ICPSR 2017 "Advanced Maximum Likelihood": Survival Analysis

Day Seven

August 15, 2017

Separation

"Separation" = "perfect prediction"

Intuition:

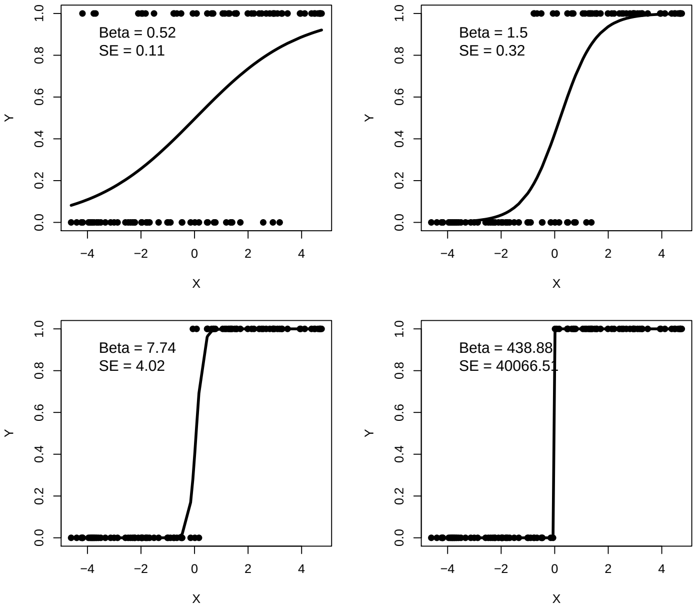
Yeas	Dems 0	1
0	178	34
1	0	219

$\Pr(Y = 1|X = 0) =?$

Separation: Effects

- $\hat{\beta}_X = \pm\infty$
- $\widehat{\text{s.e.}}_\beta = \infty$
- $\left.\frac{\partial^2 \ln L}{\partial X^2}\right|_{\hat{\beta}} = 0$

Separation Illustrated



Separation: What Happens

```
> summary(glm(Y~W+Z+X,family="binomial"))

Call:
glm(formula = Y ~ W + Z + X, family = "binomial")

Coefficients:
            Estimate Std. Error z value Pr(>|z|)
(Intercept)   -0.363      0.111   -3.26  0.00111 **
W              0.424      0.119    3.57  0.00036 ***
Z             -0.412      0.112   -3.67  0.00024 ***
X             18.746    541.835    0.03  0.97240
---
Signif. codes:  0 *** 0.001 ** 0.01 * 0.05 . 0.1   1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 684.41  on 499  degrees of freedom
Residual deviance: 464.69  on 496  degrees of freedom
AIC: 472.7

Number of Fisher Scoring iterations: 17
```

Separation: What Happens (Stata Remix)

```
. logit Y W Z X

note: X != 0 predicts success perfectly
      X dropped and 136 obs not used

Iteration 0:   log likelihood = -245.53269
Iteration 1:   log likelihood = -232.41173
Iteration 2:   log likelihood = -232.34436
Iteration 3:   log likelihood = -232.34436

Logistic regression                               Number of obs   =        364
                                                  LR chi2(2)      =      26.38
                                                  Prob > chi2     =     0.0000
Log likelihood = -232.34436                       Pseudo R2       =     0.0537

------------------------------------------------------------------------------
           Y |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
           W |   .4242117   .1187869     3.57   0.000     .1913936    .6570298
           Z |  -.4120285   .1123154    -3.67   0.000    -.6321628   -.1918943
           X |          0  (omitted)
       _cons |  -.3626348   .1112033    -3.26   0.001    -.5805892   -.1446803
------------------------------------------------------------------------------
```

Solution (?): Exact Logistic Regression

- Cox (1970, Ch. 4); Hirji et al. (1987 *JASA*); Mehta & Patel (1995 *Stat. Med.*)
- Conditions on permutations of covariate patterns
- Always has finite solutions;
- Computational issues...

Firth's (1993) Correction

Firth proposed:

$$L(\boldsymbol{\beta}|Y)^* = L(\boldsymbol{\beta}|Y)\,|\mathbf{I}(\boldsymbol{\beta})|^{\frac{1}{2}}$$

$$\ln L(\boldsymbol{\beta}|Y)^* = \ln L(\boldsymbol{\beta}|Y) + 0.5 \ln |\mathbf{I}(\boldsymbol{\beta})|$$

"Penalized likelihood":

- Consistent
- Eliminates small-sample bias
- Exist given separation
- Bayesians: "Jeffreys' prior"

Potential Drawbacks

- “Profile” (= “concentrated”) likelihood
- $L(\hat{\beta})$ can be asymmetrical...
- $\rightarrow$ inference...

Software

- R
  - `elrm` (exact logistic regression via MCMC)
  - `brlr` ("bias-reduced logistic regression")
  - `logistf` ("Firth's logistic regression")

- Stata
  - `exlogistic` (exact logistic regression)
  - `firthlogit` (Firth corrected logit)

Example: Pets as Family

- CBS/NYT Poll, April 1997
- Standard political/demographics, plus
- "Do you consider your pet to be a member of your family, or not?"
- Yes $=$ 84.4%, No $=$ 15.6%

Pets as Family: Data

```
> summary(Pets)
   petfamily        female               married
 Min.   :0.00   Female:403   Divorced/Sep:118
 1st Qu.:1.00   Male  :321   Married     :442
 Median :1.00                NBM         :118
 Mean   :0.84                Widowed     : 46
 3rd Qu.:1.00
 Max.   :1.00
        partyid             education
            : 58   < HS          : 71
 Democrat   :224   College Grad:131
 GOP        :228   HS diploma  :244
 Independent:214   Post-Grad   : 96
                   Some college:182
```

Pets as Family: Basic Model

```
> Pets.1<-glm(petfamily~female+as.factor(married)+as.factor(partyid)
             +as.factor(education),data=Pets,family=binomial)

> summary(Pets.1)

Call:
glm(formula = petfamily ~ female + as.factor(married) + as.factor(partyid) +
    as.factor(education), family = binomial, data = Pets)

Coefficients:
                                 Estimate Std. Error z value Pr(>|z|)
(Intercept)                        2.0133     0.5388    3.74  0.00019 ***
femaleMale                        -0.6959     0.2142   -3.25  0.00116 **
as.factor(married)Married         -0.0657     0.2911   -0.23  0.82147
as.factor(married)NBM              0.4599     0.3957    1.16  0.24504
as.factor(married)Widowed         -0.1568     0.4921   -0.32  0.75007
as.factor(partyid)Democrat        -0.1241     0.4286   -0.29  0.77213
as.factor(partyid)GOP             -0.0350     0.4321   -0.08  0.93537
as.factor(partyid)Independent     -0.1521     0.4299   -0.35  0.72338
as.factor(education)College Grad   0.2511     0.4121    0.61  0.54228
as.factor(education)HS diploma     0.0595     0.3685    0.16  0.87182
as.factor(education)Post-Grad      0.1946     0.4331    0.45  0.65321
as.factor(education)Some college   0.0587     0.3867    0.15  0.87928
---
Signif. codes:  0 *** 0.001 ** 0.01 * 0.05 . 0.1   1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 627.14  on 723  degrees of freedom
Residual deviance: 612.76  on 712  degrees of freedom
AIC: 636.8

Number of Fisher Scoring iterations: 4
```

Pets as Family: More Complicated Model

```
> Pets.2<-glm(petfamily~female+as.factor(married)*female+as.factor(partyid)+
              as.factor(education),data=Pets,family=binomial)

> summary(Pets.2)

Coefficients:
                                      Estimate Std. Error z value Pr(>|z|)
(Intercept)                             2.2971     0.6166    3.73   0.0002 ***
femaleMale                             -1.1833     0.5305   -2.23   0.0257 *
as.factor(married)Married              -0.3218     0.4470   -0.72   0.4716
as.factor(married)NBM                   0.1854     0.6140    0.30   0.7628
as.factor(married)Widowed              -0.7415     0.5780   -1.28   0.1995
as.factor(partyid)Democrat             -0.1575     0.4297   -0.37   0.7140
as.factor(partyid)GOP                  -0.0445     0.4334   -0.10   0.9182
as.factor(partyid)Independent          -0.1757     0.4312   -0.41   0.6837
as.factor(education)College Grad        0.2332     0.4137    0.56   0.5730
as.factor(education)HS diploma          0.0558     0.3703    0.15   0.8801
as.factor(education)Post-Grad           0.2171     0.4342    0.50   0.6171
as.factor(education)Some college        0.0358     0.3890    0.09   0.9266
femaleMale:as.factor(married)Married    0.4853     0.5908    0.82   0.4114
femaleMale:as.factor(married)NBM        0.5260     0.8051    0.65   0.5136
femaleMale:as.factor(married)Widowed   15.2516   549.3719    0.03   0.9779
---
Signif. codes:  0 *** 0.001 ** 0.01 * 0.05 . 0.1   1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 627.14  on 723  degrees of freedom
Residual deviance: 607.42  on 709  degrees of freedom
AIC: 637.4

Number of Fisher Scoring iterations: 14
```

What's Going On?

```
> with(Pets, xtabs(~petfamily+as.factor(married)+female))

, , female = Female

         as.factor(married)
petfamily Divorced/Sep Married NBM Widowed
        0            7      28   5       7
        1           67     199  58      32

, , female = Male

         as.factor(married)
petfamily Divorced/Sep Married NBM Widowed
        0           11      47   8       0
        1           33     168  47       7
```

Pets as Family: Firth Model

```
> Pets.Firth<-logistf(petfamily~female+as.factor(married)*female+as.factor(partyid)+
                      as.factor(education),data=Pets)

> Pets.Firth

Model fitted by Penalized ML
Confidence intervals and p-values by Profile Likelihood

                                            coef se(coef) lower 0.95 upper 0.95    Chisq        p
(Intercept)                               2.1589     0.60       1.05       3.40 16.17636 0.000058
femaleMale                               -1.1387     0.52      -2.19      -0.14  5.04186 0.024742
as.factor(married)Married                -0.2739     0.43      -1.19       0.53  0.41518 0.519353
as.factor(married)NBM                     0.1589     0.59      -0.99       1.37  0.07322 0.786705
as.factor(married)Widowed                -0.7263     0.56      -1.84       0.38  1.67233 0.195947
as.factor(partyid)Democrat               -0.1182     0.42      -0.99       0.66  0.08159 0.775159
as.factor(partyid)GOP                    -0.0078     0.42      -0.89       0.78  0.00034 0.985289
as.factor(partyid)Independent            -0.1364     0.42      -1.01       0.65  0.10813 0.742278
as.factor(education)College Grad          0.2390     0.40      -0.57       1.02  0.34480 0.557069
as.factor(education)HS diploma            0.0753     0.36      -0.67       0.76  0.04289 0.835933
as.factor(education)Post-Grad             0.2184     0.43      -0.63       1.05  0.26307 0.608019
as.factor(education)Some college          0.0524     0.38      -0.72       0.78  0.01888 0.890698
femaleMale:as.factor(married)Married      0.4558     0.58      -0.66       1.61  0.63550 0.425347
femaleMale:as.factor(married)NBM          0.5233     0.78      -1.02       2.05  0.45133 0.501702
femaleMale:as.factor(married)Widowed      2.4017     1.68      -0.14       7.37  3.37453 0.066212

Likelihood ratio test=17 on 14 df, p=0.24, n=724
```

- Separation $\nrightarrow$ dropping covariates!
- Firth's approach $>$ ELR
- Can also be applied to other sparse-data situations...

From the coxph Documentation

Convergence

In certain data cases the actual MLE estimate of a coefficient is infinity, e.g., a dichotomous variable where one of the groups has no events. When this happens the associated coefficient grows at a steady pace and a race condition will exist in the fitting routine: either the log likelihood converges, the information matrix becomes effectively singular, an argument to exp becomes too large for the computer hardware, or the maximum number of interactions is exceeded. (Nearly always the first occurs.) The routine attempts to detect when this has happened, not always successfully. The primary consequence for he user is that the Wald statistic = coefficient/se(coefficient) is not valid in this case and should be ignored; the likelihood ratio and score tests remain valid however.

Separation in Survival Data

```
> set.seed(7222009)
> X<-rep(0:1,times=100)
> T<-abs(rweibull(200,shape=1.2,
        scale=1/(exp(0+0.2*X))))
> C<-rbinom(200,1,0.2)
> C<-ifelse(X==0,0,C)

> table(C,X)
   X
C     0   1
  0 100  81
  1   0  19
```

Cox Results

```
> cox.fit<-coxph(Surv(T,C)~X,method="efron")
Warning message:
In fitter(X, Y, strats, offset, init, control, weights = weights,  :
  Loglik converged before variable  1 ; beta may be infinite.

> summary(cox.fit)

Call:
coxph(formula = Surv(T, C) ~ X, method = "efron")

  n= 200, number of events= 19

       coef exp(coef)  se(coef)     z Pr(>|z|)
X 2.038e+01 7.112e+08 5.630e+03 0.004    0.997

  exp(coef) exp(-coef) lower .95 upper .95
X 711225014  1.406e-09         0       Inf

Concordance= 0.761  (se = 0.064 )
Rsquare= 0.137   (max possible= 0.583 )
Likelihood ratio test= 29.37  on 1 df,   p=5.994e-08
Wald test            = 0  on 1 df,   p=0.9971
Score (logrank) test = 22.11  on 1 df,   p=2.58e-06
```

Parametric Model = No Help

```
> weib.fit<-survreg(Surv(T,C)~X,dist="weibull")
> summary(weib.fit)

Call:
survreg(formula = Surv(T, C) ~ X, dist = "weibull")
              Value Std. Error       z     p
(Intercept)  61.5536      0.337 182.851 0.000
X           -60.1634      0.000    -Inf 0.000
Log(scale)   -0.0184      0.190  -0.097 0.923

Scale= 0.982

Weibull distribution
Loglik(model)= -45.9   Loglik(intercept only)= -60.8
        Chisq= 29.94 on 1 degrees of freedom, p= 4.5e-08
Number of Newton-Raphson Iterations: 9
n= 200
```

Firth $\rightarrow$ Cox

Heinze and Schemper (2001):

$$\ln PL(\boldsymbol{\beta}|Y)^* = \ln PL(\boldsymbol{\beta}|Y) + 0.5 \ln |\mathbf{I}(\boldsymbol{\beta})|$$

with $\mathbf{I}(\boldsymbol{\beta}) = -E\left[\frac{\partial^2}{\partial\theta^2} \ln PL(X, \boldsymbol{\beta})\middle| \boldsymbol{\beta}\right]$.

Also, software: `coxphf`...

Firth-Corrected Cox

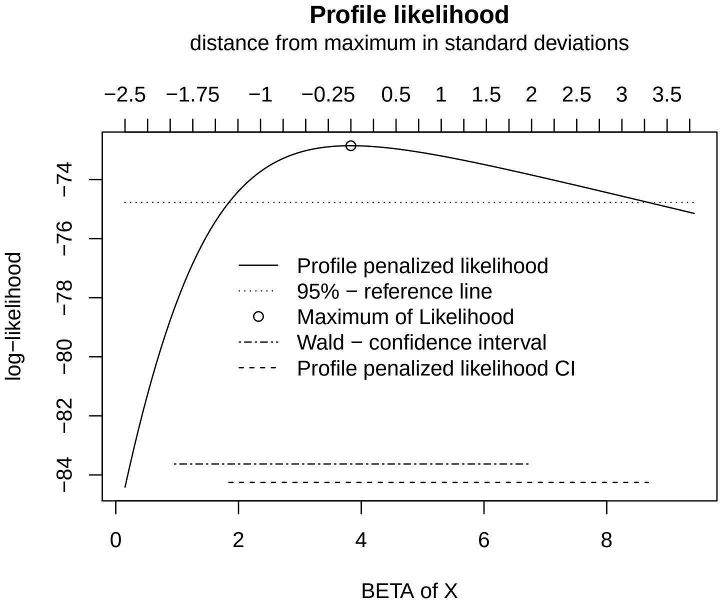
```
> SIM<-cbind(T,C,X)
> SIM<-data.frame(SIM)
> firth.fit<-coxphf(SIM,formula=Surv(T,C)~X)

> firth.fit
coxphf(formula = Surv(T, C) ~ X, data = SIM)
Model fitted by Penalized ML
Confidence intervals and p-values by Profile Likelihood

      coef se(coef) exp(coef) lower 0.95 upper 0.95    Chisq            p
X 3.830922 1.472103  46.10502   6.316689   5871.037 26.08802 3.262011e-07

Likelihood ratio test=26.08802 on 1 df, p=3.262011e-07, n=200
```

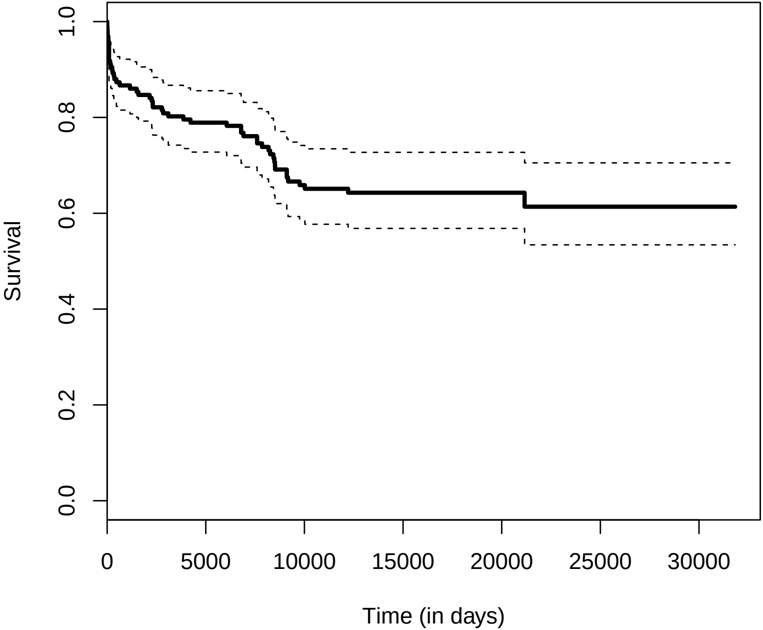
Examining the Profile Likelihood



Example: Lo et al. (2008)

- Outcome: "Cease-Fire Duration"
- Key covariate: *Foreign-Imposed Regime Change* ("FIRC")
- Data: Annual data on cease-fires, 1914-2001 (expanding Fortna 1998)
- Hypotheses:
  - FIRCs $\rightarrow$ more durable cease-fires
  - Pacifying influence of FIRCs declines over time

Lo et al.: Kaplan-Meier



From Lo et al. (2008)

Variables	*Model 1 (ARCHIGOS data)*	*Model 2 (ARCHIGOS data)*
FOREIGN-IMPOSED REGIME CHANGE	−161*** (29.3)	—
FIRC*ln(t)	16.8*** (3.03)	—
PUPPET-FIRC	—	−161*** (29.4)
PUPPET-FIRC*ln(t)	—	16.8*** (3.04)
CHANGE IN CAPABILITIES	.272 (.376)	.274 (.376)
BATTLE CONSISTENCY	−.796** (.336)	−.809** (.342)

Lo et al. Odds Ratio

$\widehat{\mathsf{OR}}_{\mathsf{FIRC}} =$

0.0000000000000000000000000000000000000000000000000000000000000000000001198

Simplified Cox Model

```
> LHR.Cox<-coxph(LHR.S~archigosFIRC+archigosFIRClnt,data=LHR,method="efron",
                iter.max=10000)
Warning message:
In fitter(X, Y, strats, offset, init, control, weights = weights,  :
  Ran out of iterations and did not converge

> LHR.Cox

Call:
coxph(formula = LHR.S ~ archigosFIRC + archigosFIRClnt, data = LHR,
    method = "efron", iter.max = 10000)

                  coef exp(coef) se(coef)     z     p
archigosFIRC    -44.11  6.99e-20    20.92 -2.11 0.035
archigosFIRClnt   4.69  1.09e+02     2.24  2.09 0.036

Likelihood ratio test=20.8  on 2 df, p=3.04e-05  n= 6368, number of events= 54
```

Firth-Corrected Cox Model

```
> LHR.CoxF<-coxphf(LHR.S~archigosFIRC+archigosFIRClnt,data=LHR,maxit=1000)

> LHR.CoxF

coxphf(formula = LHR.S ~ archigosFIRC + archigosFIRClnt, data = LHR,
    maxit = 1000)
Model fitted by Penalized ML
Confidence intervals and p-values by Profile Likelihood

                      coef  se(coef)   exp(coef)   lower 0.95
archigosFIRC    -55.591223 26.330771 7.19513e-25 4.808432e-65
archigosFIRClnt   5.848163  2.775927 3.46597e+02          NaN

                upper 0.95    Chisq           p
archigosFIRC           NaN 9.738246 0.001804731
archigosFIRClnt    7320112 8.647141 0.003275750

Likelihood ratio test=15.09131 on 2 df, p=0.0005284014, n=6368
```

What Is Going On?

```
> table(LHR$archigosFIRC,LHR$X_d)

       0    1
  0 5265   52
  1 1049    2
```

Days $\rightarrow$ Years = Little Help

	Cox	Firth-Corrected
FIRC	-53.83	-21.08
	(51.30)	(9.99)
FIRC $\times \ln(T)$	14.57	5.85
	(13.54)	(2.78)
AIC	494.07	496
Num. events	54	54