1.3 Accelerated Life Test Models

Often in reliability data analysis designed experiments for failure time data fall into the class of accelerated life tests (ALT). Accelerated life tests run test subjects at more extreme levels of the design factors than the test subjects would ever encounter under normal use. These experimental factors are called accelerating factors in an ALT. The goal of an ALT is to produce more failures than would be seen running an experiment under normal operating conditions. These tests are an important set of designed experiments in today's world as products become more reliable and therefore less likely to fail.

The key to analyzing ALT data is to determine the linearizing relationship between the accelerating factor and the parameters of the distribution being used to model the failure time. Nelson and Meeker and Escobar focus on the most appropriate way to relate the accelerating factor back to the failure distribution as being through the location parameter, μ_i. Three common relationships for relating the accelerating factor to the location parameter are:

- The Arrhenius Relationship for temperature acceleration $x_i = \frac{11605}{Temp_i(\deg Kelvin)}$
- The inverse power relationship for voltage and/or stress acceleration $x_i = \log(StressRatio) = \log(\frac{Volt(High)}{Volt(Low)})$
- The generalized Eyring relationship for one or more non-thermal accelerating variable, dependent on the number of variables and the accelerating factor (i.e. humidity or voltage)

It is important for the linearizing relationship to be based in engineering knowledge otherwise the model fit could be completely nonsensical. The methodology for modeling data from ALTs is:

1. Linearize the factors through an engineering based relationship
2. Fit model using techniques derive in section 2.1.2
3. Transform back results for interpretability in terms of design space for accelerating factors

2.2 Analysis Techniques for Exponential Family Distributions

In this section a brief description of the current literature for exponential family distribution is presented. The goal of this section is to provide insights from how these already well developed techniques for exponential families might be applied to the Weibull distribution. The section covers generalized linear models, linear mixed models, and generalized linear mixed models. McCulloch and Searle (2001) provide a straight forward approach to each of these topics. These models are important to this proposal because the generalized linear mixed model theory will provide the motivating theory for the proposed research.

2.2.1 Generalized Linear Models (GLM)

Nelder and Wedderburn (1972) introduces the area of generalized linear models (GLM). Many statisticians use GLM techniques for the analysis of non-normal data in response surface experiments. Lewis, Montgomery and Myers (2001) provide three examples where the response distribution is non-normal. They show that using a GLM analysis results in better results than transforming the data. Myers and Montgomery (1997) provide a tutorial for using GLM methods for designed experiments.

GLM analysis is applicable for any distribution that is a member of the natural exponential family, which includes the binomial, Poisson, normal, logistic, gamma, and exponential

distributions. However the Weibull distribution, which is a popular distribution for reliability data analysis, is not a member of the exponential family. The lognormal distribution, another distribution commonly used in reliability data analysis, is a member of the general exponential family through its log relationship to the normal distribution.

GLM analysis requires the specification of three model elements :

- Response distribution
- Link function
- Linear predictors

A common choice for the link function is the canonical link. The canonical link equates the location parameter of the exponential family, $\boldsymbol{\mu}$, to the linear predictor, $\mathbf{X}\boldsymbol{\beta}$. Table 2.1 below provides the canonical link function for several common exponential family distributions and the corresponding model parameters.

Table 2.1: Canonical Links for Commonly Used Exponential Family Distributions

Distribution	Canonical Link	Model
Normal	$\boldsymbol{\mu} = \mathbf{X}\boldsymbol{\beta}$	$\boldsymbol{\mu} = \mathbf{X}\boldsymbol{\beta}$
Poisson	$\log(\boldsymbol{\mu}) = \mathbf{X}\boldsymbol{\beta}$	$\boldsymbol{\mu} = \exp(\mathbf{X}\boldsymbol{\beta})$
Binomial	$\log\left(\frac{\mu_i}{1-\mu_i}\right) = \mathbf{x}_i^T\boldsymbol{\beta}$	$\mu_i = \frac{1}{1+exp(\mathbf{x}_i^T\boldsymbol{\beta})}$
Exponential	$\frac{1}{\mu_i} = \mathbf{x}_i^T\boldsymbol{\beta}$	$\mu_i = \frac{1}{\mathbf{x}_i^T\boldsymbol{\beta}}$

Many different procedures have been developed for estimating the model parameters of a GLM. Myers and Montgomery (1997) provide a discussion of iterative re-weighted least

squares which is equivalent to maximum likelihood procedures. Parameter testing and model inference can use one of three available tests, likelihood ratio test, score test, and Wald's Method. All three tests asymptotically follow a χ^2 distribution.

2.2.2 Linear Mixed Models (LMM)

A linear mixed model contains both random and fixed effects. The fixed effects model the mean of the data while the random effects control the structure of the variance-covariance matrix. Mixed modeling allows the analysis of complicated designs such as blocked designs, split plot designs and repeated measurement designs by selecting the appropriate fixed and random effects. McCulloch and Searle (2001) provide an in depth discussion on the analysis of linear mixed models.

Model and Analysis

Let $\mathbf{X}$ be the known model matrix for the fixed effects and $\boldsymbol{\beta}$ be the vector of fixed effects. Similarly, let $\mathbf{Z}$ be the known model matrix for the random effects and $\mathbf{u}$ be the vector of random effects. Then we can write:

$$E[\mathbf{y}|\mathbf{u}] = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{u} \tag{2.25}$$

for any realized value of the random vector, $\mathbf{u}$. However, because $\mathbf{u}$, is a random variable we must assign it probabilistic properties. The common assumption is $\mathbf{u} \sim N(\mathbf{0}, \mathbf{D})$, therefore

$E[\mathbf{u}] = \mathbf{0}$ and $Var(\mathbf{u}) = \mathbf{D}$. There is no loss of generality by assuming $E[\mathbf{u}] = \mathbf{0}$ because if the mean is actually different from zero the variable can be treated as both a fixed and random factor. The probabilistic assumption for $\mathbf{u}$ determines the distribution for $\mathbf{y}$. For example, suppose the response, $\mathbf{y}$, follows a normal distribution in a linear mixed model, and $\mathbf{u}$ follows a normal distribution($\mathbf{u} \sim N(\mathbf{0}, \mathbf{D})$),then

$$\mathbf{y} \sim N(\ \mathbf{X}\boldsymbol{\beta},\ \ \mathbf{ZDZ}^T + \mathbf{R}\ ) \tag{2.26}$$

where $\mathbf{R} = Var(\mathbf{y}|\mathbf{u})$. Note that the fixed effects only impact the mean and the random effects only impact the variance.

Maximum likelihood or restricted maximum likelihood (REML) are the most common methods used to find the parameter estimates. McCulloch and Searle (2001) provide a discussion of the differences between the two estimation methods and the merits of each method. REML takes the degrees of freedom for estimating the fixed effects into account. This especially important when the rank of $\mathbf{X}$ is large compared to the sample size. REML is also invariant to the levels of the fixed effects. It does not however estimate the fixed effects directly where maximum likelihood does. ANOVA estimation methods are also possible in select linear mixed models. ANOVA methods of estimation which were used historically are now seldom implemented because solutions are only available for limited cases of linear mixed models.

Split Plot Analysis - Example of a Linear Mixed Model

Vining, Kowalski and Montgomery (2005) discuss the need for split-plot structures in response surface designs when one or more hard to change factors are of interest. The split-plot design provides a practical solution for practitioners faced with time consuming setting changes that are necessary to implement a completely randomized design. Many researchers have implemented split-plot designs in industrial response surface experiments and mixture experiments including Bisgaard (2000), Cornell (1988) and Kowalski, Cornell and Vining (2002). Jones and Nachtsheim (2009) discuss the prevalence and importance of split-plot designs in the industrial experimentation.

Split-plot designs can be analyzed using a linear mixed model analysis. To use a linear mixed model to analyze a split-plot design the whole plot is treated as a random factor and a variance components covariance structure is placed on the random factor. Therefore,

$$\mathbf{D} = \begin{bmatrix} \sigma^2_{WP_1} & 0 & \dots & 0 \\ 0 & \sigma^2_{WP_2} & 0 \dots & 0 \\ \vdots & 0 & \ddots & 0 \\ 0 & \dots & 0 & \sigma^2_{WP_k} \end{bmatrix} \tag{2.27}$$

where k is the number of whole plots. This change to the variance-covariance structure of the response along with Satterthwaites approximation for degrees of freedom allows for the whole plot factor to be tested using the correct experimental error. Kowalski, Parker and

Vining (2007) provide an example as well as a tutorial for using split-plot designs.

2.2.3 Generalized Linear Mixed Models (GLMM) and Nonlinear Mixed Models (NLMM)

Model Specification GLMM

Generalized linear mixed models are a logical extension from generalized linear models and linear mixed models. In generalized linear mixed modeling random factors can be incorporated with non-normal responses. McCulloch and Searle outline the model specification for a generalized linear mixed model as:

$$y_i|\boldsymbol{\mu} \sim indep. f_{Y_i|\boldsymbol{\mu}}(y_i|\boldsymbol{\mu}) \tag{2.28}$$

where $f_{Y_i|\boldsymbol{\mu}}(y_i|\boldsymbol{\mu})$ is from the exponential distribution. Additionally, the conditional mean of y_i is given by:

$$E[y_i|\boldsymbol{\mu}] = \mu_i \tag{2.29}$$

and the link function relating the conditional mean to the fixed and random factors is given by:

$$g(\mu_i) = \mathbf{x}_i^T\boldsymbol{\beta} + \mathbf{z}_i^T\mathbf{u} \tag{2.30}$$

The model specification is complete by choosing a distribution for the responses and the random effects. McCulloch and Searle recommend maximum likelihood estimation for optimizing the likelihood function for a generalized linear mixed model. The likelihood function for any distribution is given by:

$$L(\boldsymbol{\beta}, \mathbf{u}) = \int \prod_{i=1} f_{1Y_i|\mathbf{U}}(y_i|\mathbf{u}) f_{2\mathbf{U}}(\mathbf{u}) d\mathbf{u} \tag{2.31}$$

Note the assumption here is that for a given value of the random variable the observations are independent, but they are not necessarily independent between different levels of the random factor. This allows for more complicated experimental error structures to be modeled.

McCulloch and Searle provide a very brief introduction to nonlinear mixed models. GLMMs are a subset of NLMM because NLMM allow the random effect to enter the model through any of the model parameters as opposed to just the mean. NLMM methodologies prove to be especially useful in this research because the mean of the Weibull distribution is a combination of two model parameters. Therefore, introducing the random effect through a model parameter, not the mean, is more intuitive for the Weibull distribution.

Computational Methods for Integration over the Random Effect

Numerical integration techniques have been substantially researched and applied to Generalized Linear Mixed Models (GLMMs) and Nonlinear Mixed Models (NLMMs). McCulloch and Searle provide many useful tips and ideas for computational methods for maximizing

the likelihood function with respect to the model parameters which is not a trivial task. A breif summary of the three primary techniques considered for this dissertation are covered in this literature review.

Brief Overview of Methods

There are three prominent methods for maximizing the likelihood of a NLMM: (1)Markov Chain Monte Carlo (MCMC) methods, (2)Quasi-likelihood inference; and (3)Numerical Quadrature. We discuss all three groups of techniques briefly here. Ultimately, Gauss-Hermite quadrature was chosen as the numerical integration method used in this research and the motivations for choosing this method are presented here.

Markov Chain Monte Carlo

MCMC methods can be used to stochastically converge on the MLE for NLMMs. McCulloch and Searle (2001) discuss several approaches for sampling from a difficult to calculate density. If MCMC methods are used to find the MLE of the Weibull distribution mixed model, one would want to use the Metropolis-Hastings sampling algorithm because of the unsymmetrical nature of the Weibull distribution. MCMC methods use random draws and acceptance criteria to make draws from the conditional NLMM distribution allowing us to stochastically converge on the MLE for the NLMM. A brief algorithm for implementing the M-H MCMC is outlined below.

Sample MCMC Algorithm:

1. Choose starting values for the fixed parameters and the variance.
2. Sample from the conditional distribution (Metropolis-Hastings step).
3. Update the parameters if you meet some acceptance criteria (defined by Metropolis).
4. Update step.

The algorithm repeats for a large number of steps (typically $N > 10,000$), then we remove the burn-in runs (up to 5000). The MLEs of the NLMM are found by averaging the values over the MCMC draws after the draws stabilize. There are many modifications that can be made to this algorithm to improve convergence including using expectation maximization (EM) in step 3 to update the parameters or using simulated annealing to prevent convergence of the algorithm on a local maximum instead of a global maximum.

This method was quickly ruled out for our application because it does not provide an approximate closed form solution of the log-likelihood. An important aspect of this research is the ability to make inferences on the parameter estimates of the Weibull distribution. We implement likelihood based inference methods which require a closed form approximation of the likelihood. MCMC methods, while simple to implement, avoid the evaluation of the integral over the random effect completely; therefore, they do not provide a ready method for performing inference on the MLEs.

Quasi-Likelihood Methods

Quasi-likelihood (QL) methods and their ability to obtain unbiased consistent estimates of the MLE are discussed in the literature in great detail including: Lin and Breslow (1996), Pinheiro and Bates (1995), Breslow and Lin (1995), and Breslow and Clayton (1993). QL methods approximate the likelihood using a Laplace approximation. The most common method discussed by Barndorff-Nielson and Cox (1989) expands the integrand using a Taylor series approximation. The Taylor series approximation is centered at the value of the random effect which maximizes the approximate log-likelihood. After applying the Taylor series approximation, QL applies a Laplace approximation to the approximate integrand. The Solomon-Cox approximation expands the integrand about the true mean of the random effect (zero), in a Maclaurin series as opposed to a Taylor series (Solomon and Cox, 1992).

Penalized-Quasi Likelihood (PQL) is similar to a quasi-likelihood function except a "penalty" is added to the likelihood approximations. The penalty term that Green (1987) and Breslow and Clayton (1993) subtract from the log-likelihood is: $u_i^2/(2\sigma_u)$. The penalty term prevents arbitrarily large values of the random effect from being selected. McCulloch and Searle (2001) refer to the penalty as a shrinkage effect. Much of the research comparing approximation methods focuses on PQL as opposed to quasi-likelihood.

PQL was seriously considered for our application of a NLMM where the responses follow a Weibull distribution. The mathematical details, however, for PQL methods do not work as well for the Weibull distribution as they do for exponential family distributions because a

closed form solution does not exist for the likelihood maximizing value of the random effect.

Numerical Quadrature

Gauss-Hermite quadrature is used when the random effect follows a normal distribution. If the random effect is non-normal, quadrature techniques are limited. Gauss-Hermite quadrature in discussed in detail and compared to PQL in the literature, see for example, Raudenbush, Yang and Yosef (2000) and Pinheiro and Bates (1995). Gauss-Hermite quadrature approximates the integral over the random effect in the likelihood as a weighted sum of the integrand at a specific number of evaluation points. Abramowitz and Stegun (1964) provide the tables of the quadrature points and corresponding weights. In recent years, however, these weights are calculated via mathematical software. The quadrature points are determined by the roots of the Hermite polynomials and the corresponding weights are given by the following:

$$w_k = \frac{2^{n-1} n! \sqrt{\pi}}{n^2 [H_{n-1}(x_k)]^2}$$

where $H_n(x)$ is a Hermite polynomial of degree n.

Gauss-Hermite quadrature was the other approximation seriously considered for the Weibull model with a random effect incorporated into the log-scale parameter, again because it provides a closed form solution of the approximate log-likelihood for inference. The mathematical details for this method are provided in Chapter 4 of the dissertation.

Additional Methods

There are other methods addressed in the literature for approximating the likelihood. They include: simulated maximum likelihood, which is discussed briefly by McCulloch and Searle (2001) as well as linearization methods which are implemented by SAS in PROC GLIMMIX. Additionally, there are more stochastic approximation algorithms available in addition to MCMC including genetic algorithms.

2.3 Design of Experiments for Lifetime Data

2.3.1 Lifetime Data Designs

The following criteria provide a framework for discussing planning issues for life tests:

- How many units should you test?
- How long should you run the test?

In lifetime data experimental designs, key requirements for assessing the above criteria are prior values (or planning values) for μ and β to get a ballpark idea of the distribution shape. These values should be based on the knowledge of the engineer or scientist that works with the units to be tested. The literature implements two different approaches for calculating sample sizes for life tests: Monte Carlo simulation and large sample variance approximations for maximum likelihood estimators.

The following pseudo code outlines a Monte Carlo for calculating sample sizes:

- Use the planning values of the μ and β and the corresponding distribution to simulate data for a given sample size
- Analyze the data and construct standard errors and confidence intervals to assess precision
- Repeat with several different distribution choices and planning values for μ and β
- Repeat the whole process with different sample sizes to gauge actual sample size and test length requirements

From this Monte Carlo simulation, one will be able to select a test length and sample size to achieve the desired precision.

The large sample variance approximation is another method for calculating sample size for life tests. The large sample variance approximations are convenient for determining sample size because they allow for a closed form relationship relating sample size to the precision of the estimates. The large sample variance approximation method can also be easily adapted through use of the delta method so that the sample size calculation be done to minimize the standard error for some function of μ and β, for example the estimation of the p^{th} percentile, which is often of practical interest. The information matrix for the large sample variance approximation is presented in Section 2.1.1 and given by Equation 2.13.

2.3.2 Accelerated Life Test Plans

Planning accelerated life tests require many more decisions and assumptions than planning life tests do. A key idea behind planning accelerated life tests is that often they need to be completed within tight time and cost constraints. Another key idea behind accelerated life tests is that they should always minimize the amount of extrapolation necessary from the life test levels of the accelerating variables to the use levels of the accelerating variables.

Again, in planning accelerated life tests certain information is necessary to make educated choices about the life test design. This planning information includes the expected distribution that the failures follow, planning values for μ and β, and the accelerating relationship between failure times and the accelerating variable.

Planning Accelerated Life Tests for One Accelerating Variable

To specify an accelerated life test with one accelerating variable one must specify:

- The feasible range of the accelerating variable: $[x_U, x_H]$, where x_U is the usage level of the accelerating variable and x_H is the highest level where the accelerating relationship holds for the accelerating variable.
- The total number of units available for the accelerated life test: n
- The number of levels of the accelerating variable
- The allocation of the total number of units to each of the levels of the accelerating

variable.

Again, Monte Carlo simulation or large sample variance approximations are useful in planning the accelerated life test. These two methods determine the allocation of the units to different levels of the accelerating variable.

Meeker and Escobar provide a brief discussion of statistically optimum plans which choose the levels of the accelerating variable and corresponding unit allocation to minimize variance of the maximum likelihood estimates. Statistically optimum plans can be based on several different planning criteria. Two common criteria are minimizing the standard error for a particular percentile or minimizing the determinant of the Fisher information matrix, $I_{\boldsymbol{\theta}}$. However, these plans often fail to meet practical constraints of accelerated life tests.

Meeker and Escobar (1998) make some general recommendations for accelerated life test plans that are not necessarily statistically optimum but preserve some of the design recommendations of statistically optimum plans. Their recommendations include:

- Use insurance units. Insurance units are not expected to fail because they are run at the expected use levels of the accelerating variable. Insurance units are used to check for other possible failure modes.
- Use three or four levels of the accelerating variable (this way if one level has problems there are still two or three levels left for the regression analysis)
  - Possible problems are:

    - A particular level ends up having no failures in the test
    - A level fails to follow the accelerating relationship

- Choose the lowest level of the accelerating variable subject to the constraint of seeing four or five failures to help protect against the possibility of having no failures.
- Allocate a higher percentage of units to lower levels of the accelerating variable to account for the fact that fewer will failures will occur at lower levels of the accelerating variable

Planning Accelerated Life Tests for Two Accelerating Variables

Meeker and Escobar provide a discussion of planning accelerating life tests for two accelerating variables. For planning an accelerated life test in two explanatory variables, planning values of the parameters guide the planning process.

Three types of test plans are present in the literature for two explanatory variables:

1. Test all units at normal use level conditions
    - This is only a feasible test plan if the goal is to predict a relatively low failure percentile and the probability of failure for a particular unit is high
2. Test at two or more combinations of the variable levels along a line that passes through the use conditions and the maximum conditions for each of the accelerating factor
    - This test plan does not allow for the full specification of the regression model

3. Test at three or more non-collinear combinations of the experimental variables.

The third test plan allows for the full specification of the regression model, which makes it the best test plan to implement; however, the first two test plans can provide valuable information, especially in a pilot study.

Planning Accelerated Life Tests in More than Two Variables

Accelerated life tests for more than two accelerating variables require complicated accelerating relationship and well as design plans. Meeker and Escobar advocated using traditional design of experiments designs for these types of accelerated life tests including the factorial design.

2.3.3 Response Surface Designs

Response surface designs are very popular in an industrial setting because they seek to optimize the response using small sample sizes. A first order design is the first step in the sequential RSM process. The common first order designs are the full factorial, 2^k, and the fractional factorial, 2^{k-p}, designs. These designs are presented in great detail in Myers and Montgomery (2002). Myers and Montgomery also provide many other RSM designs including Box-Behnken, Plackett-Burman, and central composite designs (CCDs).

Hamada (1995) discusses using several common response surface designs in reliability experiments. These designs include full factorial designs, fractional factorial designs and the

Box-Behnken design. He uses the maximum likelihood methodologies outlined in Section 2.1 to analyze the data obtained in these experiments. However, in several of the designs replication is present. Hamada fails to discuss whether the replicates are true replicates or if they are observational units. He treats all of the experimental errors as independent and identically distributed despite the fact that in a few of the experiments it is highly unlikely that pure replication occurred. This is great area for improvement in the current reliability data analysis methodologies as very little attention has been focused on correctly modeling experimental error versus modeling observational error.

McCool (1996) and McCool and Baran (1999) have also looked at estimating the parameters for a Weibull distribution for designed experiments. They focus on 2^2 factorial experiments, which are common response surface designs. McCool and Baran provided an analysis that begins to take the experimental design into account in their paper by fitting four different Weibull distributions using maximum likelihood estimation to each level of the 2^2 factorial experiment. This approach however does not fully incorporate the data into one model or provide a methodology for testing the significance of the factorial experiment parameters.

2.4 Literature Review Summary

This literature review covered many seemingly disjoint topics ranging from current methods of lifetime data analysis, to generalized linear mixed modeling. The goal of this research is to combine the well developed statistical techniques of GLMMs and NLMMs with reliability

data analysis. An area of concern in this research is the proper modeling of experimental error and observational error for the complicated designs that are commonly used in reliability data analysis. Another key issue is censoring. Censored data is nearly impossible to avoid when dealing with reliability data and needs to be accounted for in both the experimental design and the experimental analysis. Another important consideration for this research is the correlation between the parameters of the Weibull parameters noted by many reliability researchers. The next two chapters provide two new analysis methods based in the foundation of this literature review.

Chapter 3

Two-Stage Analysis Solution

3.1 Introduction and Current Modeling Approach

This chapter presents a two-stage analysis method that utilizes current statistical theory to analyze reliability data. This new proposed method is nice because it provides a statistically straightforward approach to handling complicated design structures. The analysis methods presented in this chapter utilize the maximum likelihood approach for analyzing reliability data applied to the Weibull distribution. The current modeling approach is first presented as a means of comparison for a new modeling approach that is presented second. The general form of the likelihood function is:

$$L(\beta, \mu) = \prod_{i=1}^{N} [f(t_i)] \tag{3.1}$$

where $f(t_i)$ is the probability density function (PDF) for the Weibull distribution. A key assumption in the derivation of this likelihood function is that the N observations are independent. We compute the log-likelihood to find:

$$\ell(\beta, \mu) = \sum_{i=1}^{N} \log\left[f(t_i)\right] \tag{3.2}$$

In reliability analysis a common goal is to determine the impact of experimental factors on product lifetime, most approaches focus on the best method for modeling the impact of the experimental factors is through the scale parameter. Therefore, the log of the PDF for the Weibull distribution, incorporating the dependance of the scale parameter on the experimental factors, can be expressed as:

$$log\left[f(t_i)\right] = \log\left(\frac{\beta}{t_i}\right) + z_i - \exp(z_i) \tag{3.3}$$

where $z_i = \beta\left[\log(t_i) - \mu_i\right]$, $\mu_i = \log(\eta_i) = \boldsymbol{x}_i^T\boldsymbol{\gamma}$, and $\boldsymbol{x}_i^T$ is the 1 x p vector of experimental factors for a given experimental run. Plugging the PDF for the Weibull Distribution into the log-likelihood we find the final form for the log-likelihood:

$$\ell(\beta, \gamma) = \sum_{i=1}^{N} \left[\log\left(\frac{\beta}{t_i}\right) + z_i - \exp(z_i)\right] \tag{3.4}$$

This log-likelihood function can then be maximized with respect to β and $\boldsymbol{\gamma}$ to obtain the

maximum likelihood estimates.

If the data contain right censoring, the log-likelihood for the Weibull distribution reduces to:

$$\ell(\beta,\gamma) = \sum_{i=1}^{N} \delta_i \left[\log\left(\frac{\beta}{t_i}\right) + z_i \right] - \exp(z_i) \tag{3.5}$$

This likelihood is then maximized with respect to β and $\boldsymbol{\gamma}$. This method is implemented in many statistical packages including Minitab, which is used in this paper in an illustrative example. Note that an important assumption that for both the uncensored and right censored likelihood derivations is that the observations are independent, therefore the treatments must be randomly applied to each test unit for this assumption to hold true.

3.2 New Modeling Approach

Our modeling approach is based on two fundamental concepts in design of experiments (DOE), experimental units and observational units. The experimental unit is the smallest unit to which the treatment is applied. The observational unit is the unit where the measurement is taken. A common design protocol in reliability experiments is to place n items on a a test stand and apply a given treatment combination to the test stand. For example, consider a temperature-humidity chamber which is used to test the shelf life of food products. The chamber holds n units. Suppose a food science engineer is interested in the impact of different temperature and humidity settings on the shelf life of chips. He places n bags

of chips in m different chambers and selects a temperature and humidity setting for each chamber. In this experiment the chamber is the experimental unit, and the bags of chips are the observational units. The total sample size is $N = nm$.

Experimental units and observational units are important concepts from DOE because they provide the basis for calculating experimental error correctly. The experimental units provide the basis for estimating the experimental error, which is the appropriate basis for all inference involving the experimental factors. The observational error contributes to the experimental error but only in part and, therefore, does not provide an appropriate basis for inferential procedures. The impact of confusing the observational units with the experimental units is manifold. First, if we treat the observational units as experimental units in the design described above we will be calculating the experimental error incorrectly which directly impacts standard error of the parameter estimates and all inferences made in the statistical analysis. Second, we will be overstating our true degrees of freedom. Therefore, when we make inferences about the significance of the experimental factors, we use an error term that is too small and overstate the significance of the factor. Additionally, this error is transmitted to the shape parameter estimate of the lifetime distribution because we are failing to model the experimental error correctly. If the experiment is looking purely at accelerating factors then the parameter estimates at the accelerated conditions will impact the predicted performance at use conditions.

The model we propose is a two-stage model that is a simple first approach to account for the experimental error correctly. This model assumes that there are n items placed on m

different test stands. Each treatment combination is applied to the test stand, and the measurements are made on each of the n items. The assumptions underlying the model are:

- The lifetimes for the individual units within a test stand follow a Weibull distribution.
- The failure mechanism for each treatment combination is the same (i.e. β is constant across test stands).
- The impact of the treatments is realized through the scale parameter.
- The test stands are independent.
- The experimental variability between the scale parameters for each treatment combination is lognormal.

3.2.1 Stage 1 Model: The model within an experimental unit:

Let t_{ij} be the observed lifetime for the j^{th} item within the i^{th} test stand. The failure times follow a Weibull distribution within a test stand, therefore:

$$f\left(t_{ij}\right) = \frac{\beta}{\eta_i}\left(\frac{t_{ij}}{\eta_i}\right)^{\beta-1} e^{-\left(\frac{t_{ij}}{\eta_i}\right)^{\beta}} \tag{3.6}$$

for a given test stand. Here $\beta > 0$ is the constant shape parameter and η_i is the scale parameter for test stand i. It can be shown that if t_{ij} follows a Weibull distribution, then the likelihood for given test stand where all of the n items fail is:

$$\mathcal{L}(\beta, \mu_i) = \prod_{j=1}^{n} f(t_{ij}) \tag{3.7}$$

We can find the MLEs for β and the η_i's by maximizing the joint log-likelihood over all m test stands. The log-likelihood over the m test stands for uncensored data is:

$$\ell(\beta, \mu_1, \ldots, \mu_m) = \sum_{i=1}^{m} \sum_{j=1}^{n} \left(\log\left(\frac{\beta}{t_{ij}}\right) + z_{ij} - e^{z_{ij}} \right) \tag{3.8}$$

where $z_{ij} = \beta\left[log(t_{ij}) - \mu_i\right]$ and $\mu_i = \log(\eta_i)$.

Right censoring can also be easily incorporated into the likelihood function. The likelihood for an individual test stand with right censoring present is:

$$\mathcal{L}(\beta, \mu_i) = \mathcal{C} \prod_{j=1}^{n} \left[f(t_{ij})\right]^{\delta_{ij}} \left[1 - F(t_{ij})\right]^{1-\delta_{ij}} \tag{3.9}$$

where $\delta_{ij} = 1$ if the item fails and $\delta_{ij} = 0$ if the item is censored. Again, $\mathcal{C}$ is a constant dependent on the type of censoring but can be take as $\mathcal{C} = 1$ when calculating maximum likelihood estimates. The joint log-likelihood for data with right censoring then becomes:

$$\ell(\beta, \mu_1, \ldots, \mu_m) = \sum_{i=1}^{m} \sum_{j=1}^{n} \left(\delta_{ij} \log\left(\frac{\beta}{t_{ij}}\right) + \delta_{ij} z_{ij} - e^{z_{ij}} \right) \tag{3.10}$$

The first stage in the analysis results in the MLE for the common shape parameter, β and

m MLEs for the scale parameter for each test stand. Additionally, under certain regularity conditions, an asymptotic variance-covariance matrix can be derived for the maximum likelihood estimates. Meeker and Escobar (1998) note that the Weibull distribution meets these regularity conditions. The estimated covariance matrix for the maximum likelihood estimates is:

$$\begin{aligned}\hat{\Sigma}_{\hat{\theta}} &= \begin{bmatrix} \widehat{Var}(\hat{\beta}) & \widehat{Cov}(\hat{\beta},\hat{\mu}_1) & \dots & \widehat{Cov}(\hat{\beta},\hat{\mu}_m) \\ \widehat{Cov}(\hat{\beta},\hat{\mu}_1) & \widehat{Var}(\hat{\mu}_1) & & \vdots \\ \vdots & & \ddots & \widehat{Cov}(\hat{\mu}_{m-1},\hat{\mu}_m) \\ \widehat{Cov}(\hat{\beta},\hat{\mu}_m) & \dots & \widehat{Cov}(\hat{\mu}_m,\hat{\mu}_{m-1}) & \widehat{Var}(\hat{\mu}_m) \end{bmatrix} \\ &= \begin{bmatrix} -\frac{\partial^2\ell(\beta,\mu_1,\dots,\mu_m)}{\partial\beta^2} & -\frac{\partial^2\ell(\beta,\mu_1,\dots,\mu_m)}{\partial\beta\partial\mu_1} & \dots & -\frac{\partial^2\ell(\beta,\mu_1,\dots,\mu_m)}{\partial\beta\partial\mu_m} \\ -\frac{\partial^2\ell(\beta,\mu_1,\dots,\mu_m)}{\partial\beta\partial\mu_1} & -\frac{\partial^2\ell(\beta,\mu_1,\dots,\mu_m)}{\partial\mu_1^2} & & \vdots \\ \vdots & & \ddots & -\frac{\partial^2\ell(\beta,\mu_1,\dots,\mu_m)}{\partial\mu_{m-1}\partial\mu_m} \\ -\frac{\partial^2\ell(\beta,\mu_1,\dots,\mu_m)}{\partial\beta\partial\mu_m} & \dots & -\frac{\partial^2\ell(\beta,\mu_1,\dots,\mu_m)}{\partial\mu_m\partial\mu_{m-1}} & -\frac{\partial^2\ell(\beta,\mu_1,\dots,\mu_m)}{\partial\mu_m^2} \end{bmatrix}^{-1} \end{aligned} \tag{3.11}$$

From the log-likelihood it can be shown that:

$$-\frac{\partial^2\ell(\beta,\mu_1,\dots,\mu_m)}{\partial\beta^2} = \sum_{i=1}^{m}\sum_{j=1}^{n}\left[\frac{\delta_{ij}}{\beta^2} + \left(\frac{z_{ij}}{\beta}\right)^2 \exp(z_{ij})\right] \tag{3.12}$$

$$-\frac{\partial^2 \ell(\beta, \mu_1, \ldots, \mu_m)}{\partial \beta \partial \mu_i} = -\sum_{j=1}^{n} \left(2\frac{z_{ij}}{\beta} \exp(z_{ij}) \right) \tag{3.13}$$

$$-\frac{\partial^2 \ell(\beta, \mu_1, \ldots, \mu_m)}{\partial \mu_i^2} = \sum_{j=1}^{n} \left(\beta^2 \exp(z_{ij}) \right) \tag{3.14}$$

Additionally, the 2^{nd} derivatives between all pairs of μ_i and μ_j are zero. This variance matrix will be used in the second stage of the model. These equations for the estimated variance matrix hold true for both uncensored and censored data if you note that $\delta_{ij} = 1$ for all points in the uncensored data case.

3.2.2 Stage 2 Model: The model between experimental units:

After obtaining the estimates for the shape parameter and the scale parameters and their corresponding variances for each experimental unit, the next step is to model the estimates of the scale parameters as a linear function of the treatments. An appropriate second stage model that accounts for the variances on the scale parameter estimates is a weight least squares model. The second stage model is:

$$\hat{\boldsymbol{\mu}} = \boldsymbol{X}\boldsymbol{\theta} + \boldsymbol{\epsilon} \tag{3.15}$$

where $\boldsymbol{X}$ is the matrix containing the treatment levels of the factors, $\boldsymbol{\theta}$ are the corre-

sponding coefficients that relate the treatment levels to the log of the scale parameter and $\boldsymbol{\epsilon} \sim MVN(\mathbf{0}, \mathbf{V})$, where the variance matrix, $\mathbf{V}$, accounts for the scale parameter variance estimates. Since this variance matrix is near diagonal a reasonable assumption is to use $\mathbf{V} =< \widehat{Var}\,(\hat{\mu}_i) >$ and then parameter estimates are given by the normal solution for weighted regression model:

$$\hat{\boldsymbol{\theta}} = \left(\mathbf{X}^T\mathbf{V}^{-1}\mathbf{X}\right)^{-1}\mathbf{X}^T\mathbf{V}^{-1}\hat{\boldsymbol{\mu}} \tag{3.16}$$

The big advantage to this approach is that you can correctly model the experimental error in current statistical packages that have the ability to fit lifetime distribution and linear models.

3.3 Percentile Predictions

A quality of interest to industrial statisticians is the prediction of the failure percentiles. Calculating the percentiles provides us with a practical implication to base the comparison between the old method and our newly proposed method. The MLE for the p^{th} percentile is:

$$\hat{t}_{p_i} = \exp\left[\hat{\mu}_i + \frac{\Phi^{-1}_{SEV}(p)}{\hat{\beta}}\right] \tag{3.17}$$

where $\Phi_{SEV}(p)$ is the inverse CDF for the smallest extreme value distribution and $\mu_i = \log(\eta_i) = \boldsymbol{x}_i^T\boldsymbol{\gamma}$. In addition, to calculating the predicted percentiles it is often useful to have bounds on these percentiles for practical implications. The normal approximation confidence interval based on Wald's Method for t_p is:

$$100(1-\alpha)\%CI = \left[\hat{t}_p/w, \quad w\hat{t}_p \right] \tag{3.18}$$

where, $w = \exp\left(z_{1-\frac{\alpha}{2}} \frac{\hat{s.e.}(\hat{t}_p)}{\hat{t}_p}\right)$. The standard error of $\hat{t}_p$ can be estimated using the multivariate delta method and is:

$$\hat{s.e.}(\hat{t}_p) = \hat{t}_p \left[\widehat{Var}(\hat{\mu}) - \frac{2\Phi_{SEV}^{-1}(p)}{\beta^2}\widehat{Cov}(\hat{\mu},\hat{\beta}) + \left[\frac{\Phi_{SEV}^{-1}(p)}{\beta^2}\right]^2 \widehat{Var}(\hat{\beta}) \right]^{1/2} \tag{3.19}$$

The variance and covariance for $\hat{\mu}$ and $\hat{\beta}$ come from straightforward functions from the estimated variance matrix based on the inverse Fisher's Information matrix for $\boldsymbol{\gamma}$ and β. For example, if $\mu_i = log(\eta_i) = \gamma_0 + \gamma_1 x_{1i} + \gamma_2 x_{2i}$, then:

$$\widehat{Var}(\hat{\mu}) = \widehat{Var}(\hat{\gamma}_0) + x_1^2\widehat{Var}(\hat{\gamma}_1) + x_2^2\widehat{Var}(\hat{\gamma}_2) + 2x_1\widehat{Cov}(\hat{\gamma}_0,\hat{\gamma}_1) + 2x_2\widehat{Cov}(\hat{\gamma}_0,\hat{\gamma}_2) + 2x_1x_2\widehat{Cov}(\hat{\gamma}_1,\hat{\gamma}_2)$$

$$\widehat{Cov}(\hat{\mu},\hat{\beta}) = \widehat{Cov}(\hat{\gamma}_0,\hat{\beta}) + x_1\widehat{Cov}(\hat{\gamma}_1,\hat{\beta}) + x_2\widehat{Cov}(\hat{\gamma}_2,\hat{\beta})$$

For the new two-stage analysis proposed in this paper it is easy to modify this expression

for t_p to calculate the estimated percentiles:

$$\hat{t}_{p_i} = \exp\left[\boldsymbol{x}_i^T\hat{\boldsymbol{\theta}} + \frac{\Phi_{SEV}^{-1}(p)}{\hat{\beta}}\right] \tag{3.20}$$

The confidence interval is again given by Equation 3.18 and the standard error is given by Equation 3.19. However, the calculation of the values for the Fisher Information matrix here is not possible because the estimates come from two completely disjoint likelihood functions. This is a major disadvantage of the two stage approach because only inferences on the parameters of the distribution are possible.

3.4 Illustrative Example

Zelen (1959) discusses a factorial experiment designed to determine the effect of voltage and temperature on the lifespan of a glass capacitor. Zelen describes the experimental setup as "n components are simultaneously placed on test." This experimental setup provides a perfect data set to compare the traditional reliability analysis to the proposed analysis, which accounts for the experimental protocol. Table 3.1 summarizes the data from the experiment.

Zelen uses two different temperature settings and four different voltages in the experiment for a total of 8 treatment combinations. Each treatment combination is applied to only one test stand, making this an unreplicated experiment from a DOE perspective. Eight capacitors are tested on each test stand, and Zelen uses Type II censoring after the first four failures.

Table 3.1: Life Test Results of Capacitors, Adapted from Zelen (1959)

	Applied Voltage			
Temperature	200 (Volts)	250 (Volts)	300 (Volts)	350 (Volts)
170°C	439	572	315	258
	904	690	315	258
	1092	904	439	347
	1105	1090	628	588
180°C	959	216	241	241
	1065	315	315	241
	1065	455	332	435
	1087	473	380	455

3.4.1 Results: Traditional Analysis

Meeker and Escboar (1998, page 447-450) provide the traditional reliability analysis for the Zelen data, which are summarized in Table 3.2 using Minitab's Lifetime data analysis function. Note that in this analysis, the estimate of the shape parameter is $\hat{\beta} = 2.75$. The analysis indicates that voltage and temperature both have a significant impact on the scale parameter and therefore the lifetime of the glass capacitor.

Table 3.2: Independent Analysis for Life-test on Glass Capacitors, Adapted from Meeker and Escobar (1998)

Regression Table

		Standard			95.0% Normal CI	
Predictor	Coef	Error	Z	P	Lower	Upper
Intercept	13.4070	2.29584	5.84	0.000	8.90726	17.9068
Voltage	-0.0059108	0.0010398	-5.68	0.000	-0.0079488	-0.0038729
Temperature	-0.0289047	0.0128970	-2.24	0.025	-0.0541822	-0.0036271
Shape	2.74869	0.418739			2.03917	3.70509

Log-Likelihood = -244.242

3.4.2 Results: New Proposed Two-Stage Analysis

The analysis we propose in this paper takes into account each observation is not independent with a two step process. The first step finds the Weibull distribution MLEs of the constant shape parameter and eight different scale parameters, one for each test stand. The second step models the log transform of the 8 different estimated scale parameters using a weighted regression model where the experimental error terms are given by the asymptotic experimental error derived in the first step for the log-scale parameters.

The results from Minitab estimating the eight different scale parameters are presented below in Table 3.3. The estimate of the shape parameter for the new two-stage analysis is $\hat{\beta}_{New} = 3.62$. This is a dramatically different estimate from the shape parameter estimate in the traditional reliability analysis. In the traditional analysis the constant shape parameter is estimated as $\hat{\beta}_{Trad.} = 2.75$. This difference in the shape parameter estimate is the first practical implication of taking the experimental design into account.

Table 3.3: Stage One Analysis Results for New Two-Stage Analysis for Life-test on Glass Capacitors

Voltage	Temperature	$\hat{\eta}$	$\hat{\mu}_i = \log(\hat{\eta}_i)$	$\hat{Var}(\hat{\mu}_i)$
200	170	1262.35	7.141	0.1387
200	180	1292.78	7.165	0.1390
250	170	1207.58	7.096	0.1386
250	180	532.85	6.278	0.1387
300	170	683.61	6.527	0.1385
300	180	431.04	6.066	0.1388
350	170	633.86	6.452	0.1384
350	180	510.10	6.235	0.1386

The second step of our proposed new analysis models the resulting MLEs for the μ_i's using a weighted regression model where the weights are determined by the asymptotic variances from the first step of this model. The second stage of this analysis can be done in any standard statistical package. Note that the variance estimates on the different μ_i are essentially equal in Table 3.3. This is a nice result because in the second stage of the model, using a weighted regression is essentially equivalent to standard least squares regression, further simplifying this two stage analysis method. This is the case because we have assumed a constant shape parameter, β, and the shape parameter is the driving parameter in the Fisher Information matrix calculations for the variances on the scale parameters, see Equation 3.12. The results from running the analysis in Minitab are displayed in Table 3.4.

Table 3.4: Stage Two Analysis Results for New Two-Stage Analysis for Life-test on Glass Capacitors

Regression Table

Predictor	Coef	SE Coef	T	P
Constant	14.613	3.249	4.50	0.006
Voltage	-0.005638	0.001644	-3.43	0.019
Temperature	-0.03682	0.01838	-2.00	0.102

S = 0.0359013 R-Sq = 75.9% R-Sq(adj) = 66.3%

Several practical differences emerge comparing the results of the new analysis back to the traditional analysis. The standard errors of the coefficients are all smaller in the traditional analysis. This is because we were overstating the true experimental degrees of freedom by treating each observation as an independent data point. The increase in standard error

Table 3.5: Independent Analysis Percentile Predictions and Confidence Intervals for Life-test on Glass Capacitors

Voltage (Volts)	Temperature (°C)	Independent Analysis Estimates			
		$t_{.01}$	$t_{.05}$	$t_{.10}$	$t_{.50}$
200	170	280.8 [246.6, 319.6]	508.0 [475.7, 542.4]	660.1 [629.5, 692.2]	1309.9 [1271.7, 1349.3]
200	180	210.3 [184.5, 239.6]	380.5 [356.5, 406.1]	494.4 [472.0, 517.9]	981.1 [955.1, 1007.8]
250	170	208.9 [185.4, 235.4]	378.0 [357.8, 399.4]	491.2 [473.5, 509.5]	974.8 [957.3, 992.6]
250	180	156.5 [138.5, 176.8]	283.1 [267.7, 299.5]	367.9 [354.4, 381.8]	730.1 [717.6, 742.7]
300	170	155.5 [137.9, 175.3]	281.3 [266.3, 297.1]	365.5 [352.5, 379.0]	725.3 [713.0, 737.9]
300	180	116.4 [102.8, 131.8]	210.7 [198.8, 223.2]	273.8 [263.4, 284.5]	543.3 [533.6, 553.1]
350	170	115.7 [101.5, 131.9]	209.3 [196.1, 223.4]	272.0 [259.6, 284.9]	539.7 [525.4, 554.5]
350	180	86.6 [75.6, 99.4]	156.8 [146.2, 168.2	203.7 [193.6, 214.3]	404.3 [392.5, 416.3]

results in the temperature not being a significant factor at $\alpha = 0.05$ level for the new analysis. Additionally, the estimates of the shape parameter are dramatically different between the two analysis methods. The coefficient estimates for the linear relationship between the log-scale parameter and temperature and pressure are also slightly different.

3.4.3 Impact on Percentile Estimation

The following tables compare the 1^{st}, 5^{th}, 10^{th} and 50^{th} percentiles. To provide a fair means of comparison, for both percentile estimates we use temperature and voltage as predictors of the scale parameter, even though temperature is not significant at the $\alpha = 0.05$ level for the new analysis. In Table 3.5 the percentile estimates and their corresponding Wald confidence intervals are displayed for the traditional maximum likelihood analysis.

Table 3.6: New Two-Stage Analysis Percentile Predictions for Zelen Data

Voltage (Volts)	Temperature (°C)	Independent Analysis Estimates			
		$t_{.01}$	$t_{.05}$	$t_{.10}$	$t_{.50}$
200	170	385.79	605.19	738.32	1242.35
200	180	266.96	418.78	510.90	859.68
250	170	291.02	456.52	556.95	937.16
250	180	201.38	315.90	385.40	648.50
300	170	219.53	344.38	420.14	706.95
300	180	151.91	238.30	290.73	489.19
350	170	165.60	259.78	316.93	533.29
350	180	114.59	179.76	219.31	369.02

In Table 3.6 the percentile predictions for the new analysis are given. The percentiles for the new analysis predict fewer failures early on, that is the first through the tenth percentiles have later predicted times. The fiftieth percentile however, occurs earlier for the new analysis. These changes in the percentile predictions make clear the impact of the change in the shape parameter estimate. Confidence intervals are not available because the inverse of the information matrix does not exist. In comparing the percentile estimates for the new method back to the confidence bounds, one can see that the percentile estimates are significantly different between the two methods. These differences are driven by the different shape parameter estimates for the two methods.

3.5 Conclusions from Two Stage Model Solution

This proposed methodology is just a first, naive approach to trying to combine the experimental protocol with reliability data analysis. The goal of this chapter was to illustrate that the experimental design has a nontrivial impact on the conclusions drawn when modeling

lifetime data with a Weibull distribution. The first implication is that we fail to correctly calculate the experimental error term if we base the experimental error on the observational units instead of the experimental units. This miscalculation will result in a lower experimental error because variation between observational units is inherently lower than between experimental units. Furthermore, if we incorrectly treat observational units as experimental units, we overstate the degrees of freedom for experimental error. The other important impact of fitting the correct model to the experimental setup is that this translates into the shape parameter estimate. In the example presented in this chapter, the shape parameter dramatically shifted between the two analysis methods, which for a practitioner could lead to dramatically different conclusions about the failure mechanism to which a product succumbs.

There is a good deal of room for improvement with this analysis method. This new approach is designed for a practitioner to be able to use now. In fact, the proposed analysis can already be done in the current version of Minitab and other common statistical packages. The only complicating factor is that the asymptotic variances need to be calculated by hand and then entered into Minitab. In the example presented in this chapter however, the variances are essentially equal and therefore do not impact the estimation and the full analysis can be done directly in current software packages. A clear next step in this research is to fully combine the estimation into a joint likelihood. This two step model is easy to implement but is most like not the optimum way to model the data. A joint likelihood approach for β and η_i's would mostly likely result in more precise estimates of the parameters. Additionally, a joint

likelihood approach would provide the ability to perform likelihood based inferences on not just the parameters but also functions of the parameters.

Chapter 4

Nonlinear Mixed Model Analysis

4.1 Introduction

Random effects arise from many DOE choices; these choices include sub-sampling, clustered data, random selection of the treatment levels, and blocking. It is important to have an analysis methodology that can properly handle these different experimental designs for life data. This chapter presents a new maximum likelihood analysis method to incorporate random effects into the analysis of life test data from a sub-sampling experimental design. We implement our new analysis method on the Zelen data and run a simulation study to further investigate the implications of properly including random effects in the data analysis.

Feiveson and Kulkarni (2000) note the need to incorporate a random effect into the model when batch effects are present in the data. Their data, originally from Gerstle and Kunz

(1983), measures burst times for Kevlar fiber strands at accelerated stress levels. The fiber strands encase pressure vessels on the Space Shuttle, and therefore, their reliability is of paramount importance. The strands are manufactured in spools, which result in a batch effect based on the spool. Feiveson and Kulkarni emphasize the need for modeling the batch effect as a random effect because there are only eight spools tested in the experiment; yet, the space shuttle pressure vessels could have fiber strands from any number of manufactured spools. They incorporate random effects through a stratified least squares approach.

Leon, Ramachandran, Ashby, and Thyagarajan (2007) also note the need for random effects in accelerated life tests of fiber strands that come from different batches. They also use data from Gerstle and Kunz (1983) to justify their model. They propose a Bayesian modeling approach for incorporating the random spool effect and conclude that the random model results in "better" estimates and predictions than the corresponding model that treats the spool as a fixed effect. They also note that both the fixed and random effect models result in a practically different estimate of the Weibull shape parameter than if the analysis ignores the batch completely. The lesson they highlight is that ignoring a vital parameter, such as spool in their case, results in bias of the shape parameter.

Leon, Li, Guess and Sawhney (2009) conduct a simulation study based on the same fiber strand data. They use the Bayesian modeling methods developed by Leon et. al (2007). They conclude that ignoring the batch effect results in overly precise estimates of quantiles and probabilities of failures.

In Chapter 3 of the dissertation, we propose a naive method to take into account the ex-

perimental protocol for a sub-sampling DOE through a two-stage analysis method. While this method is simple and straightforward to implement, it is flawed in that there is no joint likelihood, and therefore, inferences on functions of the parameters are not possible. Additionally, this two-stage method is susceptible to bias in the estimate of the shape parameter and it is limited to the sub-sampling experimental design. The method proposed in this chapter addresses the joint likelihood problem from Chapter 3 by incorporating a random effect into the model.

4.2 Nonlinear Mixed Model Methodology

4.2.1 Model

We propose a frequentist model for incorporating the random effects into the failure time model. Our specification assumes that the random effect is due to sub-sampling, but this approach is easily adaptable to the Gerstle and Kunz (1983) data, where the random effect is due to a batch effect.

One commonly incorporates random effects into a model in one of two ways; through the mean response or through the model parameters. Generalized linear mixed models (GLMMs) use the first method. Nonlinear mixed models (NLMM) are more flexible and transmit the random effect through model parameters. For the Weibull distribution, a common assumption is that all model terms (treatments, blocks, etc.) enter through a linear relationship with

the log-scale parameter. Therefore, we are using the NLMM framework for incorporating a random effect. McCulloch and Searle (2001, 286-290) provide a general outline of NLMM.

If we have $i = 1, \ldots, m$ independent experimental units and $j = 1, \ldots, n_i$ sub-samples or observational units per experimental unit, we can specify our nonlinear mixed model for the Weibull distribution with sub-sampling as:

$$\begin{aligned} t_{ij}|u_i &\sim Indep.\, Weib(\beta, \eta_i) \\ F_1(t_{ij}|\beta, \eta_i, u_i) &= 1 - exp\left[-\left(\frac{t_{ij}}{\eta_i}\right)^{\beta}\right] \\ \log(\eta_i) = \mu_i &= \boldsymbol{x}_i^T\boldsymbol{\theta} + u_i \\ f_2(u_i) &\sim iid\ N\ (0, \sigma_u^2) \end{aligned}$$

where $\boldsymbol{x}_i$ is the p x 1 vector of fixed factor levels, $\boldsymbol{\theta}$ is the vector of fixed effect coefficients, and u_i are $i = 1, ..., m$ independent random effects.

The likelihood for uncensored data for the given model specification is:

$$\mathcal{L}(\beta, \boldsymbol{\theta}|Data) = \prod_{i=1}^{m} \int \prod_{j=1}^{n_i} f_1(t_{ij}|u_i) f_2(u_i) du_i \tag{4.1}$$

where $f_1(t_{ij}|u_i)$ is the Weibull PDF for the data within an experimental unit and $f_2(u_i)$ is the normal PDF for the random effect. This likelihood could be easily adapted to model

different experimental designs. However because sub-sampling is commonly used in design of experiments for reliability data, this chapter focuses on the sub-sampling random effect model. If right censoring is present in the data, then the likelihood is:

$$\mathcal{L}(\beta, \boldsymbol{\theta}|Data) = \prod_{i=1}^{m} \int \prod_{j=1}^{n_i} [f_1(t_{ij}|u_i)]^{\delta_{ij}} [1 - F_1(t_{ij}|u_i)]^{1-\delta_{ij}} f_2(u_i) du_i \tag{4.2}$$

In this chapter we focus solely on the likelihood for right censoring because of the prevalence of right censoring in reliability data. Additionally, the right censored likelihood easily reduces to the uncensored likelihood by letting all $\delta_{ij} = 1$. Random effects models, especially nonlinear models, pose many computational issues in that in order to maximize the likelihood because it is necessary to integrate out the random effect u_i.

4.2.2 Gaussian Quadrature

There are several different mathematical techniques for integrating out the random effect for the NLMM. Gauss-Hermite (G-H) quadrature, as discussed in Chapter 2, was selected as the best method for this research. G-H quadrature is applicable when the random effect follows a normal distribution. G-H quadrature requires the random effect to have the form e^{-x^2}. Therefore, a change of variables is necessary to apply G-H quadrature to our likelihood function. Let $u_i = \sqrt{2}\sigma_u v_i$, then the likelihood before the change of variables is:

$$\mathcal{L}(\beta, \boldsymbol{\theta}|Data) = \prod_{i=1}^{m} \int_{-\infty}^{\infty} \left[\prod_{j=1}^{n_i} g(t_{ij}|u_i) \frac{e^{\frac{-u_i^2}{2\sigma_u^2}}}{\sqrt{2\pi\sigma_u^2}} \right] du_i \tag{4.3}$$

where $g(t_{ij}|u_i) = [f_1(t_{ij}|u_i)]^{\delta_{ij}} [1 - F_1(t_{ij}|u_i)]^{1-\delta_{ij}}$ for right censored data. Executing the change in variables results in the following likelihood:

$$\mathcal{L}(\beta, \boldsymbol{\theta}|Data) = \prod_{i=1}^{m} \int_{-\infty}^{\infty} \left[\prod_{j=1}^{n_i} g(t_{ij}|\sqrt{2}\sigma_u v_i) \frac{e^{-v_i^2}}{\sqrt{\pi}} \right] dv_i \tag{4.4}$$

Now we can directly apply G-H quadrature to approximate the likelihood. The G-H quadrature results in the following approximation of the likelihood:

$$\mathcal{L}(\beta, \boldsymbol{\theta}|Data) \approx \prod_{i=1}^{m} \frac{1}{\sqrt{\pi}} \left\{ \sum_{k=1}^{n_k} \left[\prod_{j=1}^{n_i} g(t_{ij}|\sqrt{2}\sigma_u q_{k_i}) w_k \right] \right\} \tag{4.5}$$

where n_k is the number of quadrature points, q_k are the evaluation points found from the roots of the Hermite polynomials, and w_k are the corresponding weights to the evaluation points given by:

$$w_k = \frac{2^{n-1} n! \sqrt{\pi}}{n^2 [H_{n-1}(q_k)]^2}.$$

A common recommendation for the number of quadrature points to minimize bias is 20 points. Pinheiro and Bates (1995) show that G-H quadrature with 100 points is as good as any other solution they investigated to the numerical optimization problem. In this research, we use 20 quadrature points in all of our analyses unless otherwise stated. This

limits computation time, especially in the simulation studies. The log-likelihood is:

$$\ell(\beta, \boldsymbol{\theta}|Data) \approx \sum_{i=1}^{m} \log \left(\frac{1}{\sqrt{\pi}} \sum_{k=1}^{n_k} \left[\prod_{j=1}^{n_i} g(t_{ij}|\sqrt{2}\sigma_u q_{k_i}) w_k \right] \right) \tag{4.6}$$

The approximate log-likelihood is maximized through standard maximization techniques. We use quasi-Newton optimization with a Broyden, Fletcher, Goldfard, and Shanno (BFGS) update of the inverse Hessian matrix.

4.2.3 Inference

An advantage of using G-H quadrature is it results in a closed-form approximate log-likelihood. Therefore, we can derive a Hessian matrix and asymptotic covariance matrix from the approximate log-likelihood. Maximum likelihood theory states that under certain regularity conditions that $\sqrt{n}(\hat{\boldsymbol{\theta}} - \boldsymbol{\theta})$ converges in distribution to a multivariate normal. Therefore, for our model let $\boldsymbol{\theta}^{*T} = [\beta, \boldsymbol{\theta}, \sigma_u]$. Then, $\hat{\boldsymbol{\theta}}^* \sim$ asymptotically $MVN\ [\boldsymbol{\theta}^*, I(\boldsymbol{\theta}^*)^{-1}]$, where

$$I(\boldsymbol{\theta}^*) = \begin{bmatrix} -\frac{\partial^2 \ell(\beta,\theta_1,\ldots,\theta_p,\sigma_u)}{\partial \beta^2} & -\frac{\partial^2 \ell(\beta,\theta_1,\ldots,\theta_p,\sigma_u)}{\partial \beta \partial \theta_1} & \cdots & -\frac{\partial^2 \ell(\beta,\theta_1,\ldots,\theta_p,\sigma_u)}{\partial \beta \partial \theta_p} & -\frac{\partial^2 \ell(\beta,\theta_1,\ldots,\theta_p,\sigma_u)}{\partial \beta \partial \sigma_u} \\ -\frac{\partial^2 \ell(\beta,\theta_1,\ldots,\theta_p,\sigma_u)}{\partial \beta \partial \theta_1} & -\frac{\partial^2 \ell(\beta,\theta_1,\ldots,\theta_p,\sigma_u)}{\partial \theta_1^2} & & \vdots & -\frac{\partial^2 \ell(\beta,\theta_1,\ldots,\theta_p,\sigma_u)}{\partial \theta_1 \partial \sigma_u} \\ \vdots & & \ddots & -\frac{\partial^2 \ell(\beta,\theta_1,\ldots,\theta_p,\sigma_u)}{\partial \theta_{p-1} \partial \theta_p} & \vdots \\ -\frac{\partial^2 \ell(\beta,\theta_1,\ldots,\theta_p,\sigma_u)}{\partial \beta \partial \theta_p} & \cdots & -\frac{\partial^2 \ell(\beta,\theta_1,\ldots,\theta_p,\sigma_u)}{\partial \theta_p \partial \theta_{p-1}} & -\frac{\partial^2 \ell(\beta,\theta_1,\ldots,\theta_p,\sigma_u)}{\partial \theta_p^2} & -\frac{\partial^2 \ell(\beta,\theta_1,\ldots,\theta_p,\sigma_u)}{\partial \theta_p \partial \sigma_u} \\ -\frac{\partial^2 \ell(\beta,\theta_1,\ldots,\theta_p,\sigma_u)}{\partial \beta \partial \sigma_u} & -\frac{\partial^2 \ell(\beta,\theta_1,\ldots,\theta_p,\sigma_u)}{\partial \theta_1 \partial \sigma_u} & \cdots & -\frac{\partial^2 \ell(\beta,\theta_1,\ldots,\theta_p,\sigma_u)}{\partial \theta_p \partial \sigma_u} & -\frac{\partial^2 \ell(\beta,\theta_1,\ldots,\theta_p,\sigma_u)}{\partial \sigma_u^2} \end{bmatrix}$$

The estimated covariance for the parameter estimates can be found by substituting the

MLEs into the information matrix, $I(\boldsymbol{\theta}^*)$. Meeker and Escobar (1998, page 622) note that the regularity conditions hold for the Weibull distribution. See Appendix A for the derivation of the information matrix for the random effects Weibull model.

4.2.4 Software

R-CRAN software is implemented for approximating the likelihood of the Weibull NLMM and the numerical optimization. Additionally, SAS PROC NLMIXED allows the user to program in their own likelihood function and specify the number of quadrature points. The default in SAS NLMIXED is to use adaptive quadrature, which is described in Pinheiro and Bates (1995). We however, choose to use 20 point G-H quadrature so our R-cran software results are directly comparable to the SAS NLMIXED results. Both the SAS and the R-cran code us the BFGS update to the Hessian matrix. However, SAS PROC NLMIXED defaults to using analytical derivatives for updating the Hessian, while R-cran's optim function uses numerical derivatives. These two methods can result in different solutions. We recommend using the analytic derivatives if possible. Appendix B provides the R-cran code and the SAS code for analyzing the NLMM.

4.3 Motivating Example

Zelen (1959) provides an example of a classic reliability DOE. Zelen describes a life test on glass capacitors under two temperature and four voltage settings that a glass capacitor

would experience under normal use. The observational units in this experiment are the eight glass capacitors on each test stand. The experimental units are the eight test stands, where the researcher applied the unique temperature, voltage treatment combination. Type II censoring, after the first four failures, is used for each test stand. Table 3.1 provides the Zelen data.

Meeker and Ecobar (1998, pages 447-450) provide a life test analysis of the Zelen data assuming the treatments were independently applied to all 64 capacitors. The results of the analysis are reproduced in Table 3.2 using Minitab. These results can also be found using SAS's Proc LIFEREG. The analysis indicates that voltage and temperature both have a significant impact on the scale parameter and therefore the lifetime of the glass capacitor.

A basic principle of experimental design is that an experimental design induces a particular probability structure. If an experiment is not a completely randomized then treating each observation as independent and multiplying the values of the PDF together to obtain the likelihood is a violation of the statistical assumptions underlying the model. Additionally, treating each observation as independent induces the wrong experimental error for testing. Including a random effect allows us to model the true experimental error and observational error correctly. In the Zelen data, the eight glass capacitors on each test stand are dependent. The analysis from Meeker and Escobar (1998) ignores the correlations between the glass capacitors on the same test stands.

The model specification presented in Section 3 of this paper allows for the sub-sampling described in the Zelen glass capacitor experimental design. The results from this analysis

using 20 point G-H quadrature to approximate the likelihood are given in Table 4.1.

Table 4.1: Nonlinear Mixed Effects Model Analysis for Life-test on Glass Capacitors

Parameter Estimates						
Parameter	**Estimate**	**Standard Error**	**t Value**	**P-value**	**95% Confidence Limits**	
Weibull Shape	2.7753	0.6622	4.19	0.0041	1.2095	4.3411
Intercept	13.5257	3.0636	4.42	0.0031	6.2816	20.7699
Voltage	-0.00589	0.001154	-5.10	0.0014	-0.00862	-0.00316
Temperature	-0.02964	0.01808	-1.64	0.1451	-0.07239	0.01310
Log(σ_u)	-3.0184	9.0655	-0.33	0.7489	-24.4549	18.4180

Incorporating random effects into the model results in similar estimates of the shape parameter, β, and the model relating temperature and voltage to the log-scale parameter, μ_i as the independent analysis. One important difference to note is that all of the standard errors are larger for the nonlinear mixed effects model. This is because we are properly modeling our experimental error and observational error in the random effects model. These larger standard errors result in temperature no longer being a significant term in the model.

Note that we estimate $\log(\sigma_u)$ as opposed to σ_u, which helps convergence of the NLMM, especially in cases where σ_u is close to zero. The invariance property of MLEs and the delta method allow us to estimate σ_u and the standard error of σ_u. The standard error is:

$$\widehat{se}\left(\hat{\sigma}_u\right) = \hat{\sigma}_u \widehat{se}\left[\log\left(\hat{\sigma}_u\right)\right] \tag{4.7}$$

The estimate of $\sigma_u = 0.0489$ for the Zelen data is small, but it is still important to include in the model to ensure that the experimental error is properly modeled.

In Chapter 3 we analyze the Zelen dataset using a two-stage modeling approach, which properly accounts for the sub-sampling experimental design. The standard errors between their analysis and the nonlinear mixed model analysis are similar in magnitude. However, the estimate of the shape parameter in the two-stage analysis is much higher, $\hat{\beta} = 3.62$, than either the independent analysis or the NLMM analysis indicating that the two-stage method is susceptible to bias in the estimation of the shape parameter.

4.4 Monte Carlo Simulation Study

While the Zelen data provides an interesting application of the random effects model, it fails to fully investigate the impact of using the random effect model over the independent model. A particular "shortfall" in the data is that the estimated variance on the random effects is small. However, since there is no true replication in Zelen data, the variance may only appear to be small due to the experimental protocol.

Recall, in the random effects model, we incorporate the treatment combinations and the random sub-sampling error into the model through the log-scale parameter, $\log(\eta_i) = \mu_i = \boldsymbol{x}_i^T\boldsymbol{\theta} + u_i$. In the Zelen data, the researcher applies each unique temperature, voltage treatment combination to only one test stand. Therefore, the fixed effects and the random sub-sampling variance are confounded and cannot be uniquely estimated. A reasonable conjecture, especially because these data were collected in 1959, is that variability between test stands is actually higher than we found in the above analysis. The simulation study pre-

sented here investigates the impact of different levels of variance on the random effect as well as the impact of model misspecification on the NLMM. We compare the NLMM results to the independent model analysis results.

4.4.1 Simulation Design

We base the simulation study heavily on the Zelen data to maintain a realistic experimental setup. The goal of the simulation study is to determine the impact of the random effect variance and model specification on the analysis. We investigate model misspecification because it is a well known fact that the Weibull distribution parameters are correlated. We wish to investigate how the possible misspecification of the scale parameter impacts that shape parameter estimate. Leon et. al (2007) observed this impact when the spool effect was not incorporated into the analysis.

The setting of all parameters for the simulation study are based on the analysis of the original Zelen data. We coded the temperature and voltage to be in the range $[-1, 1]$ so that the coefficients can be directly compared. Coding the fixed factor settings does not influence the estimate of the shape parameter for either the independent analysis or the nonlinear mixed model analysis.

The simulation study uses the following parameter values: $\theta_0 = 6.7$, $\theta_{volt} = -0.44$, $\theta_{temp} = -0.44$, $\theta_{volt*temp} = 0.15$ and $\beta = 2.78$. We selected these parameter values based on the NLMM results for the coded Zelen data. We hold these quantities constant across all of

the simulations. The changing settings for the simulation study to investigate the impact of random effect variance and model misspecification are:

- $\sigma_u^2 = [0.01, 0.1, 1]$, the variance of the random effect.
- $w_m = [0, .5, 1]$, the weight of the model misspecification. Note when $w_m = 0$ there is no model misspecification and when $w_m = 1$ the model misspecification is the most severe
- Assumed Model
  - Model 1: contains voltage and temperature ($\theta_{volt} = -0.44$, $\theta_{temp} = -0.44$)
  - Model 2: contains voltage, temperature and positive interaction ($\theta_{volt} = -0.44$, $\theta_{temp} = -0.44$, $\theta_{volt*temp} = 0.15$)

The lowest value is approximately twice as large as the estimated value for the Zelen data NLMM from Table 4.1. We base the largest variance on the maximum Weibull variance for the parameter estimates from Chapter 3. The final value, $\sigma_u = .316 = \sqrt{.1}$, provides a mid-value for the variance.

The simulation study uses a full factorial design, resulting in 18 ($3 \times 3 \times 2$) simulation runs. We maintain the same experimental design as the original Zelen data, eight test stands each with eight capacitors, Type II censoring for each test stand after the fourth failure. We run 10,000 replications of the simulation study to ensure a small simulation error.

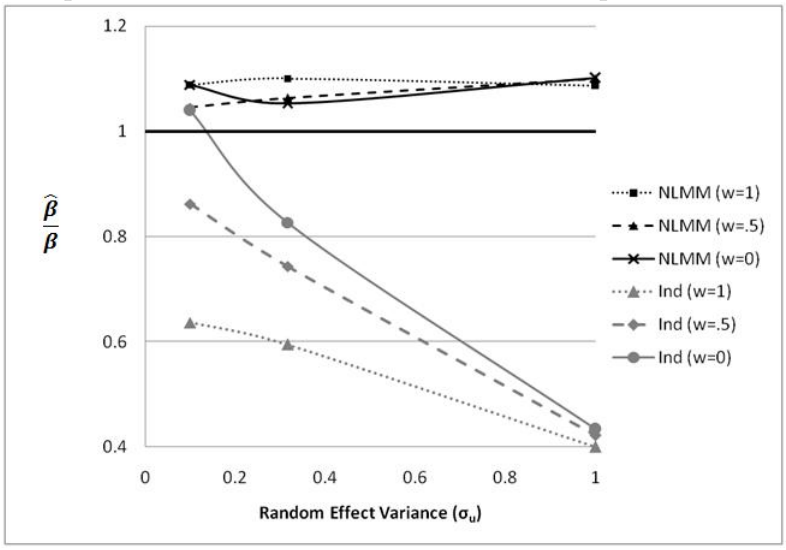
We executed the Monte Carlo simulation study in SAS. We generated the random effects within a test stand using the rand("normal") statement built into SAS. We generated the Weibull data within a test stand using the inverse CDF method and the rand("uniform") built into SAS. We stored the both the nonlinear mixed model solution for each run and the independent model solution for comparison. We confirmed the SAS results from Proc NLMIXED as well as Proc LIFEREG through code written by the author in R-cran.

4.4.2 Results

Figure 4.1 shows the results for the estimation of the Weibull shape parameter for the first simulation model, containing voltage and temperature. In Figure 4.1 the black lines are results for NLMM analysis and the grey lines are for independent analysis. We applied the model misspecification weights to temperature in the data generation step and fit the model containing voltage. Therefore, when $w_m = 1$ the coefficient for temperature used in the data generation is -0.44, when $w_m = 0.5$, the coefficient is -0.22, and when $w_m = 0$ the coefficient is 0. The model fit for these cases always contains only voltage. Therefore, when $w_m = 0$, there is no model misspecification. We present the results for $\hat{\beta}/\beta$.

Figure 4.2 shows the results for the estimation of the Weibull shape parameter for the second simulation model, containing voltage, temperature, and their interaction. In this model, we apply the model misspecification weights to the interaction term. The fit model always contains the main effects for temperature and voltage. The results for the second model are

Figure 4.1: Monte Carlo Simulation Study Investigating the Impact of Random Effect Variance and Model Misspecification on the Pivotal Weibull Shape Parameter for Model 1

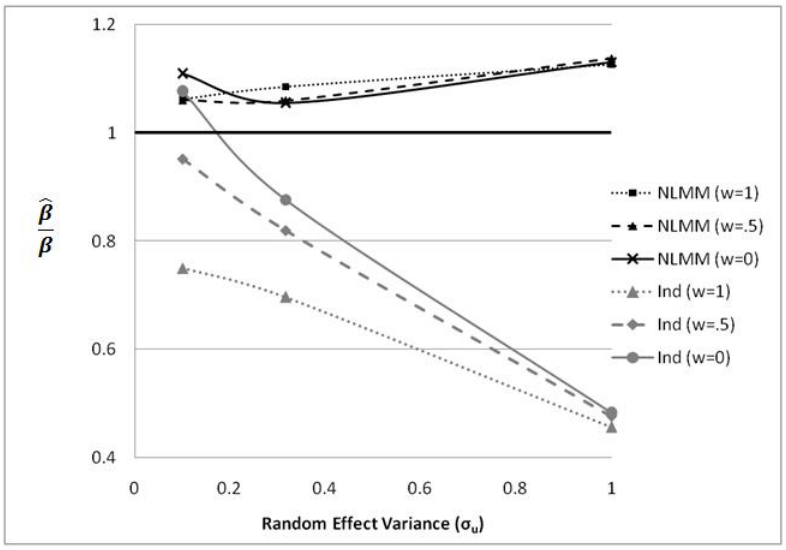


very similar to the first model. Figure 4.2 again presents the results for $\hat{\beta}/\beta$.

The results for the two different assumed models indicate that the random model results are nearly invariant to the degree of model misspecification and the variance of the random effect. The independent model estimates of β get worse as the variance of σ_u increases and as the degree of model misspecification increases. The random effects model provides a more robust estimate of the shape parameter for both model forms considered in this simulation study.

Often, in reliability data analysis we use pivotal quantities like $\hat{\beta}/\beta$ to generalize results for all values of beta. We ran the simulation study without any changes to the parameters except for using the value $\beta = 1$ to check if these pivotal quantities hold for this more complex model. Figure 4.3 shows the results of this study in terms of $\hat{\beta}/\beta = \hat{\beta}$. While

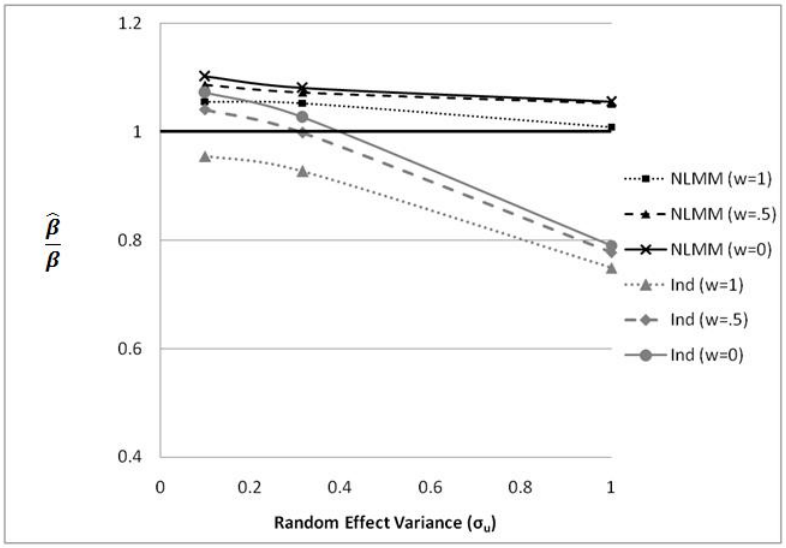
Figure 4.2: Monte Carlo Simulation Study Investigating the Impact of Random Effect Variance and Model Misspecification on the Pivotal Weibull Shape Parameter for Model 2



the general conclusions are the same for this value of β, the actual values are not equal; therefore, pivotal quantities should be interpreted with caution in this study.

In contrast to the estimates of the shape parameter, the estimates of the coefficients for the log-scale parameter are relatively robust to the analysis method. Figure 4.4 shows that our ability to estimate the log-scale parameter linear coefficient is primarily based on the level of random effect variance and the degree of model misspecification, not the modeling method. However, the statistical significance of those estimates are heavily dependent on the model analysis method. Figure 4.5 shows that as σ_u increases the ability to detect a significant effect in the model for the log-scale parameter decreases in the independent model more substantially than it does for the random model. These p-values correspond directly with the coefficient estimates in Figure 4.4. This decrease in significance is more notable for the independent case because the independent model is not using the correct experimental error

Figure 4.3: Monte Carlo Simulation Study Investigating the Impact of Random Effect Variance and Model Misspecification for Model 1, $\beta = 1$



for inference.

Finally, we note that in the initial Zelen data analysis we suggest that the NLMM underestimates the true value of σ_u. We are unable to confirm this conjecture for the Zelen data because of the lack of true replication in the data. Therefore, the estimate of σ_u is completely confounded with the estimates of $\boldsymbol{\theta}$. In the simulation study we show, how well we estimate θ_{volt} in Figure 4.4 and the confounded random variance in Figure 4.6. In Figure 4.6 the black solid line indicates no bias in the estimate of σ_u.

The results in Figure 4.4 and Figure 4.6 illustrate the importance of replication in the experimental design. We see that both θ_{volt} and σ_u are subject to bias however, under the current experimental design we cannot separate the estimates. If true replicates were present, we could obtain an estimate of σ_u independent of the log-scale parameter coefficients.

Figure 4.4: Monte Carlo Simulation Study Investigating the Impact of Random Effect Variance and Model Misspecification for Model 1 Estimate of θ_{volt}

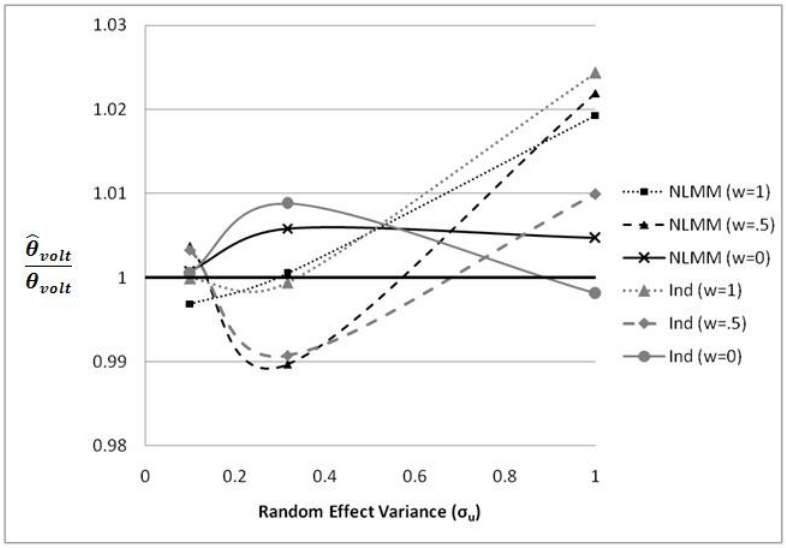


Figure 4.5: Average p-values for the Monte Carlo Simulation Study for θ_{volt} for Model 1 Specifications

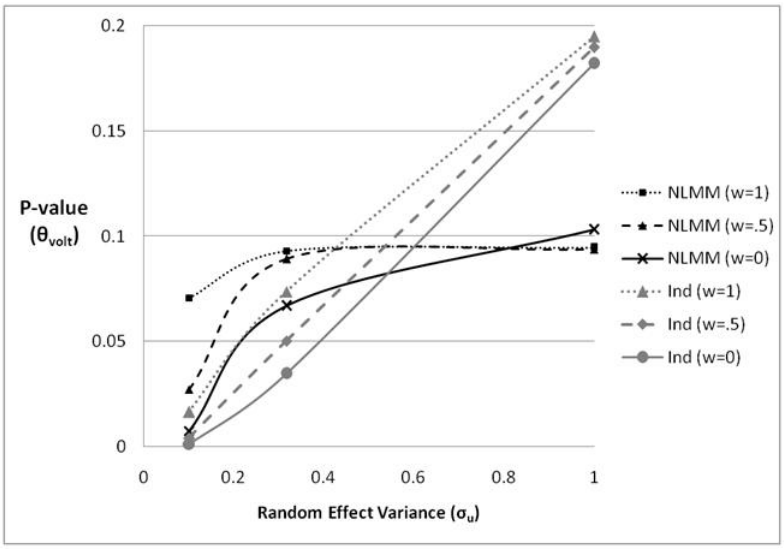
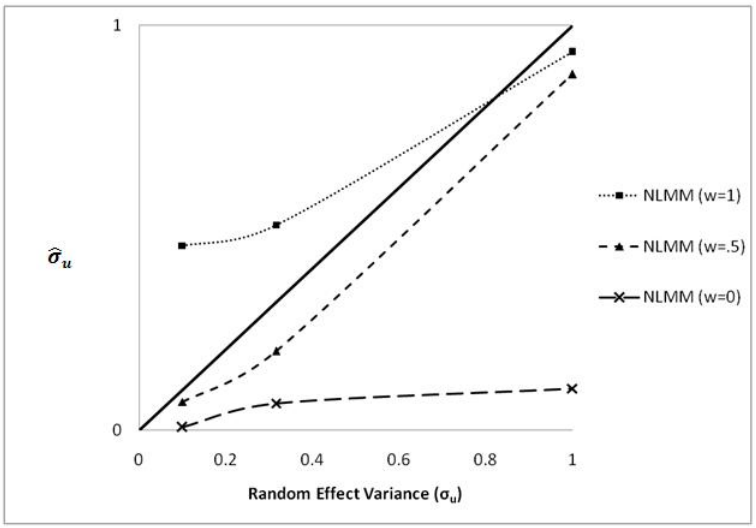


Figure 4.6: Estimated Random Standard Deviation versus the True Value for Monte Carlo Simulation Study



4.5 NLMM Conclusions and Future Directions

In this chapter we provide and methodology for incorporating random effects into life test data where sub-sampling is present. Our simulation study reveals that these models are more robust to model misspecification and increasing levels of variance in the random effect when compared to their independent model counterparts. The methods can easily be adapted to incorporate random effects other than one induced by sub-sampling.

There is a great deal of room for further exploration with these random effect models. In this paper, we applied the model to a life test experiment with sub-sampling. Clear next steps involve extending the analysis here to accelerated life tests and additional types of experimental designs that incorporate random effects.

Additionally, this new modeling technique provides a new framework for thinking about

experimental design for life tests. We note in the Zelen data no true statistical replicates exist, therefore we cannot uniquely estimate σ_u and $\boldsymbol{\theta}$ in our model. Experimental designs that allow the full model to be uniquely estimated should be investigated.

Chapter 5

Application of the Principles of Experimental Design to Reliability Data

5.1 Introduction

Fisher (1935) in "The Design of Experiments" outlines the three principles for statistical design of experiments that have guided experimental design and testing for the past 75 years. These principles are: (1) Randomization; (2) Replication; and (3) Local Control of Error.

The analysis limitations of reliability data have historically forced the analysis of reliability

experiments to assume a completely randomized designs (CRD). However, rarely is this the case in practice. Jones and Nachtsheim (2009) note how prevalent split-plot deigns are in industrial experimentation. Reliability experiments have historically focused on the questions: (1) How many test units should be run? and (2) How long should they be placed on test? These two questions have dominated the reliability field because of problems with censored data. Experimental designs outside of CRDs have generally been disregarded in the reliability community because, until recently, analysis methods were not available to handle data with more complicated randomization scheme than a CRD.

In previous chapters of this dissertation, we saw an industrial experiment from Zelen (1959) that was not a completely randomized design because it contained sub-sampling. However, the Zelen data have been analyzed as a CRD in the reliability literature, which violates the principles of experimental design. The methodologies developed in Chapters 3 and 4 of this dissertation provide two different methodologies for properly modeling the randomization and replication of a sub-sampled experimental design, resulting in different estimates of the experimental error. Chapter 3's method is limited to the sub-sampling experimental design without further modifications. Chapter 4, while structured around the sub-sampling DOE, could be extended to incorporate other types of error control including blocking and split-plot designs.

The randomization scheme is of paramount importance in the data analysis, if a design is not completely randomized it cannot be analyzed as a CRD. We provide two new analysis techniques that allow the user to properly model data from designs containing sub-sampling.

Another problem with the Zelen DOE is no true replication exists in the experiment. The lack of replication in this experiment becomes apparent in the new analysis methods presented for sub-sampled data. The final principle of experimental design, local control of error, including blocking, are beyond the scope of this dissertation. However, it is important to correctly model the experimental error and the observational error, which is the focus of error control in this dissertation.

This chapter illustrates the implication of randomization, replication and experimental error in a correctly analyzed reliability experiment. We use the most straightforward experimental design available for two experimental factors; a 2^2 factorial design. The Monte Carlo simulation studies in this chapter provide a limited introduction to the importance of incorporating the principles of DOE outlined by Fisher into lifetime tests. Additionally, we look at testing for the Weibull NLMM derived in Chapter 4 using the correct experimental error. The estimation of standard errors are central to hypothesis testing. Properly modeling the experimental error ensures a defendable test. We look at normal approximation hypothesis testing and likelihood ratio tests. Finally, a comparison is made between the different analysis methods for the Zelen data in terms of estimation, testing and prediction.

5.2 Monte Carlo Experimental Design Study

5.2.1 Comparison Study between Zelen DOE and 2^2 Factorial DOE

We use the Zelen (1959) glass capacitor data as the guiding experimental data for exploring the implications of incorporating the principles of experimental design into reliability experiments. In this chapter, we apply the NLMM analysis methodology from Chapter 4 to analyze the data from the simulation study.

Recall the model for the sub-sampling DOE in Chapter 4 is:

$$\begin{aligned} t_{ij}|u_i &\sim Indep.\, Weib(\beta, \eta_i) \\ F_1(t_{ij}|\beta, \eta_i, u_i) &= 1 - exp\left[-\left(\frac{t_{ij}}{\eta_i}\right)^{\beta}\right] \\ \log(\eta_i) = \mu_i &= \boldsymbol{x}_i^T\boldsymbol{\theta} + u_i \\ f_2(u_i) &\sim iid\ N\ (0, \sigma_u^2) \end{aligned}$$

In the Zelen data we note that since there is no true replication, the estimate of the random effect standard deviation, σ_u, is completely confounded with the fixed effect coefficient estimates. In the first part of the simulation study, we compare the Zelen DOE with a 2^2 factorial experiment replicated twice. These two experimental designs have the same number of experimental units and sub-samples. We generate data using the following parameter values:

- $\beta = 2.78$
- $\theta_0 = 6.7$
- $\theta_1 = -0.44$
- $\theta_2 = -.44$
- $\sigma_u^2 = 0.01, 0.1$ and 1.0

These values are the same values used in Chapter 4's simulation study. The only difference between the two simulation cases in this Chapter is the experimental designs.

Table 5.1 provides the average MLEs of σ_u for the NLMM over 10,000 simulation runs. Both experimental designs dramatically underestimate σ_u for the case when $\sigma_u = 0.1$. The other two values of σ_u are also underestimated but not as severely. There does not appear to be a difference in the two experimental designs in their ability to estimate the variance of the random effect, despite the fact that σ_u is mathematically confounded with $\boldsymbol{\theta}$ in the Zelen DOE and it is not for the 2^2 factorial DOE.

Table 5.1: Estimates of Random Effect Variance for Monte Carlo Simulation Study Comparing Zelen Design to Replicated 2^2 Design

σ_u	$\hat{\sigma}_u$ Replicated Design	$\hat{\sigma}_u$ Zelen Design
0.1	0.00067	0.00071
0.316	0.1795	0.1790
1	0.8903	0.8901

Figures 5.1 - 5.3 show the difference in the two experimental designs in the estimation of the other three model parameters. An important fact to remember about the Weibull

distribution is that the shape and scale parameters are correlated. Therefore, all of our parameter estimates are correlated in the NLMM.

Figure 5.1: Pivotal Coefficient Estimate for Weibull Shape Parameter, β, for Zelen Design versus Replicated 2^2 Factorial Design. Black solid line indicates no bias.

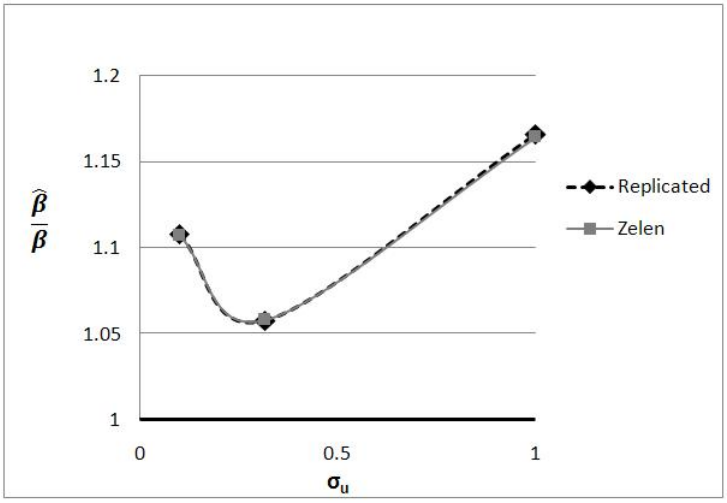
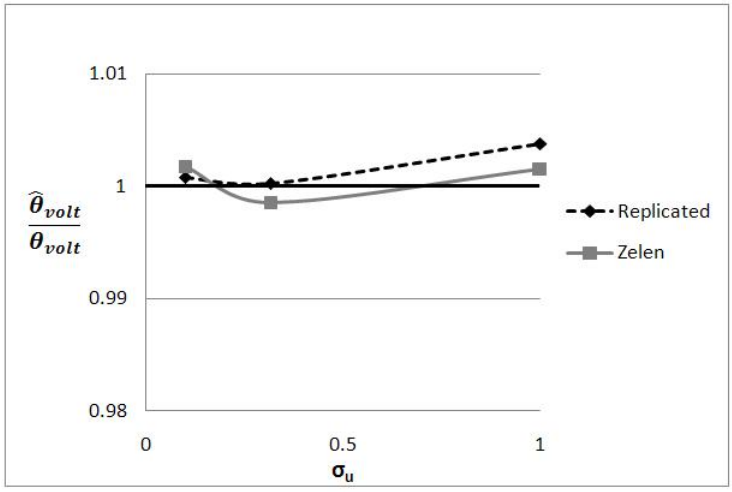
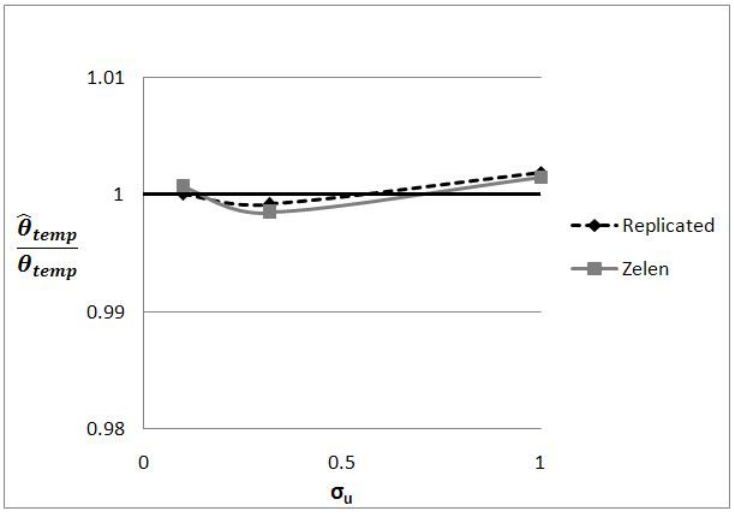


Figure 5.2: Pivotal Coefficient Estimate for Voltage in log-scale Parameter Model for Zelen Design versus Replicated 2^2 Factorial Design



The main conclusion from the experimental design comparison study is that neither experimental design outperforms the other in terms of estimation. A strong conjecture of the

Figure 5.3: Pivotal Coefficient Estimate for Temperature in log-scale Parameter Model for Zelen Design Versus Replicated 2^2 Factorial Design



reason behind this result is that both designs are lacking sufficient degrees of freedom to estimate σ_u accurately. In the analysis of the Zelen DOE and the 2^2 replicated factorial, we have only seven degrees of freedom for estimation. We need to estimate the fixed parameter coefficients, the Weibull shape parameter, and the variance of the random effect. Estimating these terms requires at least three degrees of freedom (2 for the fixed effect, 1 for the random effect variance). The shape parameter estimate comes from a combination of information within each sub-sample and between experimental units so a full degree of freedom is not required to estimate it. However, this only leaves approximately 3 degrees of freedom for experimental error, if we do not fit an interaction term in the model. The next part of the simulation study looks at exactly how much replication is needed to obtain unbiased, consistent estimates of the model parameters.

5.2.2 Monte Carlo Simulation Study 2^2 Factorial DOE with Replication

To analyze the impact of replication on the parameter estimates, we use the same experimental setup as Zelen except we use the 2^2 Factorial design and replicate it from $r = 1$ (no replication) to $r = 10$. The Zelen data use Type II right censoring; however in reliability experiments, Type I censoring provides a practical time and cost constraint. Therefore, we look at both Type I and Type II censoring in the replication study to evaluate their impact on the parameter estimates.

The Zelen data use Type II censoring after 50% of the glass capacitors fail. Therefore, we use 50% Type II censoring in the simulation study. In order to compare Type I and Type II censoring, we base our Type I censoring scheme closely on the Type II censoring scheme. We calculate the 50% percentile time for each group, resulting in 4 potential censoring times given in Table 5.2. The average time across all eight groups $\bar{t}_{.50} = 859$ which is used as the censoring time for the Type I censoring scheme.

Table 5.2: 50% Percentile Estimates for Type I Censoring

Voltage	Temperature	$t_{.50}$
-1	-1	1716.7
1	-1	712.1
-1	1	712.1
1	1	295.3

To further improve our ability to compare between censoring types we apply them to the

same uncensored data set. In the simulation study, we generate an uncensored dataset, then both censoring schemes, Type I and Type II, are applied to the uncensored data.

Table 5.3: Expected Number of Failures for Type I Censoring (Censoring Time = 859 Hours)

Voltage	Temperature	$E(N_f)$
-1	-1	0.7695
1	-1	5.5114
-1	1	5.5114
1	1	8.0000

In Type I censoring it is possible to observe no failures in a group. Table 5.3 gives the expected number of failures for each test stand in the 2^2 factorial DOE. Clearly, in the low temperature, low voltage test stand, we anticipate the possibility of observing no failures, which creates an empty cell. In the cases where no failures are observed, we can write the portion of the approximate log-likelihood for test stand i as:

$$\begin{aligned} \ell_i(\beta, \boldsymbol{\theta}|Data) &\approx \log\left(\frac{1}{\sqrt{\pi}}\sum_{k=1}^{n_k}\left[\prod_{j=1}^{n_i} g(t_{ij}|\sqrt{2}\sigma_u x_{k_i})w_k\right]\right) \\ &= \log\left(\frac{1}{\sqrt{\pi}}\sum_{k=1}^{n_k}\left[\prod_{j=1}^{n_i} \exp[-\exp(z_{ijk})]w_k\right]\right) \end{aligned}$$

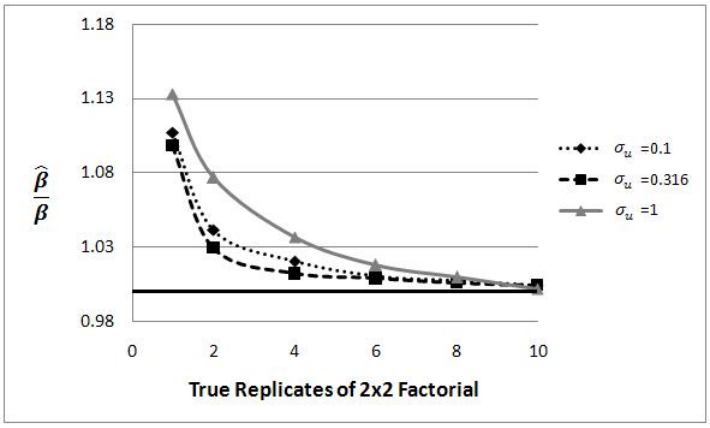
The above equation shows that there is still a contribution to the log-likelihood for an empty cell. Additionally, we can still find the maximum likelihood estimates if we observe an empty cell. However, as we will later note in the simulation study results, we observe that estimates for the unreplicated design can be of very poor quality. Replication improves the estimates of the parameters. The impacts of empty cells are investigated more in the full simulation

study.

Impact of Replication: Type I Censoring

Figures 5.4 - 5.7 show the results for the Type I censored replicated 2^2 factorial design. Figure 5.4 shows that the estimates for β are biased above the true value. Replicating the design a minimum of 4 times appears to give a good quality estimate of the Weibull shape parameter. The asymptotic properties of the MLE appear to take effect around 4-6 replicates of the 2^2 factorial.

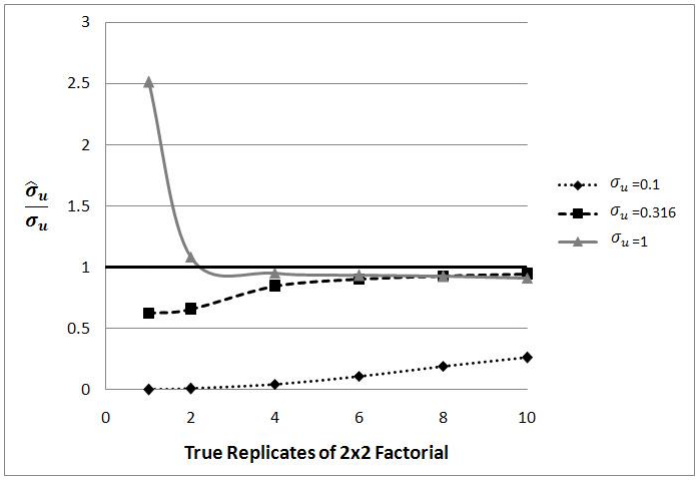
Figure 5.4: Pivotal Coefficient Estimate for Weibull Shape Parameter for Replicated 2^2 Factorial Design with Type I Censoring



Recall, the Zelen experimental design was a motivating factor for the simulation study on replicated experimental designs. The estimate of σ_u is confounded with treatment combinations in the NLMM for the Zelen design. Figure 5.5 shows the impact of replication on our ability to estimate σ_u. The simulation results show that if σ_u is small a very large sample size is required to estimate σ_u with any accuracy. Even for $r = 10$, the estimate of σ_u is

only approximately 26% of the true value. We are able to estimate σ_u with a great deal more accuracy for the larger values. However, for Type I censored data and $\sigma_u = 1$, we dramatically overestimate σ_u in the cases where empty cells occur.

Figure 5.5: Pivotal Coefficient Estimate for σ_u for Replicated 2^2 Factorial Design with Type I Censoring



Figures 5.6 and 5.7 show the average estimates of the coefficients for voltage and temperature, respectively, of the log-scale parameter linear model. For Type I censoring we notice that these estimates can be very poor when there are empty cells and a small number of replicates. In fact, the two figures do not contain the estimates for the coefficients for the case when $r = 1$ and $\sigma_u = 1$. They were omitted because the estimates were 235% and 245% the true values of the coefficients for voltage and temperature respectively and masked the other points in the figures. In addition to the log-scale parameter coefficient estimates being of poor quality in the unreplicated design, we cannot fit interaction term because the main effects model for log-scale parameter, β and σ_u result in a fully saturated model. The unreplicated 2^2 factorial design is never recommended based on these simulation results. Increasing replication, for

all values of σ_u, results in better estimates of the coefficients, θ_{volt} and θ_{temp}, of the log-scale parameter model. The estimates are within the simulation error of the simulation study for $r \geq 6$.

Figure 5.6: Pivotal Coefficient Estimate for Voltage in log-scale Parameter Model for Replicated 2^2 Factorial Design with Type I Censoring

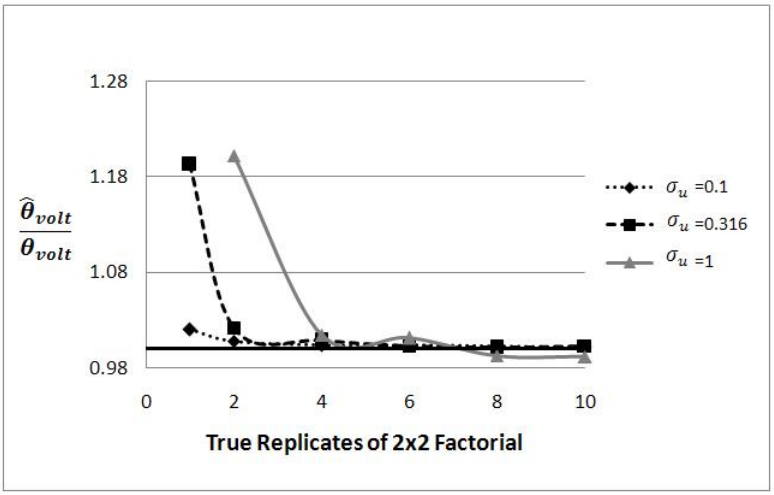
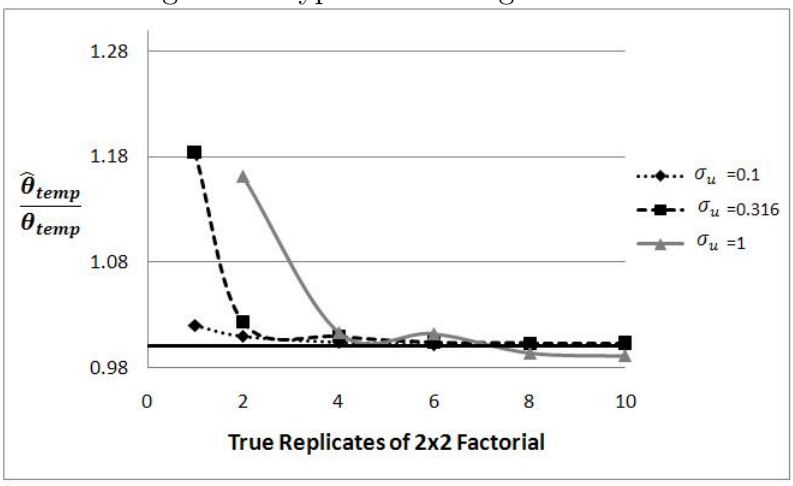


Figure 5.7: Pivotal Coefficient Estimate for Temperature in log-scale Parameter Model for Replicated 2^2 Factorial Design with Type I Censoring



In summary, for Type I censored data, 4 replicates of a 2^2 factorial DOE with 8 sub-samples

is the smallest number of reps that results in low bias and consistent estimates of the parameters. Additionally, it is interesting to note that in the unreplicated case the estimates for σ_u and $\boldsymbol{\theta}$ are poor due to empty cells, but the estimate of β is not influenced.

Impact of Replication: Type II Censoring

The results for Type II censoring for β and σ_u are in Figures 5.8 and 5.9 respectively. We omit the graphs for the coefficients for the log-scale parameter because they are within the simulation error of their true values for Type II censored data for all levels of replication considered.

In Figure 5.8 we notice that Type II censoring The estimates of β have more bias than Type I censoring case, even for the unreplicated case. Similarly to the Type I censoring case, asymptotic properties of the MLE of β appear to take affect between 4-6 replicates of the DOE.

Figure 5.8: Pivotal Coefficient Estimate for Weibull Shape Parameter for Replicated 2^2 Factorial Design with Type II Censoring

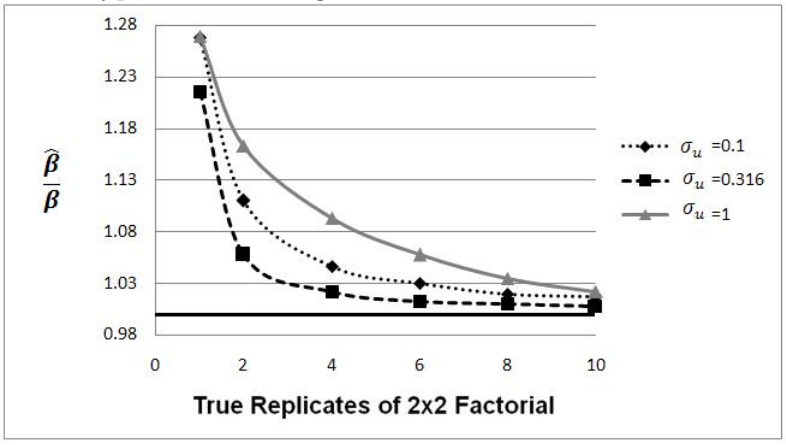
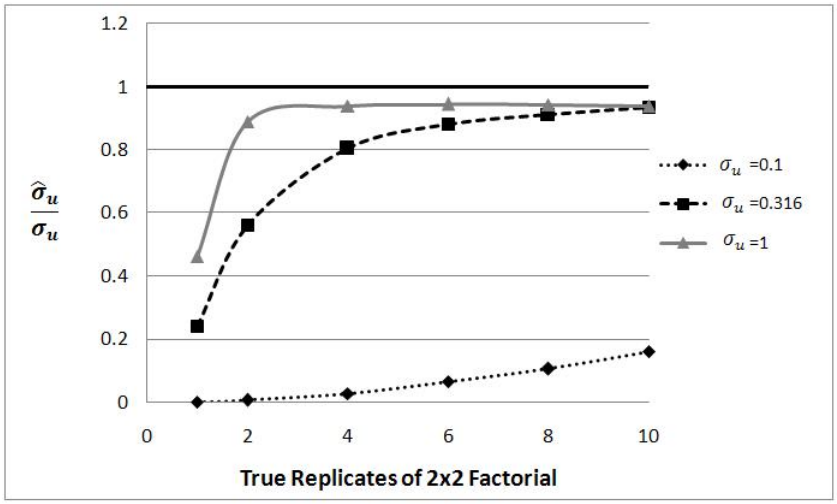


Figure 5.9 contains the simulation study results for the estimate of σ_u. The results for Type II censoring are similar to Type I censoring. Our ability to estimate σ_u is dependent its true value. For the smallest value of σ_u, a large sample size is required to estimate the parameter accurately. A major difference between the two censoring types exists in the unreplicated case. For Type II censoring we severely underestimate all three values of the σ_u in the unreplicated case. For Type I censoring, we severely overestimate σ_u for the large variance case and underestimate it for the other two cases.

Figure 5.9: Pivotal Coefficient Estimate for σ_u for Replicated 2^2 Factorial Design with Type II Censoring



5.2.3 Monte Carlo Simulation Study Conclusions

The results of the design comparison simulation study indicate that neither the Zelen design nor the 2^2 factorial design replicated twice is sufficient for estimating the parameters of the Weibull NLMM, particularly for σ_u and β. This conclusion led to a replication study of the 2^2 factorial DOE. The goal was to determine the amount of replication required to provide accurate estimates of the parameter for the Weibull NLMM. The 2^2 Factorial DOE was replicated from 1 to 10 times. The minimum number of replicates that is advisable for this type of data based on this simulation study is $r = 4$. The estimates have relatively low bias at 4 replicates and the asymptotic properties of the MLEs appear to take over.

5.3 Statistical Testing and Inference

Throughout this dissertation we have used asymptotic covariance matrix and a normal approximation for testing parameter significance. However, we have also noted through several different simulation studies, including the replication study in the previous section, that asymptotic properties are slow to take effect for the Weibull distribution, especially for the shape parameter. Therefore, the normal approximation for testing parameter significance may be a poor assumption.

ME and Lawless (2003) recommend normal approximation as well as the likelihood ratio test (LRT) for testing. In this section, we briefly review the normal approximation theory for the Weibull NLMM. We derive LRT tests for the NLMM and compare the results between the two methods.

In this section we propose three different LRTs: (1) for fixed effects; (2) for the random variance; (3) for lack of fit (LOF). We compared the fixed effects and random effects LRT back to the large-sample normal approximation test. No LOF test is readily available under normal approximation. We provide a discussion on the theoretical χ^2 distribution of the LRT. However, this theoretical distribution is a large sample property. Therefore, re-sampling techniques are proposed as an alternative to the χ^2 assumption. Re-sampling techniques may prove especially useful to practitioners who primarily work with small sample sizes. Through bootstrapping the data, we can set a cutoff which may prove to be a better test for parameter significance for small samples.

5.3.1 Normal Approximation

Recall from Chapter 4 that one can derive a Hessian matrix and asymptotic covariance matrix from the approximate log-likelihood. Maximum likelihood theory states that under certain regularity conditions that $\sqrt{n}(\hat{\boldsymbol{\theta}} - \boldsymbol{\theta})$ converges in distribution to a multivariate normal.

Therefore, for our model let $\boldsymbol{\theta}^{*T} = [\beta, \boldsymbol{\theta}, \sigma_u]$, then $\hat{\boldsymbol{\theta}}^* \sim$ Asymptotically $MVN\ (\boldsymbol{\theta}^*, I(\boldsymbol{\theta}^*)^{-1})$, where Equation 4.7 specifies $I(\boldsymbol{\theta}^*)$. The estimated covariance for the parameter estimates can be found by substituting the MLEs into the information matrix, $I(\boldsymbol{\theta}^*)$. Meeker and Escobar (1998, page 622) note that the regularity conditions hold for the Weibull distribution. Appendix A of the dissertation proves that the first and second derivatives exist and are continuous for the Weibull NLMM. The derivatives are provided in Appendix A as well.

Inference on the parameters from this information can be done through straightforward z-tests. The test statistic for testing if a given model parameter is significantly different form zero is:

$$z = \frac{\hat{\theta} - 0}{s.e.(\hat{\theta})}$$

where $s.e.(\hat{\theta})$ is the square root of the corresponding diagonal element of the covariance matrix $I(\boldsymbol{\theta}^*)^{-1}$. Notice that a frame work for a general lack of fit test is not available under normal approximation. Only tests on the parameters and functions of the estimated parameters are readily available.

5.3.2 Likelihood Ratio Test

Likelihood ratio tests are widely applicable tests related to maximum likelihood estimation. The LRT is defined by a ratio of the likelihood under null hypothesis to the likelihood under the alternative hypothesis. The test works by setting a cut-off value for the ratio between the two likelihoods, and if the ratio is less than that cutoff the test rejects the null hypothesis. Define the deviance of the LRT as $D = -2\log(\frac{\mathcal{L}_{\text{null}}}{\mathcal{L}_{\text{alt}}})$. The deviance is asymptotically χ^2 with p degrees of freedom, where p is the number of parameters being tested. Therefore asymptotically,

$$D = -2\log(\mathcal{L}_{\text{null}}) - (-2\log(\mathcal{L}_{\text{alt}})) \sim \chi^2_p \tag{5.1}$$

We use Monte Carlo simulation to examine the small sample behavior of the deviance for the three different Weibull NLMM tests. The simulation studies including in the following sections determine when the χ^2_p cutoff is reasonable for the 2^2 factorial designs.

Fixed Effects

The LRT can be used to test the significance of adding an additional parameter to the log-scale parameter model. The hypotheses for a test on fixed effects are:

$$H_o \;:\; \theta_2 = 0$$

$$H_a \;:\; \theta_2 \neq 0$$

where θ_2 is a potential coefficient for a fixed effect in the log-scale parameter model: $\mu = \boldsymbol{\theta} X$. The likelihood ratio test compares the two likelihoods for the model without θ_2 (null model) and with θ_2 (alternative model). A simulation study checks to see if the deviance for this test at what level of replication this test is approximately χ^2_1 for the 2^2 factorial design. Figure 5.10 provides a panel of Q-Q Plots for the simulation of 10,000 datasets generated under the null hypothesis for the replicated designs.

Figure 5.10 shows that the χ^2_1 distribution assumption is a reasonable assumption for around 4-6 replicates of the 2^2 factorial DOE. For less than 4 replicates the χ^2_1 approximation is liberal and will result in smaller p-values than the "true" p-value.

Random Effect

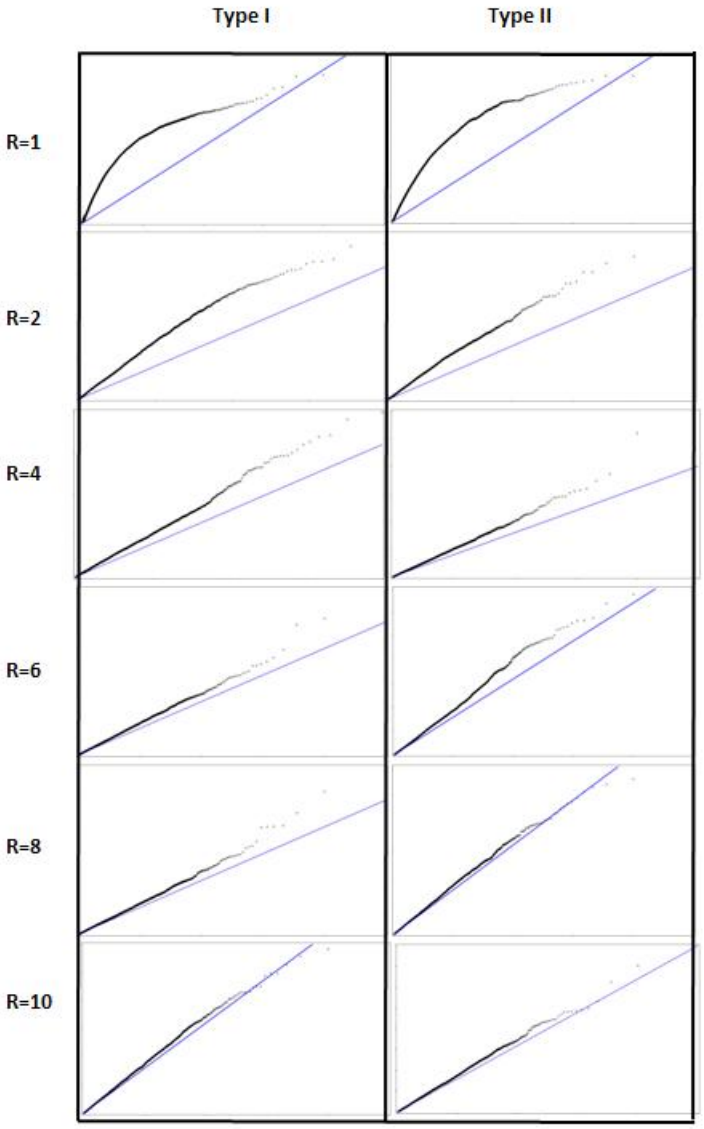
The likelihood ratio test for the random effect is different from the fixed effects test because the likelihoods have two different forms depending on whether or not the random effect is included in the model. The hypotheses for the random effect test are:

$$H_o \quad : \quad \sigma_u = 0$$

$$H_a \quad : \quad \sigma_u > 0$$

Under the null hypothesis we simply have the independent data likelihood that is commonly implemented in the reliability literature; Under the alternative hypothesis we have the likelihood for the NLMM. Therefore the deviance is given by:

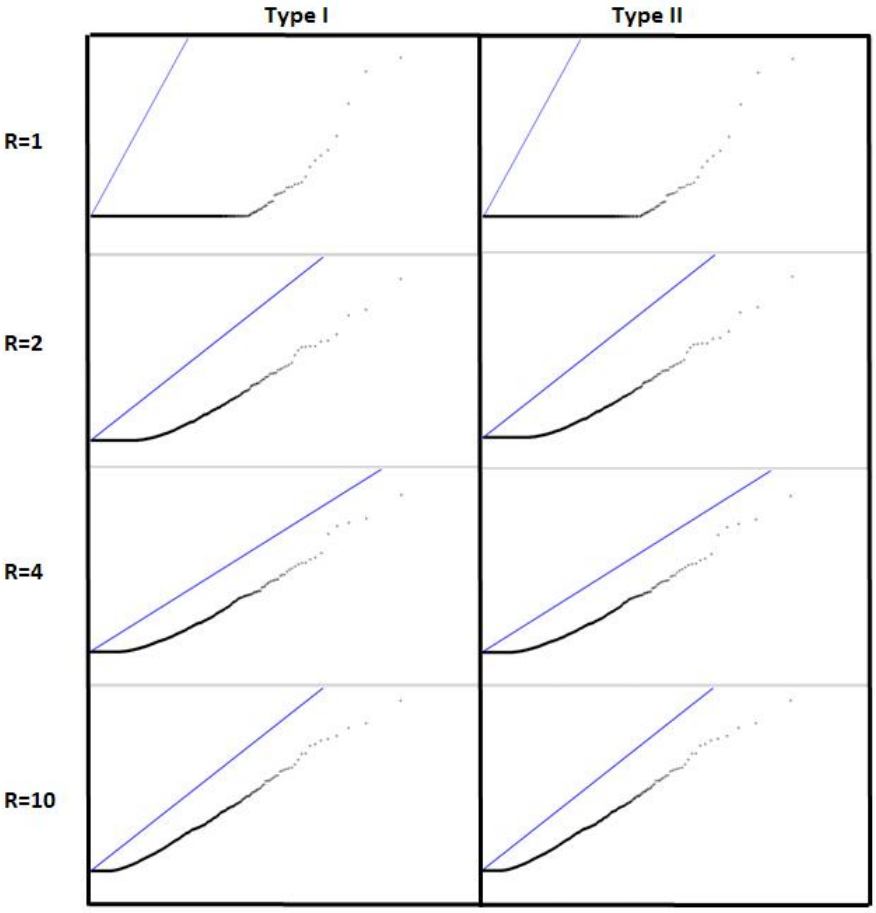
Figure 5.10: Q-Q Plots of Deviance for Fixed Effects Likelihood Ration Test. Left panels are Type I censoring, right panels are Type II censoring



$$D = -2\left(\sum_{i=1}^{N}\delta_i\left[\log\left(\frac{\beta}{t_i}\right)+z_i\right]-\exp(z_i)\right)+2\sum_{i=1}^{m}\log\left(\frac{1}{\sqrt{\pi}}\sum_{k=1}^{n_k}\left[\prod_{j=1}^{n_i}g(t_{ij}|\sqrt{2}\sigma_u x_{k_i})w_k\right]\right) \tag{5.2}$$

These models are not nested models like the fixed effect LRT; therefore, we do not expect them to follow a χ^2_1 distribution. Figure 5.11 confirms this suspicion for multiple sample sizes. The random effect LRT deviance is clearly not χ^2_1; therefore, the p-value will need to be determined empirically by the bootstrap procedure.

Figure 5.11: Q-Q Plots of Deviance for Random Effects Likelihood Ration Test. Left panels are Type I censoring, right panels are Type II censoring



We have provided a test for the random effect, but this test does not justify removing the random effect from the analysis. In this situation the random effects were induced by the experimental design. If a completely randomized design was not used, then one cannot

remove the random effect from the analysis regardless of its significance. In fact, for small values of σ_u, we showed in the previous Monte Carlo simulation that we systematically underestimate σ_u severely, which results in an insignificant hypothesis test. Including the random effect in the analysis results in a model that properly estimates the experimental error for the experimental protocol. Removing the random effect impacts the standard errors which in turn impacts inference on the other parameters. This result is illustrated on the Zelen data in the last section of this chapter.

Lack of Fit

Lack of fit (LOF) tests have typically been implement through a sums of squares approach in response surface methodologies. This requires that the experiment have true replicates. While the 2^2 factorial design proposed in this experiment does have true replication it is impossible to break out the pure error from the lack of fit under a sums of squares procedure. Therefore, we use a likelihood ratio test for testing LOF. This LOF test fits the fully saturated model by estimating a separate log-scale parameter for each setting of the fixed effects using dummy variables. In the 2^2 factorial case it simplifies the LOF analysis to note that the fully saturated model is equivalent to the model with both main effect terms and the interaction.

To verify this statement define the following dummy variables:

$$x_1 = \begin{cases} 1 & \text{if the observation has the low level of treatment A and B} \\ 0 & \text{otherwise} \end{cases}$$

$$x_2 = \begin{cases} 1 & \text{if the observation has the high level of treatment A and low level of B} \\ 0 & \text{otherwise} \end{cases}$$

$$x_2 = \begin{cases} 1 & \text{if the observation has the low level of treatment A and high level of B} \\ 0 & \text{otherwise} \end{cases}$$

Then the fully saturated model is for the log-scale parameter is $\mu_i = \gamma_0 + \gamma_1 x_{1i} + \gamma_2 x_{2i} + \gamma_3 x_{3i} + u_i$. This model is equivalent to the main effects plus interaction model for the log-scale parameter specified by: $\mu = \theta_0 + \theta_1 x_{Ai} + \theta_2 x_{Bi} + \theta_3 x_{Ai} x_{Bi}$, where x_{Ai} and x_{Bi} are the levels of factor A and B respectively of the 2^2 factorial design. The equivalence is seen by noting that:

$$\begin{aligned} \gamma_0 &= \theta_0 + \theta_1(1) + \theta_2(1) + \theta_3(1)(1) \\ \gamma_0 + \gamma_1 &= \theta_0 + \theta_1(-1) + \theta_2(-1) + \theta_3(-1)(-1) \\ \gamma_0 + \gamma_2 &= \theta_0 + \theta_1(1) + \theta_2(-1) + \theta_3(1)(-1) \\ \gamma_0 + \gamma_3 &= \theta_0 + \theta_1(-1) + \theta_2(1) + \theta_3(-1)(1) \end{aligned}$$

This equivalence was confirmed via simulation. The expressions defined above were equiva-

lent within simulation error for 10,000 simulations. The hypotheses for the LOF test for the 2^2 factorial design is:

$$H_o \ : \ \gamma_3 = 0$$

$$H_a \ : \ \gamma_3 \neq 0$$

More generally for a experimental design with d treatment combinations the LOF hypotheses are:

$$H_o \ : \ \left[\gamma_{\{p+1\}} \dots \gamma_{\{d\}}\right] = \mathbf{0}$$

$$H_a \ : \ \left[\gamma_{\{p+1\}} \dots \gamma_{\{d\}}\right] \neq \mathbf{0}$$

where p is the number of parameters fit to the model that is being tested for lack of fit. The deviance for the LOF test is:

$$D = -2\log(\mathcal{L}(\beta, \boldsymbol{\gamma}_{px1}, \sigma_u)) - (-2\log(\mathcal{L}(\beta, \boldsymbol{\gamma}_{dx1}, \sigma_u))) \sim \chi^2_{d-p} \tag{5.3}$$

The χ^2_{d-p} assumption for the 2^2 factorial experiment follow a similar pattern to Figure 5.10, therefore are omitted for brevity. We conclude that the χ^2_{d-p} is valid for the Zelen DOE and designs with more than 4-6 replicates again. It is important to note that for all of the χ^2 approximations the simulation data for fixed effect and LOF all fall above the line for the χ^2

distribution. This indicates that the LRT based on the χ^2 is a liberal test resulting in higher significance levels. This overstatement of significance can be severe if the approximation is poor; therefore, the p-values should be interpreted with caution.

Bootstrapping Procedure

The χ^2 approximation appears to be valid for the deviance of the LRT for more than 4 replicates for the LOF and fixed effects tests. However, for small sample sizes and for testing the random effect the χ^2 approximation is not valid. In these cases, Lawless (2003) recommends using bootstrapping to determine the significance of the test. Bootstrapping is a well established method for estimating standard errors and empirical hypothesis testing. Chapter 9 of ME provides a framework for implementing bootstrap techniques for reliability data. In our context there are two factors that complicate the bootstrap procedure: censored data and designed experiment. Efron (1981) extends the bootstrap procedure to censored data and verifies its validity. Aerts et al. (1994) looks at bootstrapping for fixed design regression. The bootstrap procedure outlined below combines their methods in a single bootstrap procedure for the LRTs presented in this chapter. We calculate the empirical p-value for the bootstrap procedure. The bootstrap code is available in Appendix B of the dissertation.

The bootstrap procedure for calculating empirical p-value is:

1. Take a simple random sample with replacement under the null hypothesis

- Note for designed experiments this sample is actually a stratified random sample with replacement under the null hypothesis model

2. Compute the likelihood under the null hypothesis and the alternative hypothesis and the LRT statistic

3. Re-sample M times (we use M=1000) and compute the LRT statistic each time (i.e. repeat steps 1 and 2 1000 times)

4. Compute the empirical p-value as the count of the number of re-sampled LRT statistics which are larger than the LRT from the actual data

5.4 Comparison of Analysis Methods and Testing Procedures on Zelen Data

This dissertation proposes two new analysis methods for lifetime data containing sub-sampling. Table 5.4 provides a summary of the estimates, corresponding standard errors, and p-values under the independent data model, the two-stage model (Chapter3), and the Weibull NLMM (Chapter 4) for the coded Zelen data. Additionally, we provide two different testing methods for the Weibull NLMM: normal approximation and likelihood ratio test.

Table 5.4 shows that the estimates for the log-scale parameter are relatively consistent between the three modeling approaches. The two-stage model has the largest difference in the parameter estimates for the log-scale parameter, because the linear model for the log-scale

parameter is based on the log-scale parameter for each group. Additionally, the Weibull shape parameter estimates are similar for the independent analysis and the NLMM analysis. The shape parameter is much higher for the two-stage analysis suggesting that this analysis might result in a biased shape parameter estimate. However, if one fits the NLMM with with a separate scale parameter for each group, the shape parameter estimate is nearly identical to the two-stage analysis shape parameter. This change in the shape parameter based on the model specification of the log-scale parameter highlights the problems that arise from the fact that the parameters of the Weibull distribution are correlated.

Another important result in Table 5.4 are the standard errors of the estimates. The two-stage analysis and the NLMM analysis result in more appropriate estimates of the standard error for the Zelen data than the independent analysis. The implication for testing is reflected in the p-values.

Percentile Estimation

Often, in reliability analysis the quantities of interest to a practitioner are not the parameter estimates of the Weibull distribution. Instead performance quantities may be of greater interest. Recall, from Chapter 3 that the percentile MLE for the p^{th} percentile is:

$$\hat{t}_{p_i} = \exp\left[\hat{\mu}_i + \frac{\Phi^{-1}_{SEV}(p)}{\hat{\beta}}\right] \tag{5.4}$$

where $\Phi_{SEV}(p)$ is the inverse CDF for the smallest extreme value distribution and $\mu_i =$

Table 5.4: Analysis Method Comparison for Zelen Data. *p-value determined empirically through bootstrap procedure because χ^2 approximation not available

Parameter	CRD Analysis			Two-Stage Analysis			NLMM Analysis			
	Estimate	Std. Error	P-value	Estimate	Std. Error	P-value	Estimate	Std. Error	Normal Appox. P-value	LRT P-value
β	2.75	0.4187	NA	3.62	0.5947	NA	2.78	0.6871	NA	NA
θ_0	6.7232	0.0689	<.0001	6.62009	0.0920	<.0001	6.7172	0.1152	<.0001	<.0001
θ_{volt}	-0.4433	0.0780	<.0001	-0.4233	0.1234	0.019	-0.4419	0.08702	<.0001	0.0016
θ_{temp}	-0.1445	0.0645	0.0250	-0.1840	0.09196	0.102	-0.1485	0.09337	0.1117	0.0396
σ_u	NA			NA			.0514	0.4472	0.9085	.9720*

$log(\eta_i) = \boldsymbol{x}_i^T\boldsymbol{\theta}$. In addition, to calculating the predicted percentiles it is often useful to have bounds on these percentiles for practical implications. ME provide an expression for calculating a confidence interval for t_p:

$$100(1-\alpha)\%CI = \left[\begin{array}{cc} \hat{t}_p/w, & w\hat{t}_p \end{array} \right] \tag{5.5}$$

where $w = \exp\left(z_{1-\frac{\alpha}{2}} \frac{\hat{s.e.}(\hat{t}_p)}{\hat{t}_p}\right)$. The standard error of $\hat{t}_p$ is estimated using the multivariate delta method and provided in Chapter 3.

In Chapter 3 we were unable to calculate confidence intervals for t_p for the two-stage model because a joint likelihood between β and μ_i did not exist. The Weibull NLMM solves this problem. Table 5.5 compares the independent analysis percentile estimates to the NLMM percentile estimates and provides corresponding confidence intervals. The percentile differences between the two modeling methods are not statistically different for the Zelen data illustrated by the overlap in the confidence intervals. The confidence intervals are always wider for the NLMM analysis because we are properly modeling the experimental error.

5.5 Conclusions of Design Monte Carlo Simulation Study

In this chapter we highlight the importance of randomization, replication, and experimental error estimation for reliability data. For a 2^2 factorial experiment with sub-sampling we illustrate that at least 4 replicates are required for a quality estimate of the model coefficients

Table 5.5: Percentile Estimates and Corresponding Confidence Intervals for Independent Analysis and NLMM Analysis. Percentiles are in hours.

Voltage (Volts)	Temperature (°C)	Independent Analysis				NLMM Analysis			
		$t_{.01}$	$t_{.05}$	$t_{.10}$	$t_{.50}$	$t_{.01}$	$t_{.05}$	$t_{.10}$	$t_{.50}$
200	170	280.8 [246.6, 319.6]	508.0 [475.7, 542.4]	660.1 [629.5, 692.2]	1309.9 [1271.7, 1349.3]	285.1 [218.2, 372.6]	512.4 [458.3, 573.0]	663.9 [619.6, 711.3]	1307.3 [1264.3, 1351.9]
200	180	210.3 [184.5, 239.6]	380.5 [356.5, 406.1]	494.4 [472.0, 517.9]	981.1 [955.1, 1007.8]	211.8 [179.5, 250.0]	380.8 [356.0, 407.2]	493.3 [469.3, 518.4]	971.4 [896.5, 1052.6]
250	170	208.9 [185.4, 235.4]	378.0 [357.8, 399.4]	491.2 [473.5, 509.5]	974.8 [957.3, 992.6]	212.3 [160.7, 280.6]	381.7 [340.8, 427.4]	494.5 [462.8, 528.3]	973.8 [955.0, 992.9]
250	180	156.5 [138.5, 176.8]	283.1 [267.7, 299.5]	367.9 [354.4, 381.8]	730.1 [717.6, 742.7]	157.8 [133.4, 186.7]	283.6 [267.2, 301.0]	367.4 [353.7, 381.7]	723.5 [683.2, 766.2]
300	170	155.5 [137.9, 175.3]	281.3 [266.3, 297.1]	365.5 [352.5, 379.0]	725.3 [713.0, 737.9]	158.2 [116.8, 214.2]	284.3 [250.2, 323.1]	368.3 [341.1, 397.6]	725.3 [711.9, 738.9]
300	180	116.4 [102.8, 131.8]	210.7 [198.8, 223.2]	273.8 [263.4, 284.5]	543.3 [533.6, 553.1]	117.5 [97.8, 141.2]	211.2 [197.8, 225.5]	273.7 [263.1, 284.7]	538.9 [513.9, 565.2]
350	170	115.7 [101.5, 131.9]	209.3 [196.1, 223.4]	272.0 [259.6, 284.9]	539.7 [525.4, 554.5]	117.8 [83.8, 165.6]	211.7 [181.2, 247.4]	274.3 [248.2, 303.2]	540.2 [523.7, 557.2]
350	180	86.6 [75.6, 99.4]	156.8 [146.2, 168.2	203.7 [193.6, 214.3]	404.3 [392.5, 416.3]	87.5 [70.8, 108.2]	157.3 [144.6, 171.2]	203.8 [193.1, 215.2]	401.4 [381.4, 422.4]

of a NLMM. That many replicates also ensures confidence in our statistical inferences on the model parameters.

Additionally, this chapter illustrates the importance of properly modeling the randomization scheme. For the Zelen data, if the randomization scheme is ignored and the data are analyzed like they came from a CRD, we underestimate the standard errors of the parameters. This has a negative impact on inference because our coefficient p-values will be smaller than our experimental protocol dictates. If a practitioner were interested in reliability improvement this underestimate of the p-value might lead them to conclude a particular factor decreases product reliability when in fact its impact is negligible.

Chapter 6

Conclusions and Future Work

This research is seminal because it brings together concepts from reliability analysis and statistical design of experiments that have never been combined before. The randomization theory behind statistical design of experiments demands that one take into account the randomization scheme in the modeling of data. However, before this dissertation, methods for modeling data from experimental designs more complex than a completely randomized design did not exist. This body of work provides two new analysis methods that can properly model data from a sub-sampling experimental design.

The first method is a two-stage modeling approach that properly models the experimental error for a sub-sampling DOE. The first method is nice because it can be implemented immediately by practitioners with little programming experience. We provide Minitab output to illustrate that the analysis can be completed entirely in Minitab if an equal variance assump-

tion is made between test stands. The major drawback to the two-stage analysis is that it does not provide a joint likelihood for all of the model parameters. Therefore, inferences on functions containing both the shape and scale parameters are impossible, because while point estimates can be calculated, calculating standard errors for these combination parameters is impossible for this analysis method. Additionally, the two-stage analysis method estimates β using the fully saturated model for the scale parameter. Since the two parameters of the Weibull distribution are correlated, model specification of the scale parameter impacts the estimate of the Weibull shape parameter.

The second analysis method provided in this dissertation is a nonlinear mixed model analysis. This method provides a joint likelihood for all of the parameters of the Weibull distribution. However, the incorporation of a random effect leads to a more complicated likelihood function that needs to be approximated with numerical quadrature. While this analysis is not as straightforward as the two-stage analysis, SAS does provide a procedure for handling the Weibull NLMM if one codes the log-likelihood. We illustrate that the NLMM analysis is robust to model misspecification and increasing levels of variance in the random effect when compared to the independent analysis that is currently implemented by the reliability community.

In addition to providing two new analysis methods, this dissertation provides two testing methods for inference on the parameters of the Weibull distribution. Through a study on the 2^2 factorial design, we investigate when large sample approximations are appropriate for the Weibull distribution. The principles of experimental design are also investigated through

the 2^2 factorial design.

This research is a spring board for future research topics. In this research we apply the new analysis methods to life test data. A clear future extension of this work is to apply these new analysis techniques to accelerated life tests that include an extra element of complexity due to the relationship between the accelerating factor and the log-scale parameter. Additionally, the potential for future research into statistical designs for reliability data is endless. We explored a replicated 2^2 factorial in this dissertation containing sub-sampling. Future research on robust designs and optimal designs are clear extensions on the limited design analysis contained in this dissertation.

Another area for future research is applying the Weibull nonlinear mixed model to other experimental designs in addition to the sub-sampling design. In generalized linear mixed models, random effects have been used to model blocking, split plot designs, and experimental variable selected at random. Random effects allow the user to generalize inferences to more than the levels selected in the experiment. The Kevlar fiber strand experiment provided by Gerstle and Kunz (1983) is a prime example of how these methods can be used for other types of experimental designs.

Finally, another complicating factor highlighted in this research that is ripe for future research is the impact of model misspecification in the log-scale parameter. Throughout our research we noted how the correlation between the Weibull shape parameter, β, and scale parameter, η, lead to additionally complications in the analysis. For the Zelen data, we note that if we allow the scale parameter to be different for each test stand the estimate of the

shape parameter is much higher than if a model is fit in terms of temperature and voltage for the log-scale parameter. We provided a lack of fit test in this research. Implications of lack of fit and model misspecification for the Weibull NLMM need to be examined in more detail for reliability data.

Bibliography

[1] Abernethy, R. B. *The New Weibull Handbook Fifth Edition, Reliability and Statistical Analysis for Predicting Life, Safety, Supportability, Risk, Cost and Warranty Claims*. Robert B. Abernethy, 2004.

[2] Aerts, M., Janssen, P., and Veraverbeke, N. Bootstrapping regression quantiles. *Journal of Nonparametric Statistics 4* (1994), 1–20.

[3] Bisgaard, S. The design and analysis of $2^{k-p} \times 2^{q-r}$ split plot experiments. *Journal of Quality Technology 32*, 1 (2000), 39–56.

[4] Box, G. E. P., and Wilson, K. B. On the experimental attainment of optimum conditions. *Journal of the Royal Statistical Society Series B (Methodological) 13*, 1 (1951), 1–45.

[5] Breslow, N., and Clayton, D. Approximate Inference in Generalized Linear Mixed Models. *Journal of the American Statistical Association 88*, 421 (1993), 9–25.

[6] Breslow, N., and Lin, X. Bias Correction in Generalized Linear Mixed Models with a Single-Component of Dispersion. *Biometrika 82*, 1 (1995), 81–91.

[7] Bullington, R., Lovin, S., Miller, D. M., and Woodall, W. H. Improvement of an industrial thermostat using designed experiments. *Journal of Quality Technology 25* (1993), 262–270.

[8] Cornell, J. A. Analyzing data from mixture experiments containing process variables: A split-plot approach. *Journal of Quality Technology 20*, 1 (1988), 2–23.

[9] Efron, B. Censored data and the bootstrap. *Journal of the American Statistical Association 76*, 374 (1981), 312–319.

[10] Escobar, L. A., and Meeker, W. Q. Fisher information matrix for the extreme value, normal and logisitc distributions and censored data. *Applied Statistics*, 43 (1994), 533–540.

[11] Escobar, L. A., and Meeker, W. Q. Planning accelerated life tests with two or more experimental factors. *Technometrics*, 37 (1995), 411–427.

[12] Feiveson, A., and Kulkarni, P. Reliability of Space-Shuttle Pressure Vessels with Random Batch Effect. *Technometrics 42*, 4 (2000), 332–344.

[13] Gerstle, F., and Kunz, S. *Prediction of Long Term Failure in Kevlar 49 Composite.* American Society for Testing and Materials, 1983, pp. 263–292.

[14] Hamada, M. Using statistically designed experiments to improve reliability and to achieve robust reliability. *IEEE Transactions on Reliability 44*, 2 (June 1995), 206–215.

[15] Hamada, M., and Nelder, J. A. Generalized linear models for quality-improvement experiments. *Journal of Quality Technology 29*, 3 (1997), 292–304.

[16] Hossain, A., and Howlader, H. A. Unweighted least squares estimation of weibull parameters. *Journal of Statistical Computation and Simulation 54* (1996), 265–271.

[17] Jones, B., and Nachtsheim, C. J. Split-plot designs: What, why and how. *Journal of Quality Technology 41*, 4 (2009), 340–361.

[18] Kackar, R. N. Off-line quality control, parameter design and the taguchi method. *Journal of Quality Technology 17*, 4 (1985), 176–188.

[19] Kowalski, S. M., Cornell, J. A., and Vining, G. G. Split-plot designs and estimation methods for mixture experiments with process variables. *Technometrics 44*, 1 (2002), 72–79.

[20] Kowalski, S. M., Parker, P. A., and Vining, G. G. Tutorial: Industrial split-plot experiments. *Quality Engineering 19* (2007), 1–15.

[21] Lawless, J. F. *Statistical Models and Methods for Lifetime Data*, second edition ed. John Wiley and Sons, Inc., 2003.

[22] Leon, R., Li, Y., Guess, F., and Sawhney, R. Effect of Not Having Homogeneous Test Units in Accelerated Life Tests. *Journal of Quality Technology 41*, 3 (2009), 241–246.

[23] Leon, R., Ramachandran, R., Ashby, A., and Thyagarajan, J. Bayesian Modeling of Accelerated Life Tests with Random Effect. *Journal of Quality Technology 39*, 1 (2009), 3–16.

[24] Lewis, S. L., Montgomery, D. C., and Myers, R. H. Examples of design experiments with nonnormal responses. *Journal of Quality Technology 33*, 3 (2001), 265–278.

[25] Lin, X., and Breslow, N. Bias correction in generalized linear mixed models with multiple components of dispersion. *Journal of the American Statistical Association 91*, 435 (1996), 1007–1016.

[26] Lindstrom, M., and Douglas, D. Nonliear Mixed Effects Models for Repeated Measures Data. *Biometrics 46*, 1 (1990), 673–687.

[27] McCool, J. I. The analysis of a two way factorial design with weibull response. *Communications in Statistics - Simulation and Computation 25*, 1 (1996), 263–286.

[28] McCool, J. I., and Baran, G. The analysis of 2×2 factorial fracture experiments with brittle materials. *Journal of Material Science 34* (1999), 3181–3188.

[29] McCulloch, C. E., and Searle, S. R. *Generalized, Linear, and Mixed Models*. John Wiley and Sons, Inc., 2001.

[30] Meeker, W. Q., and Escobar, L. A. A review of recent research and current issues in accelerated testing. *International Statistical Review 61*, 1 (1993), 147–168.

[31] Meeker, W. Q., and Escobar, L. A. *Statistical Methods for Reliability Data*. John Wiley and Sons, Inc., 1998.

[32] Myers, R. H. Response surface methodology - current status and future directions. *Journal of Quality Technology 31*, 1 (1999), 30–44.

[33] Myers, R. H., and Montgomery, D. C. A tutorial on generalized linear models. *Journal of Quality Technology 29*, 3 (1997), 274–291.

[34] Myers, R. H., and Montgomery, D. C. *Response Surface Methodology*, second ed. John Wiley and Sons, Inc., 2002.

[35] Myers, R. H., Montgomery, D. C., and Vining, G. G. *Generalized Linear Models with Applications in Engineering and the Sciences*. John Wiley and Sons Inc., 2002.

[36] Myers, R. H., Montgomery, D. C., Vining, G. G., Borror, C., and Kowalski, S. M. Response surface methodology: A retrospective and literature survey. *Journal of Quality Technology 36*, 1 (2004), 53–77.

[37] Nelder, J. A., and Wedderburn, R. W. Generalized linear models. *Journal of the Royal Statistical Society A*, 135 (1972), 370–384.

[38] Nelder, J. A., and Wedderburn, R. W. M. Generalized linear models. *Journal of the Royal Statistical Society Series A 135* (1972), 370–384.

[39] Nelson, W. *Accelerate Testing: Statistical Models, Test Plans and Data Analyses*. John Wiley and Sons, 1990.

[40] Pinheiro, J., and Bates, D. Approximations to the Log-Likelihood Function in the Nonlinear Mixed-Effects Model. *Journal of Computational and Graphical Statistics 4*, 1 (1995), 12–35.

[41] Raudenbush, S., Yang, M., and Yosef, M. Maximum Likelihood for Generalized Linear Models with Nested Random Effects via High-Order, Multivariate Laplace Approximation. *Journal of Computational and Graphical Statistics 9*, 1 (2000), 141–157.

[42] SAS Institute Inc. *SAS/STAT 9.2 Users Guide*. Cary, NC, 2008.

[43] Solomon, P., and Cox, D. Nonlinear Component of Variance Models. *Biometrika 79*, 1 (1992), 1–11.

[44] Somboonsavatdee, A., Nair, V. N., and Sen, A. Graphical estimators from probability plots with right-censored data. *Technometrics 49*, 4 (2007), 420–429.

[45] Taguchi, G. *System of Experimental Design*. Unipub/Kraus Int'l Publ., 1987.

[46] Vining, G. G., Kowalski, S. M., and Montgomery, D. C. Response surface designs within a split-plot structure. *Journal of Quality Technology 37*, 2 (2005), 115–129.

[47] Wikipedia. Bathtub curve — Wikipedia, the free encyclopedia, 2006. [Online; accessed 29-March-2009].

[48] Zelen, M. Factorial experiments in life testing. *Technometrics 1*, 3 (1959), 269–288.

Appendix A

Derivation of Hessian Matrix for Sub-sampling Random Effects Model

One key benefit of using numerical quadrature is that it provides a closed form approximation of the log-likelihood for the NLMM. In this Appendix we show that second derivatives exist for the log-likelihood. The existence of these derivatives makes finding an approximate asymptotic covariance matrix for the parameter estimates possible. This provides one method of inference, Wald's Method, on the model parameters.

A.1 Uncensored Data

The approximate log-likelihood for uncensored data under the Gauss-Hermite approximation is:

$$\ell(\beta, \boldsymbol{\theta}|Data) \approx \sum_{i=1}^{m} \log \left(\frac{1}{\sqrt{\pi}} \sum_{k=1}^{n_k} \left[\prod_{j=1}^{n_i} g(t_{ij}|\sqrt{2}\sigma_u q_{k_i}) w_k \right] \right)$$

where $g(t_{ij}|\sqrt{2}\sigma_u q_{k_i}) = \frac{\beta}{t_{ij}} \exp\left[z_{ijk} - \exp\left(z_{ijk}\right)\right]$, $z_{ijk} = \beta\left[\log\left(t_{ij}\right) - \mu_i - \sqrt{2}\sigma_u q_{k_i}\right]$, n_k is the number of quadrature points, q_k are the evaluation points found from the roots of the Hermite polynomials, and w_k are the corresponding weights to the evaluation points given by:

$$w_k = \frac{2^{n-1} n! \sqrt{\pi}}{n^2 [H_{n-1}(q_k)]^2}$$

. For these derivations we assume a two factor linear regression model. However, these derivations easily extend to different model forms. Therefore, $\mu_i = \log(\eta_i) = \theta_0 + \theta_1 x_{1i} + \theta_2 x_{2i}$ Substituting in $g(t_{ij})$ we get the log-likelihood for uncensored data is:

$$\ell(\beta, \boldsymbol{\theta}|Data) \approx \sum_{i=1}^{m} \log \left(\frac{1}{\sqrt{\pi}} \sum_{k=1}^{n_k} \left[\left(\prod_{j=1}^{n_i} \frac{\beta}{t_{ij}} \right) \exp \left[\sum_{j=1}^{n_i} \left[z_{ijk} - \exp\left(z_{ijk}\right) \right] \right] \right] \right)$$

The following properties are useful in taking the derivatives:

$$\begin{aligned}
\frac{\partial z_{ijk}}{\partial \beta} &= \log(t_{ij}) - \mu_i - \sqrt{2}\sigma_u q_{k_i} = \text{Linear Predictor} = L.P. \\
\frac{\partial z_{ijk}}{\partial \theta_0} &= -\beta \\
\frac{\partial z_{ijk}}{\partial \theta_1} &= -\beta x_{1i} \\
\frac{\partial z_{ijk}}{\partial \theta_2} &= -\beta x_{2i} \\
\frac{\partial z_{ijk}}{\partial \sigma_u} &= \sqrt{2} q_{k_i} \beta
\end{aligned}$$

Now we can write out the partial derivatives of the log-likelihood for each parameter. We define sums after the derivatives for making the second derivatives easier to write down.

$$\begin{aligned}
\frac{\partial \ell(\beta,\boldsymbol{\theta})}{\partial \theta_0} &= \sum_{i=1}^{m}\left[\frac{\sum_{k=1}^{d}\left[w_k \exp\left[\sum_{j=1}^{n_i}\left(z_{ijk}-\exp(z_{ijk})\right)\right]\left[\sum_{j=1}^{n_i}\left(-\beta+\beta\exp(z_{ijk})\right)\right]\right]}{\sum_{k=1}^{d}\left[w_k \exp\left[\sum_{j=1}^{n_i}\left(z_{ijk}-\exp(z_{ijk})\right)\right]\right]}\right] \\
\frac{\partial \ell(\beta,\boldsymbol{\theta})}{\partial \theta_1} &= \sum_{i=1}^{m}\left[\frac{\sum_{k=1}^{d}\left[w_k \exp\left[\sum_{j=1}^{n_i}\left(z_{ijk}-\exp(z_{ijk})\right)\right]\left[\sum_{j=1}^{n_i}\left(-\beta x_{1i}+\beta x_{1i}\exp(z_{ijk})\right)\right]\right]}{\sum_{k=1}^{d}\left[w_k \exp\left[\sum_{j=1}^{n_i}\left(z_{ijk}-\exp(z_{ijk})\right)\right]\right]}\right] \\
\frac{\partial \ell(\beta,\boldsymbol{\theta})}{\partial \theta_2} &= \sum_{i=1}^{m}\left[\frac{\sum_{k=1}^{d}\left[w_k \exp\left[\sum_{j=1}^{n_i}\left(z_{ijk}-\exp(z_{ijk})\right)\right]\left[\sum_{j=1}^{n_i}\left(-\beta x_{2i}+\beta x_{2i}\exp(z_{ijk})\right)\right]\right]}{\sum_{k=1}^{d}\left[w_k \exp\left[\sum_{j=1}^{n_i}\left(z_{ijk}-\exp(z_{ijk})\right)\right]\right]}\right] \\
\frac{\partial \ell(\beta,\boldsymbol{\theta})}{\partial \sigma_u} &= \sum_{i=1}^{m}\left[\frac{\sum_{k=1}^{d}\left[w_k \exp\left[\sum_{j=1}^{n_i}\left(z_{ijk}-\exp(z_{ijk})\right)\right]\left[\sum_{j=1}^{n_i}\left(-\sqrt{2}x_k\beta+\sqrt{2}x_k\beta\exp(z_{ijk})\right)\right]\right]}{\sum_{k=1}^{d}\left[w_k \exp\left[\sum_{j=1}^{n_i}\left(z_{ijk}-\exp(z_{ijk})\right)\right]\right]}\right] \\
\frac{\partial \ell(\beta,\boldsymbol{\theta})}{\partial \beta} &= \sum_{i=1}^{m}\left[\frac{n_i\sum_{k=1}^{d}\left[w_k S1\right]+\beta\sum_{k=1}^{d}\left[w_k S1 * \left[\sum_{j=1}^{n_i}\left(L.P.-L.P.\exp(z_{ijk})\right)\right]\right]}{\beta\sum_{k=1}^{d}\left[w_k \exp\left[\sum_{j=1}^{n_i}\left(z_{ijk}-\exp(z_{ijk})\right)\right]\right]}\right]
\end{aligned}$$

Define the following sums:

$$\begin{aligned}
S1 &= \exp\left[\sum_{j=1}^{n_i}\left(z_{ijk}-\exp(z_{ijk})\right)\right] \\
S2 &= \sum_{j=1}^{n_i}\left(-\beta+\beta\exp(z_{ijk})\right) \\
S3 &= \sum_{j=1}^{n_i}\left(-\beta x_{1i}+\beta x_{1i}\exp(z_{ijk})\right) \\
S4 &= \sum_{j=1}^{n_i}\left(-\beta x_{2i}+\beta x_{2i}\exp(z_{ijk})\right) \\
S5 &= \sum_{j=1}^{n_i}\left(-\sqrt{2}q_k\beta+\sqrt{2}q_k\beta\exp(z_{ijk})\right) \\
S6 &= \sum_{j=1}^{n_i}\left(L.P.-L.P.\exp(z_{ijk})\right)
\end{aligned}$$

Now, we can calculate the second partial derivatives with respect to each of the parameters. We'll start with the pure second order derivatives. These derivatives invoke the quotient

rule, the product rule and the chain rule from calculus.

$$\frac{\partial \ell^2(\beta,\boldsymbol{\theta})}{\partial \theta_0^2} = \sum_{i=1}^{m}\left[\frac{\left[\sum_{k=1}^{d} w_k S1\right]\left[\sum_{k=1}^{d} w_k S1 \sum_{j=1}^{n_i}\left(-\beta^2 \exp(z_{ijk})\right) + w_k S1 * S2^2\right] - \left[\sum_{k=1}^{d}\left[w_k S1 * S2\right]\right]^2}{\left[\sum_{k=1}^{d}\left[w_k S1\right]\right]^2}\right]$$

$$\frac{\partial \ell^2(\beta,\boldsymbol{\theta})}{\partial \theta_1^2} = \sum_{i=1}^{m}\left[\frac{\left[\sum_{k=1}^{d} w_k S1\right]\left[\sum_{k=1}^{d} w_k S1 \sum_{j=1}^{n_i}\left(-(\beta x_{1i})^2 \exp(z_{ijk})\right) + w_k S1 * S3^2\right] - \left[\sum_{k=1}^{d}\left[w_k S1 * S3\right]\right]^2}{\left[\sum_{k=1}^{d}\left[w_k S1\right]\right]^2}\right]$$

$$\frac{\partial \ell^2(\beta,\boldsymbol{\theta})}{\partial \theta_2^2} = \sum_{i=1}^{m}\left[\frac{\left[\sum_{k=1}^{d} w_k S1\right]\left[\sum_{k=1}^{d} w_k S1 \sum_{j=1}^{n_i}\left(-(\beta x_{2i})^2 \exp(z_{ijk})\right) + w_k S1 * S4^2\right] - \left[\sum_{k=1}^{d}\left[w_k S1 * S4\right]\right]^2}{\left[\sum_{k=1}^{d}\left[w_k S1\right]\right]^2}\right]$$

$$\frac{\partial \ell^2(\beta,\boldsymbol{\theta})}{\partial \sigma_u^2} = \sum_{i=1}^{m}\left[\frac{\left[\sum_{k=1}^{d} w_k S1\right]\left[\sum_{k=1}^{d} w_k S1 \sum_{j=1}^{n_i}\left(-2(\beta q_k)^2 \exp(z_{ijk})\right) + w_k S1 * S5^2\right] - \left[\sum_{k=1}^{d}\left[w_k S1 * S5\right]\right]^2}{\left[\sum_{k=1}^{d}\left[w_k S1\right]\right]^2}\right]$$

$$\frac{\partial \ell^2(\beta,\boldsymbol{\theta})}{\partial \beta^2} = \sum_{i=1}^{m}\left[\frac{\left[\sum_{k=1}^{d} w_k S1\right] * Der1 - \left[n_i \sum_{k=1}^{d}\left[w_k S1\right] + \beta \sum_{k=1}^{d}\left[w_k S1 * S6\right]\right] * Der2}{\left[\beta \sum_{k=1}^{d}\left[w_k S1\right]\right]^2}\right]$$

where D1 and D2 are derivatives given by:

$$\begin{aligned} D1 &= (n_i+1)\sum_{k=1}^{d}(w_k S1 * S6) + \beta \sum_{k=1}^{d}\left(w_k * S1 * S6 * \sum_{j=1}^{n_i}(L.P.)\right) \\ &- \beta \sum_{k=1}^{d}\left(w_k * S1 * S6 * \sum_{j=1}^{n_i}(L.P.\exp(z_{ijk}))\right) \\ &- \beta \sum_{k=1}^{d}\left(w_k * S1 * \sum_{j=1}^{n_i}(L.P.)^2 \exp(z_{ijk})\right) \end{aligned}$$

$$D2 = \sum_{k=1}^{d}(w_k S1) + \beta \sum_{k=1}^{d}(w_k S1 S6)$$

This concludes the pure second order derivatives, now we can move onto the mixed second

order derivatives.

$$\frac{\partial \ell^2(\beta,\boldsymbol{\theta})}{\partial\theta_0\partial\theta_1}=\sum_{i=1}^{m}\left[\frac{\left[\sum_{k=1}^{d}w_kS1\right]\sum_{k=1}^{d}w_k\left[S1*S7+S1*S2*S3\right]-\sum_{k=1}^{d}\left[w_kS1*S2\right]\sum_{k=1}^{d}\left[w_kS1*S3\right]}{\left[\sum_{k=1}^{d}\left[w_kS1\right]\right]^2}\right]$$

where $S7=\sum_{j=1}^{n_i}\left(-\beta^2x_{1i}\exp(z_{ijk})\right)$

$$\frac{\partial \ell^2(\beta,\boldsymbol{\theta})}{\partial\theta_0\partial\theta_2}=\sum_{i=1}^{m}\left[\frac{\left[\sum_{k=1}^{d}w_kS1\right]\sum_{k=1}^{d}w_k\left[S1*S8+S1*S2*S4\right]-\sum_{k=1}^{d}\left[w_kS1*S2\right]\sum_{k=1}^{d}\left[w_kS1*S4\right]}{\left[\sum_{k=1}^{d}\left[w_kS1\right]\right]^2}\right]$$

where $S8=\sum_{j=1}^{n_i}\left(-\beta^2x_{2i}\exp(z_{ijk})\right)$

$$\frac{\partial \ell^2(\beta,\boldsymbol{\theta})}{\partial\theta_0\partial\sigma_u}=\sum_{i=1}^{m}\left[\frac{\left[\sum_{k=1}^{d}w_kS1\right]\sum_{k=1}^{d}w_k\left[S1*S9+S1*S2*S5\right]-\sum_{k=1}^{d}\left[w_kS1*S2\right]\sum_{k=1}^{d}\left[w_kS1*S5\right]}{\left[\sum_{k=1}^{d}\left[w_kS1\right]\right]^2}\right]$$

where $S9=\sum_{j=1}^{n_i}\left(-\sqrt{2}q_k\beta^2\exp(z_{ijk})\right)$

$$\frac{\partial \ell^2(\beta,\boldsymbol{\theta})}{\partial\theta_0\partial\beta}=\sum_{i=1}^{m}\left[\frac{\left[\sum_{k=1}^{d}w_kS1\right]\sum_{k=1}^{d}w_k\left[S1*S10+S1*S2*S6\right]-\sum_{k=1}^{d}\left[w_kS1*S2\right]\sum_{k=1}^{d}\left[w_kS1*S6\right]}{\left[\sum_{k=1}^{d}\left[w_kS1\right]\right]^2}\right]$$

where $S10=\sum_{j=1}^{n_i}\left(-1+\exp(z_{ijk})+z_{ijk}\exp(z_{ijk})\right)$

$$\frac{\partial \ell^2(\beta,\boldsymbol{\theta})}{\partial\theta_1\partial\theta_2}=\sum_{i=1}^{m}\left[\frac{\left[\sum_{k=1}^{d}w_kS1\right]\sum_{k=1}^{d}w_k\left[S1*S11+S1*S3*S4\right]-\sum_{k=1}^{d}\left[w_kS1*S3\right]\sum_{k=1}^{d}\left[w_kS1*S4\right]}{\left[\sum_{k=1}^{d}\left[w_kS1\right]\right]^2}\right]$$

where $S11=\sum_{j=1}^{n_i}\left(-\beta^2x_{1i}x_{2i}\exp(z_{ijk})\right)$

$$\frac{\partial \ell^2(\beta,\boldsymbol{\theta})}{\partial\theta_1\partial\sigma_u}=\sum_{i=1}^{m}\left[\frac{\left[\sum_{k=1}^{d}w_kS1\right]\sum_{k=1}^{d}w_k\left[S1*S12+S1*S3*S5\right]-\sum_{k=1}^{d}\left[w_kS1*S3\right]\sum_{k=1}^{d}\left[w_kS1*S5\right]}{\left[\sum_{k=1}^{d}\left[w_kS1\right]\right]^2}\right]$$

where $S12 = \sum_{j=1}^{n_i} \left(-\sqrt{2} q_k \beta^2 x_{1i} \exp(z_{ijk})\right)$

$$\frac{\partial \ell^2(\beta, \boldsymbol{\theta})}{\partial \theta_1 \partial \beta} = \sum_{i=1}^{m} \left[\frac{\left[\sum_{k=1}^{d} w_k S1\right] \sum_{k=1}^{d} w_k \left[S1 * S13 + S1 * S3 * S6\right] - \sum_{k=1}^{d} \left[w_k S1 * S3\right] \sum_{k=1}^{d} \left[w_k S1 * S6\right]}{\left[\sum_{k=1}^{d} \left[w_k S1\right]\right]^2} \right]$$

where $S13 = \sum_{j=1}^{n_i} \left(-x_{1i} + x_{1i} \exp(z_{ijk}) + x_{1i} z_{ijk} \exp(z_{ijk})\right)$

$$\frac{\partial \ell^2(\beta, \boldsymbol{\theta})}{\partial \theta_2 \partial \sigma_u} = \sum_{i=1}^{m} \left[\frac{\left[\sum_{k=1}^{d} w_k S1\right] \sum_{k=1}^{d} w_k \left[S1 * S14 + S1 * S4 * S5\right] - \sum_{k=1}^{d} \left[w_k S1 * S4\right] \sum_{k=1}^{d} \left[w_k S1 * S5\right]}{\left[\sum_{k=1}^{d} \left[w_k S1\right]\right]^2} \right]$$

where $S14 = \sum_{j=1}^{n_i} \left(-\sqrt{2} q_k \beta^2 x_{2i} \exp(z_{ijk})\right)$

$$\frac{\partial \ell^2(\beta, \boldsymbol{\theta})}{\partial \theta_2 \partial \beta} = \sum_{i=1}^{m} \left[\frac{\left[\sum_{k=1}^{d} w_k S1\right] \sum_{k=1}^{d} w_k \left[S1 * S15 + S1 * S4 * S6\right] - \sum_{k=1}^{d} \left[w_k S1 * S4\right] \sum_{k=1}^{d} \left[w_k S1 * S6\right]}{\left[\sum_{k=1}^{d} \left[w_k S1\right]\right]^2} \right]$$

where $S15 = \sum_{j=1}^{n_i} \left(-x_{2i} + x_{2i} \exp(z_{ijk}) + x_{2i} z_{ijk} \exp(z_{ijk})\right)$

$$\frac{\partial \ell^2(\beta, \boldsymbol{\theta})}{\partial \sigma_u \partial \beta} = \sum_{i=1}^{m} \left[\frac{\left[\sum_{k=1}^{d} w_k S1\right] \sum_{k=1}^{d} w_k \left[S1 * S16 + S1 * S5 * S6\right] - \sum_{k=1}^{d} \left[w_k S1 * S5\right] \sum_{k=1}^{d} \left[w_k S1 * S6\right]}{\left[\sum_{k=1}^{d} \left[w_k S1\right]\right]^2} \right]$$

where $S16 = \sum_{j=1}^{n_i} \left(-x_{2i} + x_{2i} \exp(z_{ijk}) + x_{2i} z_{ijk} \exp(z_{ijk})\right)$ This concludes the second order derivatives for the uncensored data case.

A.2 Right Censored

The right censored data case proves to be even more challenging because of the increase complexity in the likelihood function. The approximate log-likelihood for right censored

data using Gauss-Hermite approximation is:

$$\ell(\beta, \boldsymbol{\theta}|Data) \approx \sum_{i=1}^{m} \log\left(\frac{1}{\sqrt{\pi}} \sum_{k=1}^{n_k}\left[\prod_{j=1}^{n_i} g(t_{ij}|\sqrt{2}\sigma_u q_{k_i})w_k\right]\right)$$

where $g(t_{ij}) = \left[\frac{\beta}{t_{ij}} \exp\left[z_{ijk} - \exp\left(z_{ijk}\right)\right]\right]^{\delta_{ij}} \left[\exp[-\exp\left(z_{ijk}\right)]\right]^{1-\delta_{ij}}$ and z_{ijk}, μ_i are the same as in the uncensored case. The following derivatives help in writing down the derivatives of the log-likelihood:

$$\begin{aligned}
\frac{\partial g(z_{ijk})}{\partial \theta_0} &= g(z_{ijk})\beta\left[-\delta_{ij} + \exp(z_{ijk})\right] \\
\frac{\partial g(z_{ijk})}{\partial \theta_1} &= g(z_{ijk})\beta x_{1i}\left[-\delta_{ij} + \exp(z_{ijk})\right] \\
\frac{\partial g(z_{ijk})}{\partial \theta_2} &= g(z_{ijk})\beta x_{2i}\left[-\delta_{ij} + \exp(z_{ijk})\right] \\
\frac{\partial g(z_{ijk})}{\partial \sigma_u} &= g(z_{ijk})\beta\sqrt{2}q_k\left[-\delta_{ij} + \exp(z_{ijk})\right] \\
\frac{\partial g(z_{ijk})}{\partial \beta} &= \frac{g(z_{ijk})}{\beta}\left[\delta_{ij} + \delta_{ij}z_{ijk} - z_{ijk}\exp(z_{ijk})\right]
\end{aligned}$$

The fact that each of these derivatives contains the original functions makes writing down the first derivatives using the product rule much easier. The first order derivatives are:

$$\begin{aligned}
\frac{\partial \ell(\beta, \boldsymbol{\theta}, \sigma_u)}{\partial \theta_0} &= \sum_{i=1}^{m}\left[\frac{\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta\left[-\delta_{ij} + \exp(z_{ijk})\right]}{\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})}\right] \\
\frac{\partial \ell(\beta, \boldsymbol{\theta}, \sigma_u)}{\partial \theta_1} &= \sum_{i=1}^{m}\left[\frac{\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta x_{1i}\left[-\delta_{ij} + \exp(z_{ijk})\right]}{\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})}\right] \\
\frac{\partial \ell(\beta, \boldsymbol{\theta}, \sigma_u)}{\partial \theta_2} &= \sum_{i=1}^{m}\left[\frac{\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta x_{2i}\left[-\delta_{ij} + \exp(z_{ijk})\right]}{\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})}\right] \\
\frac{\partial \ell(\beta, \boldsymbol{\theta}, \sigma_u)}{\partial \sigma_u} &= \sum_{i=1}^{m}\left[\frac{\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta\sqrt{2}q_k\left[-\delta_{ij} + \exp(z_{ijk})\right]}{\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})}\right] \\
\frac{\partial \ell(\beta, \boldsymbol{\theta}, \sigma_u)}{\partial \beta} &= \sum_{i=1}^{m}\left[\frac{\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\frac{1}{\beta}\left[\delta_{ij} + \delta_{ij}z_{ijk} - z_{ijk}\exp(z_{ijk})\right]}{\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})}\right]
\end{aligned}$$

The pure second order derivatives can be written down using the quotient rule:

$$\begin{aligned}
\frac{\partial \ell^2(\beta,\boldsymbol{\theta},\sigma_u)}{\partial \theta_0^2} &= \sum_{i=1}^{m}\left[\frac{\left(\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\right) D3 - \left(\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta\left[-\delta_{ij}+\exp(z_{ijk})\right]\right)^2}{\left(\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\right)^2}\right] \\
\frac{\partial \ell^2(\beta,\boldsymbol{\theta},\sigma_u)}{\partial \theta_1^2} &= \sum_{i=1}^{m}\left[\frac{\left(\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\right) D4 - \left(\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta x_{1i}\left[-\delta_{ij}+\exp(z_{ijk})\right]\right)^2}{\left(\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\right)^2}\right] \\
\frac{\partial \ell^2(\beta,\boldsymbol{\theta},\sigma_u)}{\partial \theta_2^2} &= \sum_{i=1}^{m}\left[\frac{\left(\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\right) D5 - \left(\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta x_{2i}\left[-\delta_{ij}+\exp(z_{ijk})\right]\right)^2}{\left(\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\right)^2}\right] \\
\frac{\partial \ell^2(\beta,\boldsymbol{\theta},\sigma_u)}{\partial \sigma_u^2} &= \sum_{i=1}^{m}\left[\frac{\left(\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\right) D6 - \left[\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta\sqrt{2}q_k\left[-\delta_{ij}+\exp(z_{ijk})\right]\right)^2}{\left(\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\right)^2}\right] \\
\frac{\partial \ell^2(\beta,\boldsymbol{\theta},\sigma_u)}{\partial \beta^2} &= \sum_{i=1}^{m}\left[\frac{\left(\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\right) D7 - \left(\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\frac{1}{\beta}\left[\delta_{ij}+\delta_{ij}z_{ijk}-z_{ijk}\exp(z_{ijk})\right]\right)^2}{\left(\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\right)^2}\right]
\end{aligned}$$

where $D3$, $D4$, $D4$, $D5$, $D6$, $D7$ are derivatives given by:

$$\begin{aligned}
D3 &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta^2\left[\delta_{ij}^2 - 2\delta_{ij}\exp(z_{ijk}) + \exp(z_{ijk})^2 - \exp(z_{ijk})\right] \\
D4 &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta^2 x_{1i}^2\left[\delta_{ij}^2 - 2\delta_{ij}\exp(z_{ijk}) + \exp(z_{ijk})^2 - \exp(z_{ijk})\right] \\
D5 &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta^2 x_{2i}^2\left[\delta_{ij}^2 - 2\delta_{ij}\exp(z_{ijk}) + \exp(z_{ijk})^2 - \exp(z_{ijk})\right] \\
D6 &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})2\beta^2 q_k^2\left[\delta_{ij}^2 - 2\delta_{ij}\exp(z_{ijk}) + \exp(z_{ijk})^2 - \exp(z_{ijk})\right] \\
D7 &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} \frac{g(z_{ijk})}{\beta^2}\left[\delta_{ij}^2\left(1+2z_{ijk}+z_{ijk}^2\right) - \delta_{ij}\left(2z_{ijk}\exp(z_{ijk}) + 2z_{ijk}^2\exp(z_{ijk}) + 1\right) + z_{ijk}^2\left(\exp(z_{ijk})^2 - \exp(z_{ijk})\right)\right]
\end{aligned}$$

The mixed second order derivatives can all be expressed using the quotient rule as:

$$\frac{\partial \ell^2(\beta,\boldsymbol{\theta},\sigma_u)}{\partial P1 \partial P2} = \sum_{i=1}^{m}\left[\frac{\left(\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\right) * A - B * C}{\left(\sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\right)^2}\right]$$

where A, B and C are specified for each mixed partial derivative.

For $P1 = \theta_0$ and $P2 = \theta_1$:

$$\begin{aligned}
A &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta^2 x_{1i} \left[\delta_{ij}^2 - 2\delta_{ij}\exp(z_{ijk}) + \exp(z_{ijk})^2 - \exp(z_{ijk})\right] \\
B &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta \left[-\delta_{ij} + \exp(z_{ijk})\right] \\
C &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta x_{1i} \left[-\delta_{ij} + \exp(z_{ijk})\right]
\end{aligned}$$

For $P1 = \theta_0$ and $P2 = \theta_2$:

$$\begin{aligned}
A &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta^2 x_{2i} \left[\delta_{ij}^2 - 2\delta_{ij}\exp(z_{ijk}) + \exp(z_{ijk})^2 - \exp(z_{ijk})\right] \\
B &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta \left[-\delta_{ij} + \exp(z_{ijk})\right] \\
C &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta x_{2i} \left[-\delta_{ij} + \exp(z_{ijk})\right]
\end{aligned}$$

For $P1 = \theta_0$ and $P2 = \sigma_u$:

$$\begin{aligned}
A &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta^2\sqrt{2}q_k \left[\delta_{ij}^2 - 2\delta_{ij}\exp(z_{ijk}) + \exp(z_{ijk})^2 - \exp(z_{ijk})\right] \\
B &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta \left[-\delta_{ij} + \exp(z_{ijk})\right] \\
C &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta\sqrt{2}q_k \left[-\delta_{ij} + \exp(z_{ijk})\right]
\end{aligned}$$

For $P1 = \theta_0$ and $P2 = \beta$:

$$\begin{aligned}
A &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \left[\left(\exp(z_{ijk}) - \delta_{ij}\right)\left(\delta_{ij} + \delta_{ij}z_{ijk} - z_{ijk}\exp(z_{ijk})\right) - \delta_{ij} + \exp(z_{ijk}) + z_{ijk}\exp(z_{ijk})\right] \\
B &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\beta \left[-\delta_{ij} + \exp(z_{ijk})\right] \\
C &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk})\frac{1}{\beta} \left[\delta_{ij} + \delta_{ij}z_{ijk} - z_{ijk}\exp(z_{ijk})\right]
\end{aligned}$$

For $P1 = \theta_1$ and $P2 = \theta_2$:

$$\begin{aligned} A &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \beta^2 x_{1i} x_{2i} \left[\delta_{ij}^2 - 2\delta_{ij} \exp(z_{ijk}) + \exp(z_{ijk})^2 - \exp(z_{ijk})\right] \\ B &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \beta x_{1i} \left[-\delta_{ij} + \exp(z_{ijk})\right] \\ C &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \beta x_{2i} \left[-\delta_{ij} + \exp(z_{ijk})\right] \end{aligned}$$

For $P1 = \theta_1$ and $P2 = \sigma_u$:

$$\begin{aligned} A &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \beta^2 x_{1i} \sqrt{2} q_k \left[\delta_{ij}^2 - 2\delta_{ij} \exp(z_{ijk}) + \exp(z_{ijk})^2 - \exp(z_{ijk})\right] \\ B &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \beta x_{1i} \left[-\delta_{ij} + \exp(z_{ijk})\right] \\ C &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \beta \sqrt{2} q_k \left[-\delta_{ij} + \exp(z_{ijk})\right] \end{aligned}$$

For $P1 = \theta_1$ and $P2 = \beta$:

$$\begin{aligned} A &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \left[x_{1i} \left(\exp(z_{ijk}) - \delta_{ij}\right) \left(\delta_{ij} + \delta_{ij} z_{ijk} - z_{ijk} \exp(z_{ijk})\right) + x_{1i} \left(-\delta_{ij} + \exp(z_{ijk}) + z_{ijk} \exp(z_{ijk})\right)\right] \\ B &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \beta x_{1i} \left[-\delta_{ij} + \exp(z_{ijk})\right] \\ C &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \frac{1}{\beta} \left[\delta_{ij} + \delta_{ij} z_{ijk} - z_{ijk} \exp(z_{ijk})\right] \end{aligned}$$

For $P1 = \theta_2$ and $P2 = \sigma_u$:

$$\begin{aligned} A &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \beta^2 x_{2i} \sqrt{2} q_k \left[\delta_{ij}^2 - 2\delta_{ij} \exp(z_{ijk}) + \exp(z_{ijk})^2 - \exp(z_{ijk})\right] \\ B &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \beta x_{2i} \left[-\delta_{ij} + \exp(z_{ijk})\right] \\ C &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \beta \sqrt{2} q_k \left[-\delta_{ij} + \exp(z_{ijk})\right] \end{aligned}$$

For $P1 = \theta_2$ and $P2 = \beta$:

$$
\begin{aligned}
A &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \left[x_{2i} \left(\exp(z_{ijk}) - \delta_{ij} \right) \left(\delta_{ij} + \delta_{ij} z_{ijk} - z_{ijk} \exp(z_{ijk}) \right) + x_{2i} \left(-\delta_{ij} + \exp(z_{ijk}) + z_{ijk} \exp(z_{ijk}) \right) \right] \\
B &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \beta x_{2i} \left[-\delta_{ij} + \exp(z_{ijk}) \right] \\
C &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \frac{1}{\beta} \left[\delta_{ij} + \delta_{ij} z_{ijk} - z_{ijk} \exp(z_{ijk}) \right]
\end{aligned}
$$

For $P1 = \sigma_u$ and $P2 = \beta$:

$$
\begin{aligned}
A &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \left[\sqrt{2} q_k \left(\exp(z_{ijk}) - \delta_{ij} \right) \left(\delta_{ij} + \delta_{ij} z_{ijk} - z_{ijk} \exp(z_{ijk}) \right) + \sqrt{2} q_k \left(-\delta_{ij} + \exp(z_{ijk}) + z_{ijk} \exp(z_{ijk}) \right) \right] \\
B &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \beta \sqrt{2} q_k \left[-\delta_{ij} + \exp(z_{ijk}) \right] \\
C &= \sum_{k=1}^{d} w_k \prod_{j=1}^{n_i} g(z_{ijk}) \frac{1}{\beta} \left[\delta_{ij} + \delta_{ij} z_{ijk} - z_{ijk} \exp(z_{ijk}) \right]
\end{aligned}
$$

Appendix B

SAS and R Code for Weibull Nonlinear Mixed Model

B.1 R Code for Uncensored NLMM

```
#Code Uses exponential trick to avoid overflow and underflow problems

library(stats4)
#quadrature weights and corresponding points for 5 point quadrature
#(5 points are used for code compactness)
wk<-c(0.01995324, 0.39361932, 0.94530872, 0.39361932, 0.01995324)
xk<-c(-2.02018287, -0.95857246, 0, 0.95857246, 2.02018287)

#read dataset and assign variable names for Zelen data
data <- read.csv( file="C:\\...\\ZelenDataUncensored.csv" )
volt <- data[,1]
temp <- data[,2]
hours <- data[,3]
group <- data[,4]

#Define negative log-likelihood function in terms of parameters
LL <- function(beta=2.75, theta0=13.4, theta1=-.0059, theta2=-.029, log.sigma=log(.036)) {

sigma=exp(log.sigma)    #log(sigma) used for maximization to avoid negative variance solutions

mu1<-theta0+volt*theta1+temp*theta2+sqrt(2)*sigma*xk[1]
mu2<-theta0+volt*theta1+temp*theta2+sqrt(2)*sigma*xk[2]
mu3<-theta0+volt*theta1+temp*theta2+sqrt(2)*sigma*xk[3]
mu4<-theta0+volt*theta1+temp*theta2+sqrt(2)*sigma*xk[4]
mu5<-theta0+volt*theta1+temp*theta2+sqrt(2)*sigma*xk[5]

z1<-beta*(log(hours)-mu1)
z2<-beta*(log(hours)-mu2)
z3<-beta*(log(hours)-mu3)
z4<-beta*(log(hours)-mu4)
z5<-beta*(log(hours)-mu5)

partsums<-array(0, c(8))

for(i in 1:8){
```

```
e11<-sum(z1[((i-1)*4):(4*i)]-exp(z1[((i-1)*4):(4*i)]))
e12<-sum(z2[((i-1)*4):(4*i)]-exp(z2[((i-1)*4):(4*i)]))
e13<-sum(z3[((i-1)*4):(4*i)]-exp(z3[((i-1)*4):(4*i)]))
e14<-sum(z4[((i-1)*4):(4*i)]-exp(z4[((i-1)*4):(4*i)]))
e15<-sum(z5[((i-1)*4):(4*i)]-exp(z5[((i-1)*4):(4*i)]))

maxabs <- max(abs(e11), abs(e12), abs(e13), abs(e14), abs(e15))
maxnorm <- max(e11, e12, e13, e14, e15)

if (maxabs > maxnorm) c1 <- min(e11, e12, e13, e14, e15) else c1 <- maxnorm

h11 <- wk[1]/sqrt(pi)*exp(e11-c1)
h12 <- wk[2]/sqrt(pi)*exp(e12-c1)
h13 <- wk[3]/sqrt(pi)*exp(e13-c1)
h14 <- wk[4]/sqrt(pi)*exp(e14-c1)
h15 <- wk[5]/sqrt(pi)*exp(e15-c1)

h1 <- c(h11, h12, h13, h14, h15)

partsums[i] <- log(beta^4/(prod(hours[((i-1)*4):(4*i)])))+log(sum(h1))+c1
}


return(-(sum(partsums))) #Return negative log-likelihood
}

#Find MLEs using built in R - function
#mle() uses numerical derivatives - can be problematic
fit<-mle(LL,start=list(beta=3.617, theta0=13.1534, theta1=-.00626, theta2=-.02904,
log.sigma=log(.155)), method="BFGS", control=list(trace))

summary(fit)   #print fit summary
vcov(fit)      #store covariance estimate from mle function


#Hessian Calculations

#set values for hessian calculations to MLEs from above
beta<-coef(fit)[1]; theta0<-coef(fit)[1]; theta1<-coef(fit)[1]; theta2<-coef(fit)[1];
log.sigma<-coef(fit)[1];

sigma=exp(log.sigma)

mu1<-theta0+volt*theta1+temp*theta2+sqrt(2)*sigma*xk[1]
mu2<-theta0+volt*theta1+temp*theta2+sqrt(2)*sigma*xk[2]
mu3<-theta0+volt*theta1+temp*theta2+sqrt(2)*sigma*xk[3]
mu4<-theta0+volt*theta1+temp*theta2+sqrt(2)*sigma*xk[4]
mu5<-theta0+volt*theta1+temp*theta2+sqrt(2)*sigma*xk[5]

z1<-beta*(log(hours)-mu1)
z2<-beta*(log(hours)-mu2)
z3<-beta*(log(hours)-mu3)
z4<-beta*(log(hours)-mu4)
z5<-beta*(log(hours)-mu5)

z<-cbind(z1,z2,z3,z4,z5)  #create matrix of z-values

H=matrix(0,5,5)  #create empty Hessian matrix

#create vectors to store sums for each calculation
sums<-array(0, c(5, 23, 8))
der22<-array(0, c(8))
der23<-array(0, c(8))
der24<-array(0, c(8))
```

```
der25<-array(0, c(8))
der21<-array(0, c(8))
der33<-array(0, c(8))
der34<-array(0, c(8))
der35<-array(0, c(8))
der31<-array(0, c(8))
der44<-array(0, c(8))
der45<-array(0, c(8))
der41<-array(0, c(8))
der55<-array(0, c(8))
der51<-array(0, c(8))
der11<-array(0, c(8))


for(i in 1:8){

bottom<-0;
top2<-0; dtop22<-0; dbottom22<-0; dtop23<-0; dbottom23<-0; dtop24<-0; dbottom24<-0;
dtop25<-0; dbottom25<-0; dtop21<-0; dbottom21<-0;
top3<-0; dtop33<-0; dbottom33<-0; dtop34<-0; dbottom34<-0; dtop35<-0; dbottom35<-0;
dtop31<-0; dbottom31<-0;
top4<-0; dtop44<-0; dbottom44<-0; dtop45<-0; dbottom45<-0; dtop41<-0; dbottom41<-0;
top5<-0; dtop55<-0; dbottom55<-0; dtop51<-0; dbottom51<-0;
top1<-0; dtop11<-0; dbottom11<-0;



for(k in 1:5){

print(i);
sums[k,1,i]<-exp(sum(z[((i-1)*4+1):(i*4),k]-exp(z[((i-1)*4+1):(i*4),k])));
sums[k,2,i]<-sum(-beta+beta*exp(z[((i-1)*4+1):(i*4),k]));
sums[k,3,i]<-sum(-beta^2*exp(z[((i-1)*4+1):(i*4),k]));
sums[k,4,i]<-sum(-beta*volt[((i-1)*4+1):(i*4)]+
                  beta*volt[((i-1)*4+1):(i*4)]*exp(z[((i-1)*4+1):(i*4),k]));
sums[k,5,i]<-sum(-beta^2*volt[((i-1)*4+1):(i*4)]*exp(z[((i-1)*4+1):(i*4),k]));
sums[k,6,i]<-sum(-beta*sqrt(2)*xk[k]+beta*sqrt(2)*xk[k]*exp(z[((i-1)*4+1):(i*4),k]));
sums[k,7,i]<-sum(-2*(xk[k]*beta)^2*exp(z[((i-1)*4+1):(i*4),k]));
sums[k,8,i]<-sum(z[((i-1)*4+1):(i*4),k]/beta-z[((i-1)*4+1):(i*4),k]/beta
                   *exp(z[((i-1)*4+1):(i*4),k]));
sums[k,9,i]<-sum(-sqrt(2)*xk[k]+sqrt(2)*xk[k]*exp(z[((i-1)*4+1):(i*4),k])+
                  sqrt(2)*xk[k]*z[((i-1)*4+1):(i*4),k]*exp(z[((i-1)*4+1):(i*4),k]));
sums[k,10,i]<-sum(-(beta*volt[((i-1)*4+1):(i*4)])^2*exp(z[((i-1)*4+1):(i*4),k]));
sums[k,11,i]<-sum(-beta*temp[((i-1)*4+1):(i*4)]+beta*temp[((i-1)*4+1):(i*4)]
                   *exp(z[((i-1)*4+1):(i*4),k]));
sums[k,12,i]<-sum(-beta^2*temp[((i-1)*4+1):(i*4)]*exp(z[((i-1)*4+1):(i*4),k]));
sums[k,13,i]<-sum(-sqrt(2)*xk[k]*beta^2*exp(z[((i-1)*4+1):(i*4),k]));
sums[k,14,i]<-sum(-1+exp(z[((i-1)*4+1):(i*4),k])+z[((i-1)*4+1):(i*4),k]
                   *exp(z[((i-1)*4+1):(i*4),k]));
sums[k,15,i]<-sum(-beta^2*volt[((i-1)*4+1):(i*4)]*temp[((i-1)*4+1):(i*4)]
                   *exp(z[((i-1)*4+1):(i*4),k]));
sums[k,16,i]<-sum(-sqrt(2)*xk[k]*beta^2*volt[((i-1)*4+1):(i*4)]*exp(z[((i-1)*4+1):(i*4),k]));
sums[k,17,i]<-sum(-volt[((i-1)*4+1):(i*4)]+volt[((i-1)*4+1):(i*4)]*exp(z[((i-1)*4+1):(i*4),k])+
                  volt[((i-1)*4+1):(i*4)]*z[((i-1)*4+1):(i*4),k]*exp(z[((i-1)*4+1):(i*4),k]));
sums[k,18,i]<-sum(-beta^2*temp[((i-1)*4+1):(i*4)]*temp[((i-1)*4+1):(i*4)]
                   *exp(z[((i-1)*4+1):(i*4),k]));
sums[k,19,i]<-sum(-sqrt(2)*xk[k]*beta^2*temp[((i-1)*4+1):(i*4)]*exp(z[((i-1)*4+1):(i*4),k]));
sums[k,20,i]<-sum(-temp[((i-1)*4+1):(i*4)]+temp[((i-1)*4+1):(i*4)]*exp(z[((i-1)*4+1):(i*4),k])+
                  temp[((i-1)*4+1):(i*4)]*z[((i-1)*4+1):(i*4),k]*exp(z[((i-1)*4+1):(i*4),k]));
sums[k,21,i]<-sum((z[((i-1)*4+1):(i*4),k]/beta)^2*exp(z[((i-1)*4+1):(i*4),k]));
sums[k,22,i]<-sum((z[((i-1)*4+1):(i*4),k]/beta));
sums[k,23,i]<-sum((z[((i-1)*4+1):(i*4),k]/beta)*exp(z[((i-1)*4+1):(i*4),k]));
```

```
bottom<-bottom+wk[k]*sums[k,1,i];

top2<-top2+wk[k]*sums[k,1,i]*sums[k,2,i];
dtop22<-dtop22+wk[k]*(sums[k,1,i]*sums[k,3,i]+sums[k,1,i]*sums[k,2,i]^2);
dbottom22<-dbottom22+wk[k]*sums[k,1,i]*sums[k,2,i];

dtop23<-dtop23+wk[k]*(sums[k,1,i]*sums[k,5,i]+sums[k,1,i]*sums[k,4,i]*sums[k,2,i]);
dbottom23<-dbottom23+wk[k]*sums[k,1,i]*sums[k,4,i];

dtop24<-dtop24+wk[k]*(sums[k,1,i]*sums[k,12,i]+sums[k,1,i]*sums[k,11,i]*sums[k,2,i]);
dbottom24<-dbottom24+wk[k]*sums[k,1,i]*sums[k,11,i];

dtop25<-dtop25+wk[k]*(sums[k,1,i]*sums[k,13,i]+sums[k,1,i]*sums[k,6,i]*sums[k,2,i]);
dbottom25<-dbottom25+wk[k]*sums[k,1,i]*sums[k,6,i];

dtop21<-dtop21+wk[k]*(sums[k,1,i]*sums[k,14,i]+sums[k,1,i]*sums[k,8,i]*sums[k,2,i]);
dbottom21<-dbottom21+wk[k]*sums[k,1,i]*sums[k,8,i];

top3<-top3+wk[k]*sums[k,1,i]*sums[k,4,i];
dtop33<-dtop33+wk[k]*(sums[k,1,i]*sums[k,10,i]+sums[k,1,i]*sums[k,4,i]^2);
dbottom33<-dbottom33+wk[k]*sums[k,1,i]*sums[k,4,i];

dtop34<-dtop34+wk[k]*(sums[k,1,i]*sums[k,15,i]+sums[k,1,i]*sums[k,11,i]*sums[k,4,i]);
dbottom34<-dbottom34+wk[k]*sums[k,1,i]*sums[k,11,i];

dtop35<-dtop35+wk[k]*(sums[k,1,i]*sums[k,16,i]+sums[k,1,i]*sums[k,6,i]*sums[k,4,i]);
dbottom35<-dbottom35+wk[k]*sums[k,1,i]*sums[k,6,i];

dtop31<-dtop31+wk[k]*(sums[k,1,i]*sums[k,17,i]+sums[k,1,i]*sums[k,8,i]*sums[k,4,i]);
dbottom31<-dbottom31+wk[k]*sums[k,1,i]*sums[k,8,i];

top4<-top4+wk[k]*sums[k,1,i]*sums[k,11,i];
dtop44<-dtop44+wk[k]*(sums[k,1,i]*sums[k,18,i]+sums[k,1,i]*sums[k,11,i]^2);
dbottom44<-dbottom44+wk[k]*sums[k,1,i]*sums[k,11,i];

dtop45<-dtop45+wk[k]*(sums[k,1,i]*sums[k,19,i]+sums[k,1,i]*sums[k,6,i]*sums[k,11,i]);
dbottom45<-dbottom45+wk[k]*sums[k,1,i]*sums[k,6,i];

dtop41<-dtop41+wk[k]*(sums[k,1,i]*sums[k,20,i]+sums[k,1,i]*sums[k,8,i]*sums[k,11,i]);
dbottom41<-dbottom41+wk[k]*sums[k,1,i]*sums[k,8,i];

top5<-top5+wk[k]*sums[k,1,i]*sums[k,6,i];
dtop55<-dtop55+wk[k]*(sums[k,1,i]*sums[k,7,i]+sums[k,1,i]*sums[k,6,i]^2)
dbottom55<-dbottom55+wk[k]*sums[k,1,i]*sums[k,6,i]

dtop51<-dtop51+wk[k]*(sums[k,1,i]*sums[k,9,i]+sums[k,1,i]*sums[k,8,i]*sums[k,6,i]);
dbottom51<-dbottom51+wk[k]*sums[k,1,i]*sums[k,8,i];

ni<-4
top1<-top1+ni*wk[k]*sums[k,1,i]+beta*wk[k]*sums[k,1,i]*sums[k,8,i]
dtop11<-dtop11+(ni+1)*wk[k]*sums[k,1,i]*sums[k,8,i]+beta*wk[k]*sums[k,1,i]*sums[k,8,i]*sums[k,22,i]
        -beta*wk[k]*sums[k,1,i]*sums[k,8,i]*sums[k,23,i]-beta*wk[k]*sums[k,1,i]*sums[k,21,i]
dbottom11<-dbottom11+wk[k]*sums[k,1,i]+beta*wk[k]*sums[k,1,i]*sums[k,8,i]


}
der22[i]<-(bottom*dtop22-top2*dbottom22)/(bottom^2)
der23[i]<-(bottom*dtop23-top2*dbottom23)/(bottom^2)
der24[i]<-(bottom*dtop24-top2*dbottom24)/(bottom^2)
der25[i]<-(bottom*dtop25-top2*dbottom25)/(bottom^2)
der21[i]<-(bottom*dtop21-top2*dbottom21)/(bottom^2)
der33[i]<-(bottom*dtop33-top3*dbottom33)/(bottom^2)
der34[i]<-(bottom*dtop34-top3*dbottom34)/(bottom^2)
```

```
der35[i]<-(bottom*dtop35-top3*dbottom35)/(bottom^2)
der31[i]<-(bottom*dtop31-top3*dbottom31)/(bottom^2)
der44[i]<-(bottom*dtop44-top4*dbottom44)/(bottom^2)
der45[i]<-(bottom*dtop45-top4*dbottom45)/(bottom^2)
der41[i]<-(bottom*dtop41-top4*dbottom41)/(bottom^2)
der55[i]<-(bottom*dtop55-top5*dbottom55)/(bottom^2)
der51[i]<-(bottom*dtop51-top5*dbottom51)/(bottom^2)
der11[i]<-(beta*bottom*dtop11-top1*dbottom11)/(beta*bottom)^2

}
H[1,1]<--sum(der11)
H[1,2]<--sum(der21); H[2,1]<--sum(der21)
H[1,3]<--sum(der31); H[3,1]<--sum(der31)
H[1,4]<--sum(der41); H[4,1]<--sum(der41)
H[1,5]<--sum(der51); H[5,1]<--sum(der51)
H[2,2]<--sum(der22)
H[2,3]<--sum(der23); H[3,2]<--sum(der23)
H[2,4]<--sum(der24); H[4,2]<--sum(der24)
H[2,5]<--sum(der25); H[5,2]<--sum(der25)
H[3,3]<--sum(der33)
H[3,4]<--sum(der34); H[4,3]<--sum(der34)
H[3,5]<--sum(der35); H[5,3]<--sum(der35)
H[4,4]<--sum(der44)
H[4,5]<--sum(der45); H[5,4]<--sum(der45)
H[5,5]<--sum(der55)
print(H) #output Hessian matrix
```

B.2 R Code for Censored NLMM

```
#Censored Weibull with log sum of exponentials rules

library(stats4)

wk<-c(0.01995324, 0.39361932, 0.94530872, 0.39361932, 0.01995324)
xk<-c(-2.02018287, -0.95857246, 0, 0.95857246, 2.02018287)

data <- read.csv( file="C:\\...\\ZelenData.csv" )
volt <- data[,1]
temp <- data[,2]
hours <- data[,3]
group <- data[,4]
delta <- data[,5]

LL <- function(beta=2.75,theta0=13.4,theta1=-.0059,theta2=-.029,log.sigma=log(.036)){

#negative log-likelihood function

sigma=exp(log.sigma)

mu1<-theta0+volt*theta1+temp*theta2+sqrt(2)*sigma*xk[1]
mu2<-theta0+volt*theta1+temp*theta2+sqrt(2)*sigma*xk[2]
mu3<-theta0+volt*theta1+temp*theta2+sqrt(2)*sigma*xk[3]
mu4<-theta0+volt*theta1+temp*theta2+sqrt(2)*sigma*xk[4]
mu5<-theta0+volt*theta1+temp*theta2+sqrt(2)*sigma*xk[5]

z1<-beta*(log(hours)-mu1)
z2<-beta*(log(hours)-mu2)
z3<-beta*(log(hours)-mu3)
z4<-beta*(log(hours)-mu4)
```

```
z5<-beta*(log(hours)-mu5)

partsums<-array(0, c(8))

for(i in 1:8){

e11<-sum(z1[((i-1)*4):(4*i)]-exp(z1[((i-1)*4):(4*i)]))
e12<-sum(z2[((i-1)*4):(4*i)]-exp(z2[((i-1)*4):(4*i)]))
e13<-sum(z3[((i-1)*4):(4*i)]-exp(z3[((i-1)*4):(4*i)]))
e14<-sum(z4[((i-1)*4):(4*i)]-exp(z4[((i-1)*4):(4*i)]))
e15<-sum(z5[((i-1)*4):(4*i)]-exp(z5[((i-1)*4):(4*i)]))

maxabs <- max(abs(e11), abs(e12), abs(e13), abs(e14), abs(e15))
maxnorm <- max(e11, e12, e13, e14, e15)

if (maxabs > maxnorm) c1 <- min(e11, e12, e13, e14, e15) else c1 <- maxnorm

h11 <- wk[1]/sqrt(pi)*exp(e11-c1)
h12 <- wk[2]/sqrt(pi)*exp(e12-c1)
h13 <- wk[3]/sqrt(pi)*exp(e13-c1)
h14 <- wk[4]/sqrt(pi)*exp(e14-c1)
h15 <- wk[5]/sqrt(pi)*exp(e15-c1)

h1 <- c(h11, h12, h13, h14, h15)

partsums[i] <- log(beta^4/(prod(hours[((i-1)*4):(4*i)])))+log(sum(h1))+c1
}


return(-(sum(partsums)))
}

fit<-mle(LL,start=list(beta=3.617, theta0=13.1534, theta1=-.00626, theta2=-.02904,
log.sigma=log(.155)), method="BFGS", control=list(trace))

summary(fit)
vcov(fit5)

#Hessian Calculations are done similarly to uncensored case and are omitted
```

B.3 SAS Code for Censored NLMM

```
proc nlmixed data=work.data method=gauss noad noadscale QPOINTS=20 tech=quanew
             update=bfgs cov;
parms beta=2.78 theta0=6.7 theta1=-.44 logsigma=-3;
z = beta*(log(t)-theta0-theta1*volt - u);
f1= beta/t*exp(z-exp(z));
F2=exp(-exp(z));
ll=log(f1)*(Censored=0)+log(F2)*(Censored=1);
sigma2=exp(logsigma)**2;
model t ~general(ll);
random u ~ normal(0, sigma2) subject=group;
ods output ParameterEstimates=mydata.parmest;
run;
```

B.4 SAS Code for Random Effect Bootstrapping in NLMM

```
*Construct Resampled data-------------------------------------------------------------;

proc sort data=work.ZELENCENSORED;
by group;
run;

proc surveyselect data=work.ZELENCENSORED method=URS n=8 out=sample1 rep=10000 outhits;
strata group;
run;

proc sort data=work.sample1;
by Replicate;
run;


 proc nlmixed data=work.sample1 method=gauss noad noadscale QPOINTS=20 tech=quanew
              update=bfgs cov;
by Replicate;
parms beta=2.78 theta0=6.7 theta1=-.44 theta2=-.44 logsigma=-1.2;
z = beta*(log(hours)-theta0-theta1*voltcode-theta2*tempcode - u);
f1= beta*exp(z-exp(z));
F2=exp(-exp(z));
ll=log(f1)*(Censored=0)+log(F2)*(Censored=1);
sigma2=(exp(logsigma))**2;
model hours ~general(ll);
random u ~ normal(0, sigma2) subject=group;
ods output FitStatistics=work.loglikesample1;
run;

proc lifereg data=work.sample1;
by replicate;
model hours*Censored(1)=voltcode tempcode;
ods output ModelInfo=work.loglikesample1null;
run;



data work.loglikesample1;
set work.loglikesample1;
where Descr='-2 Log Likelihood';
model='alt';
altvalue=value;
drop value;
run;

data work.loglikesample1null;
set work.loglikesample1null;
where Label1='Log Likelihood';
model='null';
run;


data work.LRTsample1;
merge work.loglikesample1null work.loglikesample1;
by Replicate;
if altvalue = . then delete;
if cvalue1 = . then delete;
LRT=-2*cvalue1-altvalue;
run;
```

```
proc means data=work.lrtsample1 n;
var Replicate;
ods output Summary = work.replicatesize;
run;

data work.lrtdata;
merge work.lrtdata work.replicatesize;
run;

data work.test;
retain rep replicate teststat;
set work.lrtdata;
n = replicate_n;

do replicate = 1 to n;
rawteststat=LRT;
output;
end;

drop LRT replicate_n;
run;

data work.pvalue;
merge work.lrtsample1 work.test;
count=LRT>=rawteststat;
run;

proc means data=work.pvalue n mean;
var count;
ods output summary = work.pvalues;
run;
```