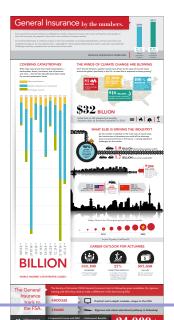
Today

- data presentation Michael
- In the news
- Semi-parametric regression
- HW 3: due March 21
- Final Exam: April 11 2:00 5:00 pm SS 1085
 - 4 questions
 - one theory question
 - one applied question
 - one question from HW
 - one question about a study
 - one question with computer output
 - detailed list of SM sections coming
 - See Final Exam from 2012 on course web page

link



STA 2201: Applied Statistics II March 14, 2014

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CBC News

Can a new test to identify the likelihood of Alzheimer's lead to better treatment?

Wednesday, March 12, 2014 | Categories: Episodes 💭 0





Nature Medicine News Release



Nature Medicine Advance Publication

medicine

nature.com > journal home > advance online publication > letter > full text

NATURE MEDICINE | LETTER

Plasma phospholipids identify antecedent memory impairment in older adults

Mark Mapstone, Amrita K Cheema, Massimo S Fiandaca, Xiaogang Zhong, Timothy R Mhyre, Linda H MacArthur, William J Hall, Susan G Fisher, Derick R Peterson, James M Haley, Michael D Nazar, Steven A Rich, Dan J Berlau, Carrie B Peltz, Ming T Tan, Claudia H Kawas & Howard J Federoff

Affiliations | Contributions | Corresponding author

Nature Medicine (2014) | doi:10.1038/nm.3466

Received 27 August 2013 | Accepted 09 January 2014 | Published online 09 March 2014

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STA 2201: Applied Statistics II March 14, 2014

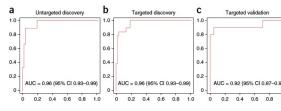
Althoundr's discass causes a progressive demontia that currently affects over 35 million

Nature Medicine

- 525 patients, followed for five years
- 46 patients had AD or pre-AD("aMCI") at entry; 28 converters
- in year 3 53 patients with aMCI/AD selected for plasma testing
- matched with 53 normal controls
- looked for biomarkers of disease, using logistic regression and lasso
- used the most promising to test on a further set of 21 patients with 20 matched controls
- ROC curve: plot of sensitivity (True Positives) against 1specificity (False Positives) as cut-off varies

... nature medicine

Figure 2 ROC results for the lipidomics analyses. (a–c) Plots of ROC results from the models derived from the three phases of the lipidomics analysis. Simple logistic models using only the metabolites identified in each phase of the lipidomics analysis were developed and applied to determine the success of the models for classifying the Cpre and NC groups. The red line in each plot represents the AUC obtained from the discovery-phase LASSO analysis (a), the targeted analysis of the ten metabolites in the discovery ohase (b) and the application



of the ten-metabolite panel developed from the targeted discovery phase in the independent validation phase (c). The ROC plots represent sensitivity (i.e., true positive rate) versus 1 – specificity (i.e., false positive rate).

Lasso for choosing explanatory variables

penalized least squares

$$\min_{\beta} \left(\Sigma \{ y_i - \beta_0 - \Sigma_{j=1}^{p} x_{ij} \beta_j \}^2 + \lambda \Sigma_{j=1}^{p} |\beta_j| \right)$$

equivalent to

$$\min_{\beta} \Sigma \{ y_i - \beta_0 - \Sigma_{j=1}^{\rho} x_{ij} \beta_j \}^2 \quad \text{s.t. } \Sigma |\beta_j| \le t$$

- quadratic programming problem
- $\hat{\beta}^{lasso}$ is nonlinear function of y

Tibshirani (1996), JRSS B and (2011), JRSS B

- http://www-stat.stanford.edu/~tibs/lasso.html
- extends to generalized linear models, implemented in glmnet

Extensions of semi-parametric regression

• original model
$$y_j = g(x_j) + \epsilon_j$$

- fit by local polynomial regression: $g(x_0) \doteq \beta_0 + \beta_1(x_i - x_0) + \dots + \beta_k(x_i - x_0)^k, \quad \hat{g}(x_0) = \hat{\beta}_0$
- $\triangleright \hat{\beta}$ maximizes

$$\ell(\beta,\sigma;\mathbf{x}_0,h) = \sum \frac{1}{h} w\left(\frac{\mathbf{x}_j - \mathbf{x}_0}{h}\right) \ell_j(\beta,\sigma;\mathbf{x}_0)$$

•
$$\ell_j(\beta, \sigma; x_0) = -\frac{1}{2\sigma^2} \{ y_j - \beta_0 - \beta_1(x_j - x_0) - \dots - \beta_k(x_j - x_0)^k \}^2 - \frac{1}{2} \log \sigma^2$$

- local log-likelihood fitting
- extend to more general models by replacing ℓ_i by the appropriate log-likelihood contribution

Example 10.32

toxoplasmosis data; response – incidence;
 x – yearly rainfall

SM Figure 10.12

- $y_j = r_j/m_j$, $r_j \sim \text{Binom}\{m, \pi(x_j)\}$
- $\pi(x) = \exp[\theta(x)/\{1 + \exp\{\theta(x)\}]$ $\theta(x) \doteq \beta_0 + \beta_1(x - x_0) + \dots + \beta_k(x - x_0)^k/k!, \quad \hat{\theta}(x_0) = \hat{\beta}_0$
- local log-likelihood

$$\ell(\beta; x_0, h) = \sum \frac{1}{h} w\left(\frac{x_j - x_0}{h}\right) m_j \{y_j x_j^{\mathrm{T}} \beta - \log(1 + e^{x_j^{\mathrm{T}} \beta})\}$$

or possibly allow for over-dispersion

$$\ell(\beta,\phi;x_0,h) = \sum \frac{1}{h} w\left(\frac{x_j - x_0}{h}\right) \frac{m_j}{\phi} \{y_j x_j^{\mathrm{T}} \beta - \log(1 + e^{x_j^{\mathrm{T}} \beta})\}$$

Example 10.32

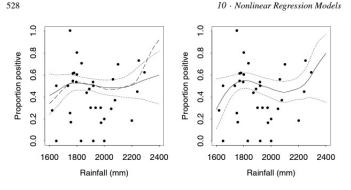
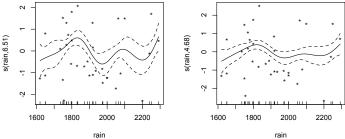


Figure 10.17 Local fit to the toxoplasmosis dat The left panel shows fitt probabilities $\widehat{\pi}(x)$, with the fit of local linear logistic model with h = 400 (solid) and 0.95 pointwise confidence bands (dots). Also show is the local linear fit with h = 300 (dashes). The right panel shows the loc quadratic fit with h = 40and its 0.95 confidence band. Note the increased variability due to the quadratic fit, and its stronger curvature at the boundaries.

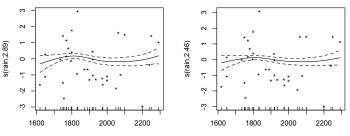
... Ex 10.32

```
> library(mgcv)
> library(SMPracticals)
> data(toxo)
> ?gam
> toxo.gam <- gam(cbind(r,m-r) ~ s(rain), family = binomial, data = toxo)</pre>
> summary(toxo.gam)
Family: binomial
Link function: logit
Formula.
cbind(r, m - r) \sim s(rain)
Parametric coefficients:
           Estimate Std. Error z value Pr(>|z|)
(Intercept) -0.09015 0.08573 -1.052 0.293
Approximate significance of smooth terms:
         edf Ref.df Chi.sg p-value
s(rain) 6.515 7.57 23.05 0.00259 **
> par(mfrow=c(2,2))
> toxo.gam$sp
    s(rain)
0.008141828
> plot(gam(cbind(r,m-r) ~ s(rain),sp=toxo.gam$sp, family = binomial, data = toxo), residuals=
> plot(gam(cbind(r,m-r) ~ s(rain),sp=0.05, family = binomial, data = toxo), residuals=TRUE, p
> plot(gam(cbind(r,m-r) ~ s(rain),sp=0.5, family = binomial, data = toxo), residuals=TRUE, pc
> plot(gam(cbind(r,m-r) ~ s(rain),sp=1, family = binomial, data = toxo), residuals=TRUE, pch=
```











... Ex 10.32

- gam uses spline smoothing terms, rather than local polynomials
- smoothing parameter replaces bandwidth h
- kgplm in librarygplm computes kernel smooths, but for Bernoulli data
- note from output that $\phi = 1$
- quasibinom is a valid choice of family
- ► gives estimate of φ as 1.8 (with default choice of smoothing)
- smooth fit no longer significant

... Ex 10.32

►

- estimation of smoothing parameter using generalized cross-validation
- or generalization of AIC

$$GCV(h) = \sum \left\{ \frac{y_j - \hat{g}(x_j)}{1 - \operatorname{tr}(S_h)/n} \right\}^2$$
$$AIC_c(h) = n\log \hat{\sigma}^2(h) + n \frac{1 + \operatorname{tr}(S_h)/n}{1 - \{\operatorname{tr}(S_h) + 2\}/n}$$

for generalized linear models

$$AIC_{c}(h) = \sum d_{j}\{y_{j}; \hat{\mu}_{j}(h)\} + n \frac{1 + tr(S_{h})/n}{1 - \{tr(S_{h}) + 2\}/n}$$

Flexible modelling using basis expansions §10.7.2

$$\flat \ y_j = g(x_j) + \epsilon_j$$

Flexible linear modelling

$$g(x) = \sum_{m=1}^{M} \beta_m h_m(x)$$

- This is called a linear basis expansion, and h_m is the mth basis function
- For example if X is one-dimensional: $g(x) = \beta_0 + \beta_1 x + \beta_2 x^2$, or $g(x) = \beta_0 + \beta_1 \sin(x) + \beta_2 \cos(x)$, etc.
- Simple linear regression has $h_1(x) = 1$, $h_2(x) = x$

Piecewise polynomials

▶ piecewise constant basis functions $h_1(x) = I(x < \xi_1), \quad h_2(x) = I(\xi_1 \le x < \xi_2),$ $h_3(x) = I(\xi_2 \le x)$

equivalent to fitting by local averaging

- piecewise linear basis functions , with constraints $h_1(x) = 1$, $h_2(x) = x$ $h_3(x) = (x - \xi_1)_+$, $h_4(x) = (x - \xi_2)_+$
- windows defined by knots ξ_1, ξ_2, \ldots
- ► piecewise cubic basis functions $h_1(x) = 1, h_2(x) = x, h_3(x) = x^2, h_4(x) = x^3$
- continuity $h_5(x) = (x \xi_1)^3_+, \quad h_6(x) = (x \xi_2)^3_+$

 continuous function, continuous first and second derivatives

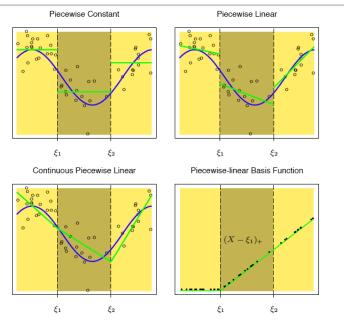


FIGURE 5.1. The top left panel shows a piecewise constant function fit to some artificial data. The broken vertical lines indicate the positions of the two knots ξ_1 and ξ_2 . The blue curve represents the true function, from which the data were

Piecewise Cubic Polynomials

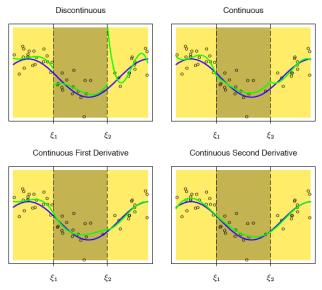
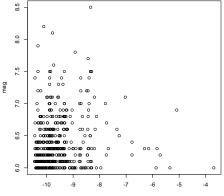


FIGURE 5.2. A series of piecewise-cubic polynomials, with increasing orders of continuity.

Example: earthquake data

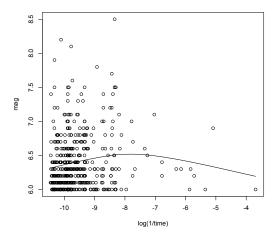
> with (quake, plot (log (1/time), mag)) ## using a different measure of intensity here than in Fi



log(1/time)

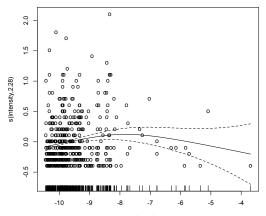
... earthquake

- > eq.gam <- gam(mag ~ s(intensity), data = quake)
- > with (quake, lines (intensity, eq.gam\$fitted.values))



... earthquake

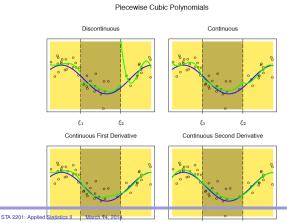
> plot(eq.gam, residual=TRUE, pch = "o")
standard errors plotted by default



intensity

Cubic splines

- truncated power basis of degree 3
- ► need to choose number of knots *K* and placement of knots ξ_1, \dots, ξ_K SM uses *n* knots
- construct features matrix using truncated power basis set
- use constructed matrix as set of predictors



... cubic splines

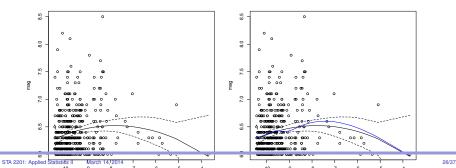
```
> with(quake, bs(log(1/time))[1:10,])
#bs(x) with no other arguments just gives a single cubic polyn
              1
                         2
                                   3
 [1,] 0.0000000 0.0000000 1.0000000
 [2,] 0.1018013 0.3903714 0.4989780
 [3.] 0.1359705 0.4189773 0.4303434
 [4,] 0.1884790 0.4408886 0.3437743
 [5,] 0.2056632 0.4436068 0.3189471
. . .
attr(, "degree")
[1] 3
attr(, "knots")
numeric(0)
attr(, "Boundary.knots")
[1] -10.454784 -3.690961
attr(,"intercept")
[1] FALSE
attr(,"class")
[1] "bs" "basis" "matrix"
```

... cubic splines

```
> with(quake,bs(log(1/time), df=5)[1:10,])
# gives a proper cubic spline basis, here with 5 df
      1
                 2
                           3
                                      4
                                                5
 [1,] 0 0.0000000 0.000000 0.0000000 1.000000
 [2,] 0 0.01110655 0.1250814 0.4247847 0.4390274
 [3,] 0 0.01846075 0.1661869 0.4486889 0.3666635
 [4,] 0 0.03370916 0.2283997 0.4600092 0.2778819
 [5,] 0 0.03989014 0.2484715 0.4585984 0.2530400
. . .
attr(, "degree")
[1] 3
attr(, "knots")
33.33338 66.66667%
-9.943294 - 9.520987
attr(, "Boundary.knots")
[1] -10.454784 -3.690961
```

... earthquake data

```
> guake.bs = lm(mag ~ bs(log(1/time),df=5),data = guake)
> guake.pred = predict(guake.bs, se.fit = TRUE, interval = "confidence")
> quake.pred
Śfit
         fit
                 lwr
                           upr
   5.962665 5.216283 6.709047
2
  6.279641 5.979190 6.580092
З
   6.323859 6.042772 6.604946
> lines(log(1/quake$time),quake.pred[[1]][,1])
> lines(log(1/guake$time), guake.pred[[1]][,2], lty=2)
> lines(log(1/quake$time),quake.pred[[1]][,3], lty=2)
> guake.lo = loess(mag ~ log(1/time), data = guake)
> quake.lopred = predict(quake.lo, se=T)
```



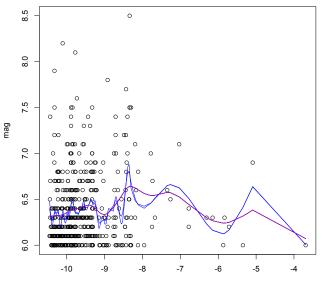
Smoothing splines §10.7.2

•
$$y_j = g(t_j) + \epsilon_j, \quad j = 1, \ldots, n$$

• choose $g(\cdot)$ to solve

$$\min_{g} \sum_{j=1}^{n} \frac{\{y - g(t_j)\}^2}{2\sigma^2} - \frac{\lambda}{2\sigma^2} \int_{a}^{b} \{g''(t)\}^2 dt, \quad \lambda > 0$$

- solution is a cubic spline, with knots at each observed x_i value
- see Figure 10.18 for a non-regularized solution
- has an explicit, finite dimensional solution
- $\hat{g} = \{\hat{g}(t_1), \dots, \hat{g}(t_n)\} = (I + \lambda K)^{-1} y$
- *K* is a symmetric $n \times n$ matrix of rank n 2



log(1/time)

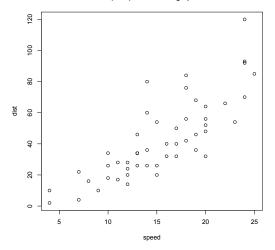
... smoothing splines

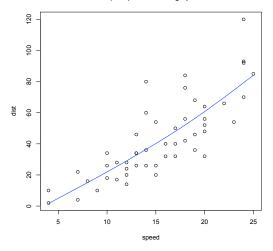
```
> guake$int = log(1/guake$time)
> guake[1:4,]
       time mag int
1 40.08333 6.0 -3.690961
2 162.38889 6.9 -5.089994
3 210.22917 6.0 -5.348198
4 303.85417 6.2 -5.716548
> attach(guake)
> plot(int, mag)
> guake.ss2 = smooth.spline(x = int, y = mag, df = 5)
> lines(guake.ss2, col="red")
> guake.ss3
Call:
smooth.spline(x = int, y = mag, cv = TRUE)
Smoothing Parameter spar= 1.499945 lambda= 0.0001340604 (25 iterations)
Equivalent Degrees of Freedom (Df): 11.35023
Penalized Criterion: 64 57512
PRESS: 0.1730025
> lines(guake.ss3, col="blue")
```

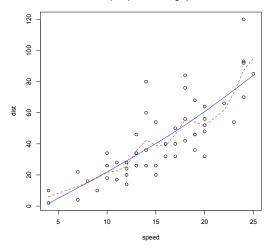
... smoothing splines

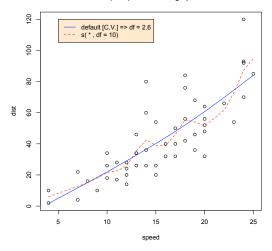
An example from the R help file for smooth.spline:

```
> data(cars)
> attach(cars)
> plot(speed, dist, main = "data(cars) & smoothing splines")
> cars.spl <- smooth.spline(speed, dist)</pre>
> (cars.spl)
Call·
smooth.spline(x = speed, v = dist)
Smoothing Parameter spar= 0.7801305 lambda= 0.1112206 (11 iterations)
Equivalent Degrees of Freedom (Df): 2.635278
Penalized Criterion: 4337.638
GCV: 244.1044
> lines(cars.spl, col = "blue")
       lines(smooth.spline(speed, dist, df=10), lty=2, col = "red")
\sim
      legend(5,120,c(paste("default [C.V.] => df =",round(cars.spl$df,1)),
>
                      "s( * , df = 10)"), col = c("blue", "red"), ltv = 1:2,
+
              bg='bisgue')
+
> detach()
```









Multidimensional splines

- so far we are considering just 1 X at a time
- for regression splines we replace each X by the new columns of the basis matrix
- for smoothing splines we get a univariate regression
- it is possible to construct smoothing splines for two or more inputs simultaneously, but computational difficulty increases rapidly
- these are called thin plate splines
- alternative:

 $E(Y | X_1, ..., X_p) = f_1(X_1) + f_2(X_2) + \cdots + f_p(X_p)$ additive models

► binary response: logit{ $E(Y | X_1, ..., X_p)$ } = $f_1(X_1) + f_2(X_2) + \cdots + f_p(X_p)$ generalized additive models

Which smoothing method?

- basis functions: natural splines, Fourier, wavelet bases
- regularization via cubic smoothing splines
- kernel smoothers: locally constant/linear/polynomial
- adaptive bandwidth, running medians, running *M*-estimates
- Dantzig selector, elastic net, rodeo (Lafferty & Wasserman, 2008)
- Faraway (2006) Extending the Linear Model:
 - with very little noise, a small amount of local smoothing (e.g. nearest neighbours)
 - with moderate amounts of noise, kernel and spline methods are effective
 - with large amounts of noise, parametric methods are more attractive
- "It is not reasonable to claim that any one smoother is better than the rest"
 - loess is robust to outliers, and provides smooth fits
 - spline smoothers are more efficient, but potentially sensitive



Happy St. Patrick's Day!

