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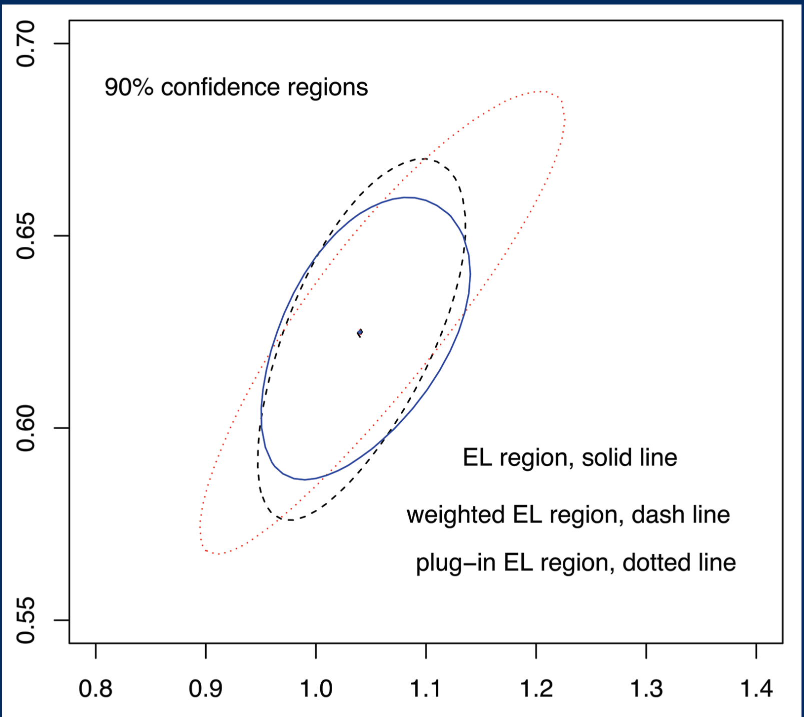

Mai Zhou

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Preface

The first book on empirical likelihood was published in 2001 (by Owen and also from CRC), thirteen years after Owen published his first paper on empirical likelihood in 1988 [78].

This fascinating methodology attracted a lot of researchers and has been under rapid development ever since. Numerous papers have been published since then and the list is getting longer every day.

It is now fourteen years since the publication of Owen's 2001 book on empirical likelihood. I feel the time is perhaps ripe for another book on empirical likelihood.

Aside from the obvious accumulation of research progress in the fourteen years since, another obvious development is the vastly improved computing power and universal availability of computers. No longer are expensive workstations in the labs available only to a few. They are everywhere and in every student's backpack.

During the last 14 years, the software R became the most popular choice of language among statistics researchers, and went from version 1.x.x to 3.x.x. I feel the easy-to-use, widely available R software for calculating empirical likelihood will boost the everyday use of empirical likelihood and in turn stimulate more research in this area.

This book includes many worked out examples with the associated R code. You can copy and paste them into an R command window.

The R packages used in this book include `emplik`, `survival`, `KMsurv`, `ELYP`. We also briefly mention related packages `km.ci`, `kmc`, `gmm`, `rms`, `el.convex`. The latter group of packages is not crucial when reading this book. The package `emplik` is version 1.01 at the time of writing this book. This package has over 12 years of history. On the other hand, the package `ELYP` is less refined and is version 0.72.

We use the `survival` package for both its datasets and some of the estimation functions (for example, to obtain the Cox partial likelihood estimate). The package `KMsurv` contains only datasets, and we use them in several examples. The package `emplik` is the main package for calculations related to empirical likelihood, except for those related to the Cox model, which are in the package `ELYP`. The package `kmc` contains the functions that implement the recursive algorithm we describe in Chapter 6. It is still quite fluid and should eventually be integrated into `emplik` in the future. Finally, the package `km.ci` provides empirical likelihood confidence intervals and confidence bands for the Kaplan–Meier survival probabilities.

I will keep updating and uploading the package `emplik` and `ELYP` to the public repository CRAN after the publication of the book, and maintain a Web page for any updates:

```
http://www.ms.uky.edu/~mai/EmpLik.html
```

The empirical likelihood method has its root in survival analysis. The very first paper originating the empirical likelihood method [112] is about empirical likelihood with the Kaplan–Meier estimator. So it seems to me that the empirical likelihood method naturally fits in with survival analysis. Also, over the years I have worked mostly on the empirical likelihood applications in survival analysis. So I chose to concentrate on this area.

Owen [81] covers much wider topics and also contains several sections about empirical likelihood with various censored, truncated, or other incomplete data. He discussed many forms of censoring, including interval censoring and double censoring. This book deals only with right censored data. Also, we do not discuss high-order asymptotic results for the empirical likelihood ratio. I feel the practical usefulness of high-order results in survival analysis concerning empirical likelihood ratio is not clear at this moment.

The core content of the book is Chapters 1, 2, 3, 4 (less Section 4.5), and 6. Chapter 1 discuss the empirical likelihood for right censored data, Chapter 6 for some computational tricks for censored data empirical likelihood, and the rest of the materials are pretty much standard survival analysis topics, treated with empirical likelihood. Basic knowledge of survival analysis is assumed.

Chapter 5 covers semi-parametric accelerated failure time models. This subject has a long history, but somehow standard software does not usually include this model and it is less used in practice (compared to the Cox regression model).

Section 4.5 discusses a recent extension of the Cox model by Yang and Prentice [129]. I include it here because I believe the empirical likelihood method is particularly suited for the statistical inference of this model.

Chapter 7 is about the optimality of confidence regions derived from empirical likelihood ratio tests or plug-in empirical likelihood ratio tests. It is a bit of a surprise that confidence regions can be so different in shape and orientation based on censored data. Chapter 8 collects mainly several empirical likelihood confidence band results, among other things.

There is a long list of people to whom I want to say THANK YOU. I am afraid the list is so long that I won't be able to stop for a long time. So instead of all the names, I shall list several categories.

First, all my colleagues. I have benefited tremendously over the years by reading your work and writings, by personal interactions, and in some cases, by collaborating on research. Some of the names appear in the reference list at the end of this book, but there are many more whose names do not appear in the references. THANK YOU!

I am also grateful to my students. I enjoyed working with you all.

I also want to acknowledge the support of an NSF grant.

I want to thank the many people who helped me put together this manuscript, correcting numerous typos and awkward grammar. All the remaining errors are my own.

Finally, I want to thank my family; they helped in this book project in numerous ways.

Mai Zhou

Chapter 1

Introduction

Survival analysis has long been a classic area of statistical study. For example, the famous Kaplan–Meier estimator got its name from a paper published in the year 1958. Many textbooks on survival analysis are available and the list is still growing. The main survival analysis procedures are available in all major statistical software packages. On the other hand, empirical likelihood is a methodology that has only recently been developed. The name "empirical likelihood" seems to appear first in Owen's 1988 paper. Only one book so far is available on empirical likelihood and most commercial statistical software does not yet include empirical likelihood procedures.

1.1 Survival Analysis

What is survival analysis? One might say "survival analysis is the statistical analysis of failure time data." In fact, some books are titled exactly as such. It is certainly correct, but it begs people to ask "what is failure time data?," which then takes longer to explain.

One might also say that "survival analysis is Kaplan–Meier estimator + log-rank test + Cox proportional hazards model." This description is too simplistic, but certainly very specific and constructive.

Perhaps we should be asking: what is the difference between survival analysis and regular statistical analysis? Or what are the unique features of survival analysis not seen in other branches of statistics?

We can list several features unique to survival analysis:

1. In survival analysis, the parameters of interest are often the "hazard" instead of cumulative distribution function (CDF) or mean.

2. In survival analysis, the available data is subject to censoring.

3. In survival analysis, nonparametric procedures are more common.

Empirical likelihood is a nonparametric method and thus fits into the third point above for survival analysis. We also point out that the Kaplan–Meier estimator, log-rank test and Cox model are all nonparametric procedures. Let us discuss the above features in more detail.

1.1.1 Hazard Function

Let $F(t)$ denote the CDF of the random variable X of interest; then the cumulative hazard function is defined as

$$\Lambda(t) = \int_{-\infty}^{t} \frac{dF(s)}{1-F(s-)} \ . \tag{1.1}$$

We comment that this definition is valid for either continuous or discrete CDF $F(t)$, and for X that can take negative values. If $F(t)$ is discrete, the integration is the Stieljes integral. When the CDF is continuous, $F(s-) = F(s)$, the integration on the right-hand side can be simplified to $-\log(1-F(t))$ and thus we have (for the continuous case)

$$\Lambda(t) = -\log(1-F(t)). \tag{1.2}$$

If the CDF has a density $f(s)$, then

$$\Lambda(t) = \int_{-\infty}^{t} \frac{f(s)}{1-F(s)} ds$$

and

$$\frac{\partial}{\partial t}\Lambda(t) = \frac{f(t)}{1-F(t)} \ .$$

If we define the *hazard function* $h(t)$ as

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

then the relation between $\Lambda(t)$ and $h(t)$ is similar to that of CDF $F(t)$ to the density $f(t)$, i.e., $\Lambda(t) = \int_{-\infty}^{t} h(s)ds$ and $\frac{\partial}{\partial t}\Lambda(t) = h(t)$.

The probabilistic interpretation of hazard $h(t)$ is that $h(t)dt$ is the conditional probability of the random variable taking a value in $[t, t+dt)$, given it is larger than or equal to t:

$$h(t)dt = \frac{f(t)dt}{1-F(t-)} = P(t \le X < t+dt | X \ge t) \ .$$

Compare this to the similar interpretation for the density $f(t)$:

$$f(t)dt = P(t \le X < t+dt) \ .$$

The hazard $h(t)$ must be nonnegative but does not have an upper bound. The cumulative hazard function $\Lambda(t)$ must be nonnegative and nondecreasing, but again can be unbounded. In fact, if the CDF is continuous, then $\Lambda(t)$ must be unbounded. This can be seen from $\Lambda(t) = -\log(1-F(t))$. On the other hand, if the CDF is discrete, then $\Lambda(t)$ does not increase to infinity as t increases, but the last jump is always of size one. This can be seen by (supposing t^* is the last jump point)

$$\Delta\Lambda(t_{last}) = \Delta\Lambda(t^*) = \frac{\Delta F(t^*)}{1-F(t^*-)} = 1 \ ,$$

because $\Delta F(t^*) = F(t^*+) - F(t^*-) = 1 - F(t^*-)$.

The inverse formula that recovers the CDF given a cumulative hazard is a bit awkward in the sense that the continuous and discrete versions look quite different: if the CDF/cumulative hazard is continuous, then

$$1 - F(t) = e^{-\Lambda(t)} . \tag{1.3}$$

If the CDF/cumulative hazard is purely discrete, then we have

$$1 - F(t) = \prod_{s \le t} (1 - \Delta\Lambda(s)) , \tag{1.4}$$

where $\Delta\Lambda(s) = \Lambda(s+) - \Lambda(s-)$. We notice that there are at most a countable many terms in the product, because there are at most a countable number of jumps in a monotone function.

In the case of a partly continuous, partly discrete CDF/cumulative hazard, we have to combine the two formulae:

$$1 - F(t) = e^{-\Lambda_c(t)} \prod_{s \le t} (1 - \Delta\Lambda(s)) \tag{1.5}$$

where $\Lambda_c(t)$ is the continuous part of the cumulative hazard:

$$\Lambda_c(t) = \Lambda(t) - \sum_{s \le t} \Delta\Lambda(s) .$$

Our discussion later in this book will mostly focus either on the continuous case or the purely discrete case, not on the mixed case.

The nonparametric estimation of the cumulative hazard function leads to the Nelson–Aalen estimator. The two sample log-rank test can be viewed as comparing the two hazard functions from two samples. The Cox proportional hazards model is a regression model which models how the ratio of hazards relates to the covariates. We shall discuss the Cox model in Chapter 4 and review the Nelson–Aalen estimator and log-rank test in subsections later in the present chapter.

Remark: At first glance, it is not clear how a rather innocent looking transformation of CDF to hazard has such an influence on survival analysis. For one thing, it removed the constraint that the jumps of a CDF must sum to one. Second, by working on conditional probabilities, it localized the parameters and made the estimation problem easier with censoring. This also leads to the application of martingales in survival analysis.

1.1.2 Censored Observations

The random variable of interest in survival analysis is "time to failure," denoted by X. Typically this is a positive, continuous random variable. Between the start and the end of a "life," a lot can happen, and often there are some conditions that prevent us from following up the "life" to its eventual failure. This leads to censoring.