Smoothing Spline ANOVA Models

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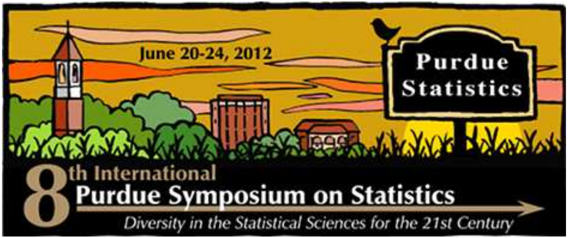

Outline

1. Introduction
   - Cubic Spline and Penalized Likelihood
   - Functional ANOVA Decomposition
   - R Package gss
2. Estimation and Inference
   - Splines as Bayes Estimates
   - Efficient Approximation
   - Cross-Validation
   - Bayesian Confidence Intervals
   - Kullback-Leibler Projection
3. Regression Models
   - Non-Gaussian Regression
   - Regression with Correlated Data
4. Density and Hazard Estimation
   - Density and Conditional Density
   - Hazard and Relative Risk

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Cubic Smoothing Spline

- Problem: Observing $Y_i = \eta(x_i) + \epsilon_i$, $i = 1, \ldots, n$, where $x_i \in [0,1]$ and $\epsilon_i \sim N(0, \sigma^2)$, one is to estimate $\eta(x)$.
- Method: Minimize $\frac{1}{n}\sum_{i=1}^{n}\left(Y_i - \eta(x_i)\right)^2 + \lambda \int_0^1 \left(\eta''(x)\right)^2 dx$.
- Solution: Piecewise cubic polynomial, with $\eta^{(3)}(x)$ jumping at knots $\xi_1 < \xi_2 < \cdots < \xi_q$ (ordered distinctive x_i); linear on $[0, \xi_1] \cup [\xi_q, 1]$.
- Smoothing Parameter: As $\lambda \uparrow$, $\eta(x)$ gets smoother; at $\lambda = 0_+$, one interpolates data, at $\lambda = \infty$, $\eta(x) = \beta_0 + \beta_1 x$.

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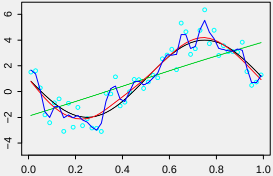
Role of Smoothing Parameter

- Simulation: $n = 50$, equally spaced x_i, $\eta(x) = 1 + 3\sin(2\pi x - \pi)$, $\sigma^2 = 1$.
- Cubic spline estimates calculated with $\log_{10} n\lambda = 0$, -3, and -6.



Penalized Likelihood Method

- Problem: Estimate $\eta(x)$ on generic domain $\mathcal{X}$ using stochastic data.
- Method: Minimize $L(\eta) + \lambda J(\eta)$, where $L(\eta)$ is minus log likelihood and $J(\eta)$ is a roughness functional such as $\int_0^1 \big(\eta''(x)\big)^2 dx$.
- Equivalence of penalized and constrained MLE:
$$\min L(\eta) + \lambda J(\eta) \;\Leftrightarrow\; \min L(\eta), \text{ subject to } J(\eta) \le \rho,$$
with λ being the Lagrange multiplier.

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Examples of Penalized Likelihood Estimation

- Gaussian Regression: $Y_i \sim N\big(\eta(x_i), \sigma^2\big)$; $L(\eta) = \frac{1}{n}\sum_{i=1}^n \big(Y_i - \eta(x_i)\big)^2$, with σ^2 absorbed into λ.
- Logistic Regression: $Y_i \sim \text{Bin}\big(m_i, p(x_i)\big)$; for $\eta(x) = \log\frac{p(x)}{1-p(x)}$, $L(\eta) = -\frac{1}{n}\sum_{i=1}^n \big\{Y_i\eta(x_i) - m_i \log(1+e^{\eta(x)})\big\}$.
- Density Estimation: $X_i \sim f(x)$ on $\mathcal{X}$, where $f(x) = e^{\eta(x)}/\int_{\mathcal{X}} e^{\eta(x)}dx$; $L(\eta) = -\frac{1}{n}\sum_{i=1}^n \eta(X_i) + \log\int_{\mathcal{X}} e^{\eta(x)}dx$.

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Functional ANOVA Decomposition

- ANOVA: $Y_{ijk} = \mu_{ij} + \epsilon_{ijk}$, where $\mu_{ij} = \mu + \alpha_i + \beta_j + (\alpha\beta)_{ij}$.
- ANOVA (cont.): Rewrite μ_{ij} as function on $\mathcal{X} = \mathcal{X}_1 \times \mathcal{X}_2$ discrete, $f(x) = f(x_{\langle 1 \rangle}, x_{\langle 2 \rangle}) = f_\emptyset + f_1(x_{\langle 1 \rangle}) + f_2(x_{\langle 2 \rangle}) + f_{12}(x_{\langle 1 \rangle}, x_{\langle 2 \rangle})$.
- ANOVA (cont.): On generic domain $\mathcal{X} = \mathcal{X}_1 \times \mathcal{X}_2$,
$$\begin{aligned} f(x) &= (I - A_1 + A_1)(I - A_2 + A_2)f \\ &= A_1A_2f + (I - A_1)A_2f + A_1(I - A_2)f + (I - A_1)(I - A_2)f \\ &= f_\emptyset + f_1(x_{\langle 1 \rangle}) + f_2(x_{\langle 2 \rangle}) + f_{12}(x_{\langle 1 \rangle}, x_{\langle 2 \rangle}), \end{aligned}$$
where A_1, A_2 are averaging operators on $\mathcal{X}_1$, $\mathcal{X}_2$, respectively.
- Side Conditions: $A_1 f_1 = A_1 f_{12} = A_2 f_2 = A_2 f_{12} = 0$.

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Examples of Averaging Operators

- $\mathcal{X} = \{1, \dots, K\}$: $Af = \frac{1}{K}\sum_x f(x)$; $Af = f(1)$.
- $\mathcal{X} = [a, b]$: $Af = \frac{1}{b-a}\int_a^b f(x)dx$; $Af = f(a)$.

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Examples of Two-Way ANOVA Decomposition

- $\mathcal{X} = [0,1]^2$, $A_1 f = \int_0^1 f\, dx_{\langle 1\rangle}$, $A_2 f = \int_0^1 f\, dx_{\langle 2\rangle}$:

$$f_\emptyset = A_1 A_2 f = \int_0^1 \int_0^1 f\, dx_{\langle 1\rangle} dx_{\langle 2\rangle},$$
$$f_1 = (I - A_1) A_2 f = \int_0^1 \Big(f - \int_0^1 f\, dx_{\langle 1\rangle}\Big) dx_{\langle 2\rangle},$$
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- $\mathcal{X} = \{1, \dots, K\} \times [0,1]$, $A_1 f = \frac{1}{K} \sum_{x_{\langle 1\rangle}} f(x_{\langle 1\rangle})$, $A_2 f = \int_0^1 f dx_{\langle 2\rangle}$:

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$$= f - \int_0^1 f\, dx_{\langle 2\rangle} - \frac{1}{K} \sum_{x_{\langle 1\rangle}} f + \frac{1}{K} \sum_{x_{\langle 1\rangle}} \int_0^1 f\, dx_{\langle 2\rangle}.$$

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- Two-Way ANOVA decomposition on $\mathcal{X} = \mathcal{X}_1 \times \mathcal{X}_2$ implies one-way ANOVA decomposition on $\mathcal{X}$, with $A = A_1 A_2$.
- Multi-way ANOVA decompositions can be defined directly, or recursively via 2-way decompositions.
- ANOVA structures can be built into penalized likelihood estimation, yielding tensor product splines.

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- Multi-way ANOVA decompositions can be defined directly, or recursively via 2-way decompositions.
- ANOVA structures can be built into penalized likelihood estimation, yielding tensor product splines.
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- Elimination of higher order terms lessens curse of dimensionality.

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- Write $\eta(x) = \sum_\beta \eta_\beta$ for an ANOVA decomposition, with generic index β.
- Schematically, $J(\eta) = \sum_\beta \theta_\beta^{-1} J_\beta(\eta_\beta)$, where $J_\beta(\eta_\beta)$ measure the roughness of η_β and θ_β adjust their relative weights in $J(\eta)$.
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Gaussian Regression with gss

- `gss` suites have syntax similar to `lm` and `glm`.
- Gaussian Regression: `ssanova` suite.

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Implicit and Explicit Model Configurations

- Vector: Cubic, or periodic cubic via `type=list(x=list("per",c(a,b)))`.
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Example: Water Acidity in Lakes

- Data: Water acidity measurements were recorded for 112 lakes in the Blue Ridge along with calcium concentrations.
- Modeling: A model of the following form was considered,

$$\text{pH} = \eta_{\emptyset} + \eta_c(\text{cal}) + \eta_g(\text{geog}) + \eta_{c,g}(\text{cal}, \text{geog}) + \epsilon,$$

  but $\eta_{c,g}$ is "insignificant" so an additive model is fitted.
- Notes: i) η_c is linear; ii) η_g is 2-D, isotropically invariant.

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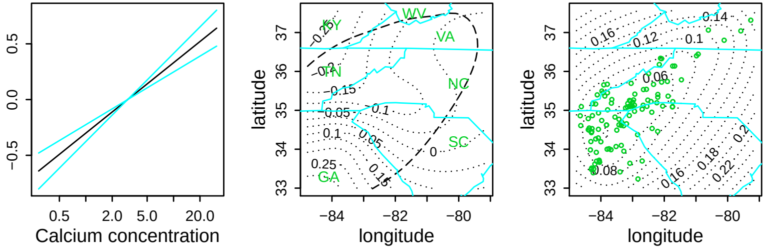

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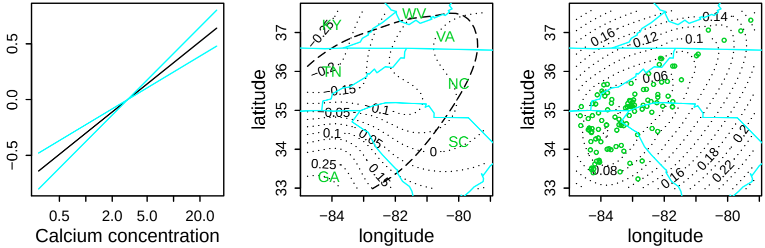

A Sample Session with ssanova

First load data frame LakeAcidity with elements ph, cal, and geog.

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data(LakeAcidity); lake <- LakeAcidity
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Next fit a model of form $\eta = \eta_\emptyset + \eta_c + \eta_g + \eta_{c,g}$.

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fit0 <- ssanova(ph~log(cal)*geog,data=lake)
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ff <- matrix(est.g$fit,31,31)
filled.contour(xx,xx,ff,asp=1,plot.axes={points(acid$geog)})
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Outline

Empirical Bayes Models

- Shrinkage Estimate: Set $J(\eta) = \eta^T B \eta$ on $\mathcal{X} = \{1, \dots, K\}$; minimizer of $\frac{1}{n}\sum_i \big(Y_i - \eta(x_i)\big)^2 + \lambda J(\eta)$ is Bayes under prior $\eta \sim N(\mathbf{0}, cB^+)$.

- Univariate Spline: $\lambda J(\eta)$ acts like minus log likelihood of Gaussian process prior on $\mathcal{X}$, with $E\big[\eta(x)\big] = 0$ and $E\big[\eta(x)\eta(y)\big] \propto R_J(x, y)$, where the "inverse" $R_J(x, y)$ of $J(\eta)$ is a reproducing kernel.

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Normal Priors

- $B = I - \frac{1}{K} \mathbf{1}\mathbf{1}^T$: $J(\eta) = \sum_x \big(\eta(x) - \bar{\eta}\big)^2$; $Y_{ij} = \mu + \alpha_i + \epsilon_{ij}$, $\boldsymbol{\alpha} \sim N(\mathbf{0}, cB)$.
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Gaussian Process Priors

- Cubic Spline: $R_J(x, y) = k_2(x)k_2(y) - k_4(|x - y|)$ is the "inverse" of $J(\eta) = \int_0^1 \big(\eta''(x)\big)^2 dx$, with $k_\nu(x) = B_\nu(x)/\nu!$ scaled Bernoulli polynomials.
- Thin-Plate Spline: "Inverse" of $\int\int \Big(\frac{\partial^2 f}{\partial z_{\langle 1\rangle}^2} + 2\frac{\partial^2 f}{\partial z_{\langle 1\rangle}\partial z_{\langle 2\rangle}} + \frac{\partial^2 f}{\partial z_{\langle 2\rangle}^2}\Big)^2 dz_{\langle 1\rangle} dz_{\langle 2\rangle}$.

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Models on Product Domains

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$$R(x,y) = R^{\langle 1\rangle}(x_{\langle 1\rangle}, y_{\langle 1\rangle})R^{\langle 2\rangle}(x_{\langle 2\rangle}, y_{\langle 2\rangle}),$$
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- With an ANOVA decomposition $\eta = \sum_\beta \eta_\beta$, the "inverse" of $J(\eta) = \sum_\beta \theta_\beta^{-1} J_\beta(\eta_\beta)$ is $R_J(x,y) = \sum_\beta \theta_\beta R_\beta(x,y)$, where $R_\beta(x,y)$ are "inverses" of $J_\beta(\eta)$; η_β have independent priors.
- The minimizer of $\frac{1}{n}\sum_{i=1}^{n}\big(Y_i - \eta(x_i)\big)^2 + \lambda J(\eta)$ is of form,
$$\eta(x) = \sum_{\nu=1}^{m} d_\nu \phi_\nu(x) + \sum_{i=1}^{n} c_i R_J(x_i, x),$$
where $\{\phi_\nu(x)\}$ is a basis of $\mathcal{N}_J = \{\eta : J(\eta) = 0\}$.
- One needs explicit forms of $\phi_\nu(x)$ and $R_J(x,y)$ for computation, but not of $J(\eta)$.

Outline

Asymptotic Convergence

- As $n \to \infty$ and $\lambda \to 0$, $(V + \lambda J)(\hat{\eta} - \eta) = O_p(\lambda^p + n^{-1}\lambda^{-1/r})$, where $V(\hat{\eta} - \eta)$ is a quadratic loss, $r > 1$, and $p \in [1, 2]$.

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share the same convergence rates with $\hat{\eta} \in \mathcal{H} = \{\eta : J(\eta) < \infty\}$, with $\{z_j\} \subseteq \{x_i\}$ a random subset and $q\lambda^{2/r} \to \infty$.
- For $r = 4$, $p = 2$, the optimal $O_p(n^{-8/9})$ is achieved at $\lambda \asymp n^{-4/9}$; it suffices to have $q \asymp n^{2/9+\epsilon}$, $\forall \epsilon > 0$. Computation is $O(nq^2)$.

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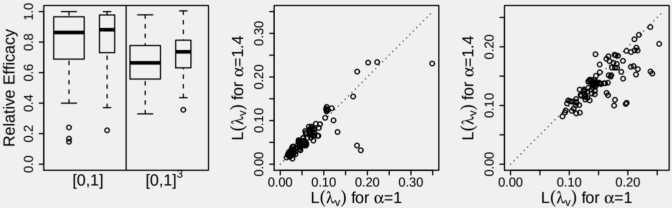
Empirical Performance of CV in Density Estimation

- Simulations: $n = 100$ on $[0,1]$, $n = 300$ on $[0,1]^3$; 100 replicates each.
- $L(\lambda) = \text{SKL}(\eta, \eta_\lambda)$ is minimized at λ_o. $V(\lambda)$ is minimized at λ_v for $\alpha = 1, 1.4$. $L(\lambda_o)/L(\lambda_v)$ defines the relative efficacy of $V(\lambda)$.



Outline

Bayesian Confidence Intervals

- Under a Gaussian process prior on $\mathcal{X}$ with $E\big[\eta(x)\big] = 0$ and $E\big[\eta(x)\eta(y)\big] \propto R_J(x,y)$, $L(\eta) + (\lambda/2)J(\eta)$ is posterior likelihood.
- With $L(\eta)$ quadratic as in Gaussian regression, the posterior is Gaussian with $E\big[\eta(x)\big] = \hat{\eta}(x)$, which, together with $\mathrm{Var}\big[\eta(x)\big]$, yield Bayesian confidence intervals for $\eta(x)$.
- For $L(\eta)$ non-quadratic, substitute $L(\eta)$ by its quadratic approximation $Q_{\hat{\eta}}(\eta)$ at $\hat{\eta}$, and the approximate likelihood $Q_{\hat{\eta}}(\eta) + (\lambda/2)J(\eta)$ is Gaussian with $E\big[\eta(x)\big] = \hat{\eta}(x)$.
- Posterior means and variances can be calculated for partial sums of $\eta(x)$, say $\eta_1 + \eta_2$ of $\eta = \eta_\emptyset + \eta_1 + \eta_2 + \eta_3 + \eta_{12}$.
- For an `ssanova fit`, one may use

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  with `se=TRUE` asking for standard errors and `inc` specifing terms to be included in the (partial) sum.

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- Need to "test" $H_0 : \eta \in \mathcal{H}_0$ versus $H_a : \eta \in \mathcal{H}_0 \oplus \mathcal{H}_1$.

- With $\mathcal{H}_0$ infinite-D, Neyman-Pearson tests are unavailable.
- KL Projection: Given $\hat{\eta} \in \mathcal{H}_0 \oplus \mathcal{H}_1$, minimize $\mathrm{KL}(\hat{\eta}, \eta)$ over $\eta \in \mathcal{H}_0$ to obtain $\tilde{\eta}$, then inspect the "entropy" decomposition,
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- If $\rho = \mathrm{KL}(\hat{\eta}, \tilde{\eta}) / \mathrm{KL}(\hat{\eta}, \eta_c)$ is small, one loses little by cutting out $\mathcal{H}_1$.
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Kullback-Leibler Projection

- Need to "test" $H_0 : \eta \in \mathcal{H}_0$ versus $H_a : \eta \in \mathcal{H}_0 \oplus \mathcal{H}_1$.
- Additive Models: $\eta = \eta_\emptyset + \eta_1 + \eta_2 + \eta_{12}$.
- With $\mathcal{H}_0$ infinite-D, Neyman-Pearson tests are unavailable.
- KL Projection: Given $\hat{\eta} \in \mathcal{H}_0 \oplus \mathcal{H}_1$, minimize $\mathrm{KL}(\hat{\eta}, \eta)$ over $\eta \in \mathcal{H}_0$ to obtain $\tilde{\eta}$, then inspect the "entropy" decomposition,

$$\mathrm{KL}(\hat{\eta}, \eta_c) = \mathrm{KL}(\hat{\eta}, \tilde{\eta}) + \mathrm{KL}(\tilde{\eta}, \eta_c),$$

  where $\eta_c \in \mathcal{H}_0$ can be a constant regression or a uniform density.
- If $\rho = \mathrm{KL}(\hat{\eta}, \tilde{\eta}) / \mathrm{KL}(\hat{\eta}, \eta_c)$ is small, one loses little by cutting out $\mathcal{H}_1$.
- For an `ssanova fit`, one may calculate KL projection using

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Outline

Regression with Exponential Family Responses

- For $Y \sim f(y)$, one may use $L(\eta) = \frac{1}{n}\sum_{i=1}^{n} l_i(\eta(x_i); Y_i)$ in $L(\eta) + \lambda J(\eta)$, where $l(\eta; y) \propto -\log f(y)$ for η the link.

- In gss, use something like `gssanova(y~x,family="binomial")`; only one link is used for each family, with η free of constraint.
- `predict` and `project` also work for `gssanova` fits, with calculations taking place on the link scale.

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Exponential Family Regression

- Logistic Regression: $f(y) = \binom{m}{y} p^y (1-p)^{m-y}$; $\eta = \log \frac{p}{1-p}$; $l(\eta; y) = -y\eta + m\log(1+e^{\eta})$.
- Poisson Regression: $f(y) = \lambda^y e^{-\lambda}/y!$; $\eta = \log\lambda$; $l(\eta; y) = -y\eta + e^{\eta}$.
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Example: Colorectal Cancer Mortality Rate

- Data: Colorectal cancer mortality during 2000 – 2004 were registered in the 92 counties of Indiana; Census 2000 is also available.
- Modeling: $Y \sim \text{Poisson}(e^{\eta} p)$, with p the population, and η is modeled as a function of sex, location, racial composition, etc.

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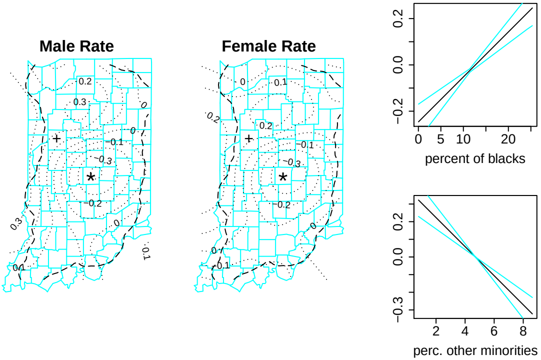

Example: Colorectal Cancer Mortality Rate

First load data frame ColoCan with elements pop, event, sex, brt, ort, scrn, and geog, then fit an initial model.

```
data(ColoCan)
fit0 <- gssanova(event~sex*(geog+brt+ort+scrn),"poisson",
                  offset=log(pop),data=ColoCan,nbasis=40)
```

Check for the "significance" of some terms, then fit an additive model.

```
project(fit.cc.0,c("sex","geog","sex:geog","brt","ort"))
fit1 <- gssanova(event~sex*geog+brt+ort,"poisson",
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Now compare mortality rates in Tippecanoe and Marion counties.

```
est1 <- predict(fit.cc,ColoCan[c(49,79,141,171),],
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exp(est1[2]-est1[1])
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Regression with Accelerated Life Models

- Consider life time T with survival function $P(T > t) = S(t)$ and hazard function $\lambda(t) = -d \log S(t)/dt$; $S(t) = \exp\left\{-\int_0^t \lambda(u)du\right\}$.
- When $\log T \sim f(z) = f\left(\frac{\log t - \mu}{\sigma}\right)$, one has an accelerated life model.

Accelerated Life Models

- Weibull: $f(z) = we^{-w}$, for $w = e^z$; $\lambda(t) = \frac{\nu}{t}e^z = \nu t^{\nu-1}e^{-\nu\mu}$, for $\nu = 1/\sigma$.
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Example: Stanford Heart Transplant

- Load data frame `stan` with elements `time`, `status`, and `age`.

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data(stan)
```

- Fit a Weibull regression model

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fit <- gssanova(cbind(time+.01,status)~age,"weibull",
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- With $\lambda(t,u)=\nu t^{\nu-1}e^{-\nu(\eta_\emptyset+\eta_u)}=\lambda_0(t)\lambda_1(u)$, the Weibull model is a proportional hazard model.
- One may evaluate the fitted η_u,

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gd <- seq(min(stan$age),max(stan$age),length=51)
est <- predict(fit,data.frame(age=gd),se=TRUE,inc="age")
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and plot the relative risk $\lambda_1(u)=e^{-\nu\eta_u}$,

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- With $\lambda(t,u) = \nu t^{\nu-1} e^{-\nu(\eta_\emptyset+\eta_u)} = \lambda_0(t)\lambda_1(u)$, the Weibull model is a proportional hazard model.
- One may evaluate the fitted η_u,

```
gd <- seq(min(stan$age),max(stan$age),length=51)
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and plot the relative risk $\lambda_1(u) = e^{-\nu\eta_u}$,

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Example: Stanford Heart Transplant

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data(stan)
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Outline

Random Effects and Mixed-Effect Models

- Consider $Y_i = \eta(x_i) + \mathbf{z}_i^T \mathbf{b} + \epsilon_i$, $\mathbf{b} \sim N(\mathbf{0}, \sigma^2 B)$, $\epsilon \sim N(0, \sigma^2)$.

- In general, replace $\eta(x_i)$ by $\zeta_i = \eta(x_i) + \mathbf{z}_i^T \mathbf{b}$, and minimize
$$\frac{1}{n}\sum_{i=1}^{n} l_i\big(\eta(x_i) + \mathbf{z}_i^T\mathbf{b}; Y_i\big) + \mathbf{b}^T\Sigma\mathbf{b} + \lambda J(\eta),$$
where $\Sigma \propto B^{-1}$, usually structured, contains correlation parameters.

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Random Effects

- The random effects $\mathbf{z}^T\mathbf{b}$ are also known as variance components; $\mathrm{Var}(\mathbf{Y}) = \sigma^2(I + ZBZ^T)$, for $Z^T = (\mathbf{z}_1, \dots, \mathbf{z}_n)$.
- For longitudinal data from subjects $s_i \in \mathcal{S}$, $\mathbf{z}_i^T\mathbf{b} = b_{s_i}$, $b_s \sim N(0, \tau^2)$.
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Example: Treatment of Bacteriuria

- Load bacteriuria with elements infect, trt, and time.

```
data(bacteriuria); bact <- bacteriuria
```

- Fit logistic regression model with subject random effect.

```
id.z <- (1:820)[bact$id%in%c(3,38)]
fit0 <- gssanova(infect~trt*time,"binomial",data=bact,
                 random=~1|id,id.basis=id.z)
```

- Check the "significance" of interaction, then fit an additive model.

```
project(fit0,c("trt","time"))
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```

- Check the magnitudes of b_s, noticing disparity between trt levels.

```
var(fit1$b[1:36]); var(fit1$b[37:72])
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- Attach different γ for the two groups, $\Sigma \propto \mathrm{diag}(\gamma_1 I, \gamma_2 I)$.

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Outline

Density Estimation

- For $X_i \sim f(x) = \frac{e^{\eta(x)}}{\int_{\mathcal{X}} e^{\eta(x)}}$, use $L(\eta) = -\frac{1}{n}\sum_i \eta(X_i) + \log \int_{\mathcal{X}} e^{\eta(x)}$ in $L(\eta) + \lambda J(\eta)$, for $\mathcal{X}$ generic.
  - With $\eta = \eta_\emptyset + \eta_x$, $f(x) = e^{\eta_x(x)} / \int_{\mathcal{X}} e^{\eta_x(x)}$.
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```
data(buffalo); buff <- buffalo
fit0 <- ssden(~buff,domain=data.frame(buff=c(0,150)))
fit1 <- ssden(~buff,domain=data.frame(buff=c(20,130)))
plot(0:150,dssden(fit0,0:150),type="l"); abline(h=0,lty=2)
lines(20:130,dssden(fit1,20:130),col=4)
pp <- qssden(fit1,(0:5)/5); pssden(fit1,pp)
```

Example: AIDS Incubation

- Load `aids` with elements `incu`, `infe`, and `age`.

```
data(aids); aids1 <- aids[aids$age>=60,]
```

- Generate quadrature on $\mathcal{X} = \{X_{\langle 1 \rangle} \leq X_{\langle 2 \rangle}\}$.

```
qd.pt <- expand.grid(incu=2*(1:50)-1,infe=2*(1:50)-1)
qd.pt <- qd.pt[qd.pt$incu<=qd.pt$infe,]
qd.wt <- rep(1,nrow(qd.pt));
qd.wt[qd.pt$incu==qd.pt$infe] <- .5
my.qd <- list(pt=qd.pt,wt=qd.wt)
```

- Calculate fits with and without η_{12}.

```
dm <- data.frame(incu=c(0,100),infe=c(0,100))
fit0 <- ssden(~incu*infe,data=aids1,domain=dm,quad=my.qd)
project(fit0,c("incu","infe"))
fit1 <- ssden(~incu+infe,data=aids1,domain=dm,quad=my.qd)
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- $X_{\langle 1 \rangle}$ and $X_{\langle 2 \rangle}$ are always dependent with truncation; $\eta_{12} = 0$ implies pre-truncation independence.

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fit1 <- ssden(~incu+infe,data=aids1,domain=dm,quad=my.qd)
```

- $X_{\langle 1\rangle}$ and $X_{\langle 2\rangle}$ are always dependent with truncation; $\eta_{12} = 0$ implies pre-truncation independence.

Example: AIDS Incubation

- Load `aids` with elements `incu`, `infe`, and `age`.

```
data(aids); aids1 <- aids[aids$age>=60,]
```

- Generate quadrature on $\mathcal{X} = \{X_{\langle 1 \rangle} \leq X_{\langle 2 \rangle}\}$.

```
qd.pt <- expand.grid(incu=2*(1:50)-1,infe=2*(1:50)-1)
qd.pt <- qd.pt[qd.pt$incu<=qd.pt$infe,]
qd.wt <- rep(1,nrow(qd.pt));
qd.wt[qd.pt$incu==qd.pt$infe] <- .5
my.qd <- list(pt=qd.pt,wt=qd.wt)
```

- Calculate fits with and without η_{12}.

```
dm <- data.frame(incu=c(0,100),infe=c(0,100))
fit0 <- ssden(~incu*infe,data=aids1,domain=dm,quad=my.qd)
project(fit0,c("incu","infe"))
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Example: AIDS Incubation

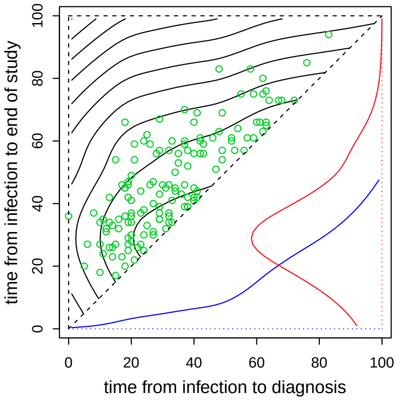
- Evaluate conditional densities $f(x_{\langle 1\rangle}|x_{\langle 2\rangle})$ and $f(x_{\langle 2\rangle}|x_{\langle 1\rangle})$.

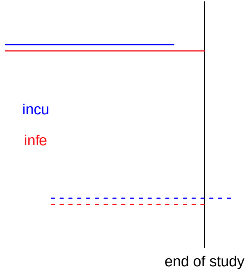
```
xx <- 2*(1:50)-1
f.incu <- cdssden(fit1,xx,data.frame(infe=50))$pdf
f.infe <- cdssden(fit1,xx,data.frame(incu=50))$pdf
```

Example: AIDS Incubation

- Evaluate conditional densities $f(x_{\langle 1 \rangle}|x_{\langle 2 \rangle})$ and $f(x_{\langle 2 \rangle}|x_{\langle 1 \rangle})$.

```
xx <- 2*(1:50)-1
f.incu <- cdssden(fit1,xx,data.frame(infe=50))$pdf
f.infe <- cdssden(fit1,xx,data.frame(incu=50))$pdf
```





Conditional Density Estimation

- To estimate $f(y|x) = \frac{e^{\eta(x,y)}}{\int_{\mathcal{Y}} e^{\eta(x,y)}}$ on $\mathcal{X} \times \mathcal{Y}$ from (X_i, Y_i), use $L(\eta) = -\frac{1}{n}\sum_i \left\{\eta(X_i, Y_i) - \log \int_{\mathcal{Y}} e^{\eta(X_i,y)}\right\}$ in $L(\eta) + \lambda J(\eta)$.
- In `gss`, use something like `sscden(~x*y,~y)`, where `~x*y` specifies model terms and `~y` designates y-variables; terms in η_x are removed.
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Regression with Cross-Classified Responses

- For $\mathcal{Y} = \{0, 1\}$, this reduces to logistic regression.
- In general, this "unwinds" contingency tables along an "x-axis" and estimates table probabilities as functions of covariates.

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Example: Penny Thickness

- Load `penny` with elements `mil` and `year`.

  ```
  data(penny); ydm <- data.frame(mil=c(49,61))
  ```

- Calculate fits with and without break.

  ```
  fit0 <- sscden(~year*mil,~mil,data=penny,ydomain=ydm)
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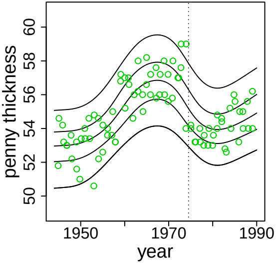

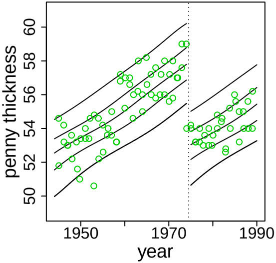

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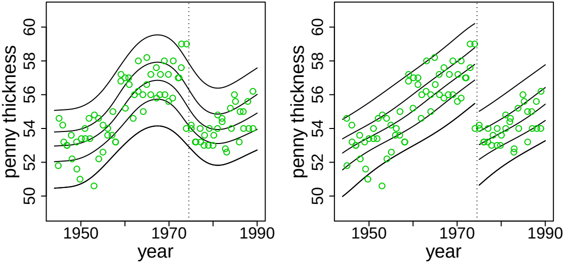

Outline

Hazard Estimation

- For life time T with covariate U, consider $S(t,u) = P(T > t|U = u)$, $\lambda(t,u) = e^{\eta(t,u)} = -\partial \log S(t,u)/\partial t$; $S(t,u) = \exp\left\{-\int_0^t e^{\eta(s,u)} ds\right\}$.
- Observing $(X_i, \delta_i, Z_i, U_i)$, for $X = \min(T, C)$, $\delta = I_{[X \leq C]}$, and $Z < X$, use $L(\eta) = -\frac{1}{n}\sum_i \left\{\delta_i \eta(X_i, U_i) - \int_{Z_i}^{X_i} e^{\eta(t,U_i)} dt\right\}$ in $L(\eta) + \lambda J(\eta)$.
- In gss, use something like `sshzd(Surv(x,delta,z)~x*u)`, where η_t must be included in model terms; here t is represented by `x` in `x*u`.

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- With an additive $\eta = \eta_\emptyset + \eta_t + \eta_u$, one has a proportional hazard model.
- Adding random effects $\mathbf{z}^T\mathbf{b}$ to $\eta(t,u)$, one has frailty models.
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- Use `hzdrate.sshzd(fit,data.frame(x=tt,u=uu),se,inc)` to evaluate fits, much like `predict` for `ssanova`/`gssanova` fits.
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Example: Stanford Heart Transplant

- Calculate fits with and without η_{tu}.

```
fit0 <- sshzd(Surv(futime,status)~futime*age,data=stan)
project(fit0,inc=c("futime","age"))
fit1 <- sshzd(Surv(futime,status)~futime+age,data=stan)
```

  where `futime` is on the $t^* = \sqrt{t}$ scale; $\tilde{\lambda}(t,u) = \lambda(t^*,u)/2t^*$.

- Evaluate e^{η_u} on a grid, with `e.a$fit` on e^{η_u} and `e.a$se` on η_u.

```
e.a <- hzdrate.sshzd(fit1,data.frame(age=11:64),
                     se=TRUE,inc=c("age"))
```

- Evaluate $e^{\eta_\emptyset + \eta_t}$ on a grid.

```
e.b <- hzdrate.sshzd(fit1,data.frame(futime=0:60),
                     se=TRUE,inc=c("1","futime"))
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```
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                     se=TRUE,inc=c("age"))
```

```
plot(11:64,e.a$fit,type="l",ylim=c(0,5))
lines(11:64,e.a$fit*exp(1.96*e.a$se),col=5)
lines(11:64,e.a$fit/exp(1.96*e.a$se),col=5)
```

- Evaluate $e^{\eta_\emptyset+\eta_t}$ on a grid.

```
e.b <- hzdrate.sshzd(fit1,data.frame(futime=0:60),
                     se=TRUE,inc=c("1","futime"))
```

Example: Stanford Heart Transplant

- Calculate fits with and without η_{tu}.

```
fit0 <- sshzd(Surv(futime,status)~futime*age,data=stan)
project(fit0,inc=c("futime","age"))
fit1 <- sshzd(Surv(futime,status)~futime+age,data=stan)
```

where `futime` is on the $t^* = \sqrt{t}$ scale; $\tilde{\lambda}(t,u) = \lambda(t^*,u)/2t^*$.

- Evaluate e^{η_u} on a grid, with `e.a$fit` on e^{η_u} and `e.a$se` on η_u.

```
e.a <- hzdrate.sshzd(fit1,data.frame(age=11:64),
                     se=TRUE,inc=c("age"))
```

```
plot(11:64,e.a$fit,type="l",ylim=c(0,5))
lines(11:64,e.a$fit*exp(1.96*e.a$se),col=5)
lines(11:64,e.a$fit/exp(1.96*e.a$se),col=5)
```

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Estimation of Relative Risk

- For $\lambda(t,u)=\lambda_0(t)\lambda_1(u)$, one may treat $\lambda_0(t)$ as a nuisance and estimate $\lambda_1(u)=e^{\eta_u(u)}$ via partial likelihood, using in $L(\eta)+\lambda J(\eta)$ $L(\eta)=-\frac{1}{n}\sum_{i=1}^{n}\delta_i\{\eta(U_i)-\log\sum_{j=1}^{n}I_{[Z_j<X_i\leq X_j]}e^{\eta(U_j)}\}$.
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Example: Stanford Heart Transplant

- Calculate the fit, which is invariant to the scaling of t.

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fit2 <- sscox(Surv(time,status)~age,data=stan)
```

- Evaluate e^{η_u} on data points, then estimate $\lambda_0(t)$.

```
risk <- predict(fit2,stan)
fit3 <- sshzd(Surv(futime,status)~futime,data=stan,
              offset=log(risk))
```

- Evaluate $\lambda_1(u)$ and $\lambda_0(t)$ on grids.

```
e.a0 <- predict(fit2,data.frame(age=11:64),se=T,inc=c("age"))
e.b0 <- hzdcurve.sshzd(fit3,0:60,se=TRUE)
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Thank You!