



#### Advanced School and Conference on Statistics and Applied Probability in Life Sciences

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Sampling bias in logistic models

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# Sampling bias in logistic models

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Trieste, October 2007

Auto-generated units

www.stat.uchicago.edu/~pmcc/reports/bias.pdf

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# Outline



- Gaussian models
- Binary regression model
- Properties of conventional models
- 2 Auto-generated units
  - Point process model
- 3 Consequences of auto-generation
  - Sampling bias
  - Non-attenuation
  - Inconsistency
  - Estimating functions
  - Robustness
  - Interference



Arguments pro and con



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Gaussian models Binary regression model Properties of conventional models

# Conventional regression model

Fixed set  $\mathcal{U}$  (usually infinite):  $u_1, u_2, \ldots$  subjects, plots,... Covariate  $x(u_1), x(u_2), \ldots$  (non-random, vector-valued) Response  $Y(u_1), Y(u_2), \ldots$  (random, real-valued)

Regression model:

For each sample  $u_1, \ldots, u_n$  with  $\mathbf{x} = (x(u_1), \ldots, x(u_n))$ Distribution  $p_{\mathbf{x}}(\mathbf{y})$  on  $\mathcal{R}^n$  depends on  $\mathbf{x}$ 

Example:

$$\mathcal{D}_{\mathbf{x}}(\mathbf{y} \in \mathbf{A}; \theta) = \mathcal{N}_n(\mathbf{X}\beta, \sigma_0^2 \mathbf{I}_n + \sigma_1^2 \mathbf{K})(\mathbf{A})$$

 $A \subset \mathcal{R}^n$ ,  $K_{ij} = K(x_i, x_j)$ block-factor models, spatial models, generalized spline models,...



Gaussian models Binary regression model Properties of conventional models

# Binary regression model

Units:  $u_1, u_2, ...$  subjects, patients, plots (labelled) Covariate  $x(u_1), x(u_2), ...$  (non-random,  $\mathcal{X}$ -valued) Process  $\eta$  on  $\mathcal{X}$  (Gaussian, for example) Responses  $Y(u_1), ...$  conditionally independent given  $\eta$ 

$$logit pr(Y(u) = 1 | \eta) = \alpha + \beta x(u) + \eta(x(u))$$

Joint distribution

$$p_{\mathbf{x}}(\mathbf{y}) = E_{\eta} \prod_{i=1}^{n} \frac{e^{(\alpha + \beta x_i + \eta(x_i))y_i}}{1 + e^{\alpha + \beta x_i + \eta(x_i)}}$$

parameters 
$$\alpha, \beta, K$$
.  $K(x, x') = cov(\eta(x), \eta(x'))$ .



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Binary regression model: computation

Computational problem:

$$p_{\mathbf{x}}(\mathbf{y}) = \int_{\mathcal{R}^n} \prod_{i=1}^n \frac{e^{(\alpha + \beta x_i + \eta(x_i))y_i}}{1 + e^{\alpha + \beta x_i + \eta(x_i)}} \phi(\eta; K) d\eta$$

Options:

Taylor approx: Laird and Ware; Schall; Breslow and Clayton, McC and Nelder, Drum and McC,...

Laplace approximation: Wolfinger 1993; Shun and McC 1994 Numerical approximation: Egret

E.M. algorithm: McCulloch 1994 for probit models Monte Carlo: Z&L,...



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#### Just a minute...

But ...  $p_{\mathbf{x}}(\mathbf{y})$  is not the correct distribution!

Why not?



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Gaussian models

Binary regression model

Properties of conventional models

Gaussian models Binary regression model Properties of conventional models

# Binary regression model (contd)

logit pr(
$$Y(u) = 1 | \eta$$
) =  $\alpha + \beta x(u) + \eta(x(u))$ 

Approximate one-dimensional marginal distribution

logit pr(
$$Y(u) = 1$$
) =  $\alpha^* + \beta^* x(u)$ 

 $|\beta^*| < |\beta|$  (parameter attenuation) Subject-specific approach versus population-average approach

$$E(Y(u)) = \frac{e^{\alpha^* + \beta^* x(u)}}{1 + e^{\alpha^* + \beta^* x(u)}}$$
$$\operatorname{cov}(Y(u), Y(u')) = V(x(u), x(u'))$$

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PA more acceptable than SS?

Gaussian models Binary regression model Properties of conventional models

# Properties of conventional regression model

- (i) Population  ${\mathcal U}$  is a fixed set of labelled units
- (ii) Two samples having same **x** also have same response distribution. (exchangeability, no unmeasured confounders,...)
- (iii) Distribution of Y(u) depends only on x(u), not on x(u')(no interference, Kolmogorov consistency)
- (iv) sample  $u_1, \ldots, u_n$  is a fixed set of units  $\Rightarrow \mathbf{x}$  fixed No concept of random sampling of units
- (v) Does not imply independence of components: fitted value  $E(Y(u')) \neq$  predicted E(Y(u') | data)

What if ...  $u_1, \ldots, u_n$  were generated at random?

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Point process model

#### Point process model for auto-generated units

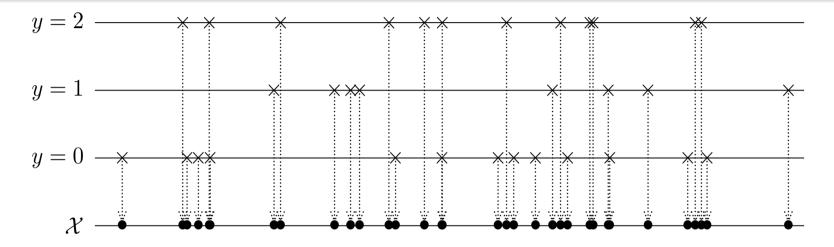


Figure 1: A point process on  $\mathcal{C} \times \mathcal{X}$  for k = 3, and the superposition process on  $\mathcal{X}$ . Intensity  $\lambda_r(x)$  for class r

*x*-values auto-generated by the superposition process with intensity  $\lambda_{\bullet}(x)$ . To each auto-generated unit there corresponds an *x*-value and a *y*-value. *y*-value Peter McCullagh Auto-generated units

#### Binary point process model

Intensity process  $\lambda_0(x)$  for class 0,  $\lambda_1(x)$  for class 1 Log ratio:  $\eta(x) = \log \lambda_1(x) - \log \lambda_0(x)$ Events form a PP with intensity  $\lambda$  on  $\{0, 1\} \times \mathcal{X}$ . Conventional calculation (Bayesian and frequentist):

$$pr(Y = 1 | x, \lambda) = \frac{\lambda_1(x)}{\lambda_1(x)} = \frac{e^{\eta(x)}}{1 + e^{\eta(x)}}$$
$$pr(Y = 1 | x) = E\left(\frac{\lambda_1(x)}{\lambda_1(x)}\right) = E\left(\frac{e^{\eta(x)}}{1 + e^{\eta(x)}}\right)$$

Calculation is correct in a sense, but irrelevant...

 $\ldots$  there might not be an event at x!



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Point process model

#### Correct calculation for auto-generated units

pr(event of type r in dx |  $\lambda$ ) =  $\lambda_r(x) dx + o(dx)$ pr(event of type r in dx) =  $E(\lambda_r(x)) dx + o(dx)$ pr(event in SPP in dx |  $\lambda$ ) =  $\lambda_{\cdot}(x) dx + o(dx)$ pr(event in SPP in dx) =  $E(\lambda_{\cdot}(x)) dx + o(dx)$ 

$$\operatorname{pr}(Y(x) = r | \operatorname{SPP} \operatorname{event} \operatorname{at} x) = \frac{E\lambda_r(x)}{E\lambda_r(x)} \neq E\left(\frac{\lambda_r(x)}{\lambda_r(x)}\right)$$

Sampling bias:

Distn for fixed x versus distn for autogenerated x.



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Point process model

# Two ways of thinking

First way: waiting for Godot! Fix  $x \in \mathcal{X}$  and wait for an event to occur at x  $pr(Y = 1 | \lambda, x) = \frac{\lambda_1(x)}{\lambda_{\bullet}(x)}$  $pr(Y = 1; x) = E\left(\frac{\lambda_1(x)}{\lambda_{\bullet}(x)}\right)$ 

Conventional, mathematically correct, but seldom relevant

Second way: come what may!

SPP event occurs at x, a random point in  $\mathcal{X}$ joint density at (y, x) proportional to  $E(\lambda_y(x)) = m_y(x)$ x has marginal density proportional to  $E(\lambda_{\cdot}(x)) = m_{\cdot}(x)$ 

$$\operatorname{pr}(Y = 1 \mid x) = \frac{E\lambda_1(x)}{E\lambda_1(x)} \neq E\left(\frac{\lambda_1(x)}{\lambda_1(x)}\right)$$



Sampling bias Non-attenuation Inconsistency Estimating functions Robustness Interference

Log Gaussian illustration of sampling bias

$$\begin{aligned} \eta_0(x) &\sim & GP(0,K), & \lambda_0(x) = \exp(\eta_0(x)) \\ \eta_1(x) &\sim & GP(\alpha + \beta x,K), & \lambda_1(x) = \exp(\eta_1(x)) \\ \eta(x) &= \eta_1(x) - \eta_0(x) &\sim & GP(\alpha + \beta x, 2K), & K(x,x) = \sigma^2 \end{aligned}$$

One-dimensional sampling distributions:

$$\rho(x(u)) = \operatorname{pr}(Y(u) = 1) = E\left(\frac{e^{\alpha + \beta x(u) + \eta(x)}}{1 + e^{\alpha + \beta x(u) + \eta(x)}}\right)$$

$$\operatorname{logit}(\rho(x)) \simeq \alpha^* + \beta^* x \quad (|\beta^*| < |\beta|)$$

$$\pi(x) = \operatorname{pr}(Y = 1 \mid x \in \operatorname{SPP}) = \frac{E\lambda_1(x)}{E\lambda_1(x)} = \frac{e^{\alpha + \beta x + \sigma^2/2}}{e^{\sigma^2/2} + e^{\alpha + \beta x + \sigma^2/2}}$$

$$\operatorname{logit} \operatorname{pr}(Y = 1 \mid x \in \operatorname{SPP}) = \alpha + \beta x$$

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# Explanation of sampling bias

Fix x, x' non-random points in  $\mathcal{X}$ No reason to think that  $\lambda_{\cdot}(x) > \lambda_{\cdot}(x')$  versus  $\lambda_{\cdot}(x') > \lambda_{\cdot}(x)$ Now let  $x^*$  be the point where first superposition event occurs Good reason to think that  $\lambda_{\cdot}(x^*) > \lambda_{\cdot}(x)$ 

because x-values have density  $\lambda_{\cdot}(x)$ 

Correct calculation for predetermined non-random **x**:

$$p_{\mathbf{x}}(\mathbf{y}) = E \prod_{j=1}^{n} \frac{\lambda_{y_j}(x_j)}{\lambda_{\boldsymbol{\cdot}}(x_j)}$$

Correct calculation for random autogenerated  ${\boldsymbol x}$ 

$$p(\mathbf{y} \mid \mathbf{x}) = \frac{E \prod \lambda_{y_j}(x_j)}{E \prod \lambda_{\boldsymbol{\cdot}}(x_j)}$$
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# Attenuation

Quota sampling: Conventional calculation for fixed subject *u* 

logit pr(Y(u) = 1 |  $\eta$ , x) =  $\alpha + \beta x(u) + \eta(x(u))$ 

implies marginally after integration

logit pr(Y(u) = 1; x)  $\simeq \alpha^* + \beta^* x(u)$ 

with  $\tau = |\beta^*|/|\beta| < 1$ , sometimes as small as 1/3.

Calculation is correct for quota samples (x fixed) Both probabilities specific to unit u No averaging over units  $u \in \mathcal{U}$ Nevertheless  $\beta$  is called the subject-specific effect  $\beta^*$  is called population averaged effect



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Quota sampling:

Conventional calculation for fixed subject u

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# Non-attenuation

Sequential sampling for auto-generated units

logit pr(
$$Y(x) = 1 | \lambda$$
, event at  $x$ ) =  $\alpha + \beta x + \eta(x)$ 

implies marginally after integration

logit pr(
$$Y(x) = 1 | x$$
 in superposition) =  $\alpha + \beta x$ 

#### Calculation is correct for autogenerated units

Both probabilities specific to unit at x

No averaging over units

No parameter attenuation for autogenerated units



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Sampling bias Non-attenuation Inconsistency Estimating functions Robustness Interference

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#### Consequences: inconsistency

Conventional Bayesian likelihood for predetermined x:

$$p_{\mathbf{x}}(\mathbf{y}) = E \prod_{j=1}^{n} \frac{\lambda_{y_j}(x_j)}{\lambda_{\boldsymbol{\cdot}}(x_j)}$$

'Correct' likelihood for auto-generated  $\boldsymbol{x}$ 

$$p(\mathbf{y} | \mathbf{x}) = \frac{E \prod \lambda_{y_j}(x_j)}{E \prod \lambda_{x_j}(x_j)}$$

If conventional likelihood is used with autogenerated  ${\boldsymbol x}$ 

parameter estimates based on  $p_{\mathbf{x}}(\mathbf{y})$  are inconsistent bias is approximately  $1/\tau > 1$ 



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Consequences: estimating functions

Mean intensity for class r:  $m_r(x) = E(\lambda_r(x))$  $\pi(x) = m_1(x)/m_1(x); \quad \rho(x) = E(\lambda_1(x)/\lambda_1(x))$ 

For predetermined x,  $E(Y) = \rho(x)$ 

$$\sum_{x} h(x)(Y(x) - \rho(x))$$

(PA estimating function for  $\rho(x)$ )

For autogenerated x,  $E(Y|x \in \text{SPP}) = \pi(x) \neq \rho(x)$ 

$$T = \sum_{x \in \text{SPP}} h(x)(Y(x) - \pi(x))$$

has zero mean for auto-generated **x**.





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#### Consequences: robustness of PA

Bayes/likelihood has the right target parameter initially but ignores sampling bias in the likelihood estimates the right parameter inconsistently.

Population-average estimating equation establishes the wrong target parameter  $\rho(x) = E(Y; x)$ misses the target because sampling bias is ignored but consistently estimates  $\pi(x) = E(Y | x \in \text{SPP})$ because conventional notation E(Y | x) is ambiguous

PA is remarkably robust but does not consistently estimate the variance



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## variance calculation: binary case

 $(\mathbf{y}, \mathbf{x})$  generated by point process;

$$T(\mathbf{x},\mathbf{y}) = \sum_{x \in \mathrm{SPP}} h(x)(Y(x) - \pi(x))$$

$$E(T(\mathbf{x}, \mathbf{y})) = 0; \qquad E(T \mid \mathbf{x}) \neq 0$$
  

$$\operatorname{var}(T) = \int_{\mathcal{X}} h^{2}(x)\pi(x)(1 - \pi(x)) m_{\cdot}(x) dx$$
  

$$+ \int_{\mathcal{X}^{2}} h(x)h(x') V(x, x') m_{\cdot}(x, x') dx dx'$$
  

$$+ \int_{\mathcal{X}^{2}} h(x)h(x')\Delta^{2}(x, x')m_{\cdot}(x, x') dx dx'$$

V: spatial or within-cluster correlation;

 $\Delta$ : interference

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# What is interference?

Physical interference: distribution of Y(u) depends on x(u')

Sampling interference for autogenerated units  $m_r(x) = E(\lambda_r(x)); \quad m_{rs}(x, x') = E(\lambda_r(x)\lambda_s(x'))$ Univariate distributions:  $\pi_r(x) = m_r(x)/m_.(x)$ Bivariate:  $\pi_{rs}(x, x') = m_{rs}(x, x')/m_..(x, x')$  $\pi_{rs}(x, x') = \operatorname{pr}(Y(x) = r, Y(x') = s | x, x' \in SPP)$ 

Hence  $\pi_{r.}(x, x') = pr(Y(x) = r | x, x' \in SPP)$   $\Delta_r(x, x') = \pi_{r.}(x, x') - \pi_r(x)$ No second-order sampling interference if  $\Delta_r(x, x') = 0$ 



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#### Autogeneration of units in observational studies

Q: Subject was observed to engage in behaviour *X*.

What form *Y* did the behaviour take?

Application	X	Y
Marketing	car purchase	brand
Ecology	Sex	activity class
Ecology	play	relatives or non-relatives
Traffic study	highway use	speed
Traffic study	highway speeding	colour of car/driver
Law enforcement	burglary	firearm used?
Epidemiology	birth defect	type of defect
Epidemiology	cancer death	cancer type

Units/events auto-generated by the process



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## Auto-generation as a model for self-selection

Economics:

Event: single; in labour force; seeks job training Attributes (*Y*): (age, job training (Y/N), income)

Epidemiology:

Event: birth defect

Attributes: (age of M, type of defect, state)

Clinical trial:

Event: seeks medical help; diagnosed C.C.; informed consent;

Attributes: (age, sex, treatment status, survival)

What is the population of statistical units?



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#### Mathematical considerations

Restriction: if  $p_k()$  is the distribution for k classes, what is the distribution for k - 1 classes? Does restricted model have same form? Answer:

Weighted sampling

Closure under weighted or case-control sampling

Closure under aggregation of homogeneous classes



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