UNIVERSITÄT BERN

Towards continuous domain models in Spatial Epidemiology

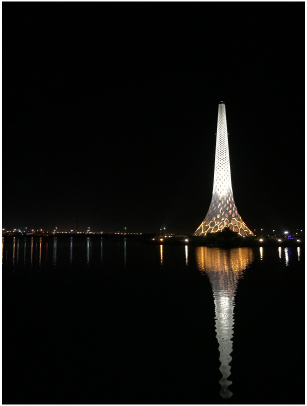
Garyfallos Konstantinoudis

Institute of Social and Preventive Medicine

October 28, 2018

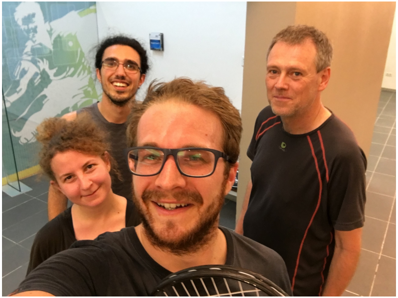
Outline

The campus

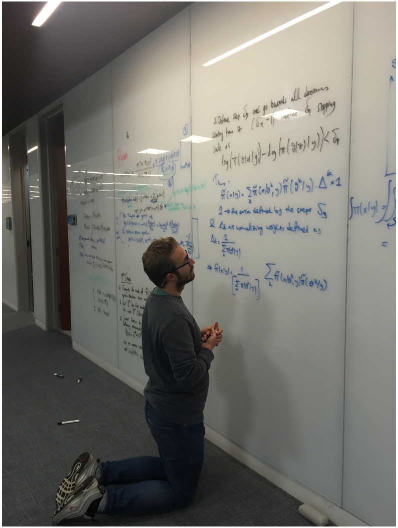


The food

The People



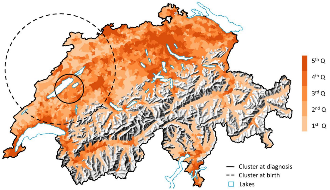
The Frustration



Introduction

Geographical Analysis in Spatial Epidemiology

- Generate hypotheses
- Identify hotspots of environmental contamination



Konstantinoudis *Cancer Causes Control* 2018

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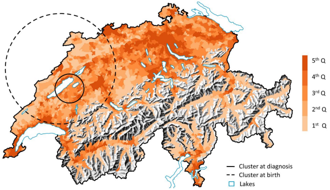

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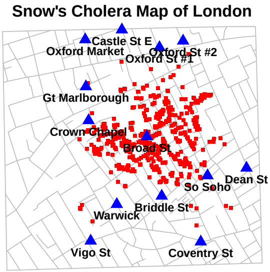

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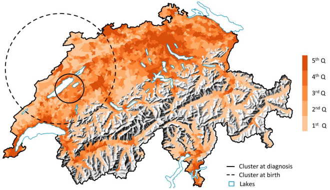

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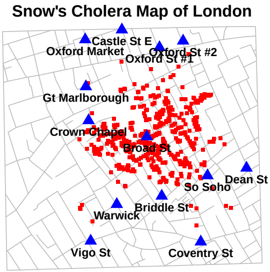
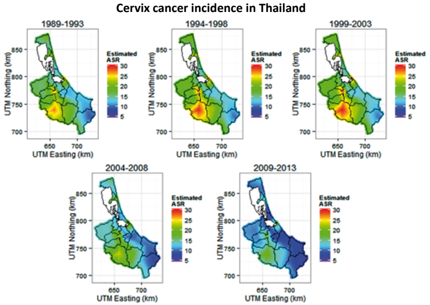
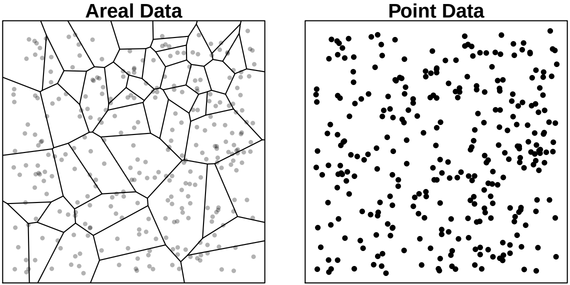




Zhao *Health Policy and Planning* 2017

Types of data

- Areal data and Besag York Mollie (BYM) models
- Point data and Log-Gaussian Cox processes (LGCPs)



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- Childhood leukaemia: 5.4 per $100,000$ person years
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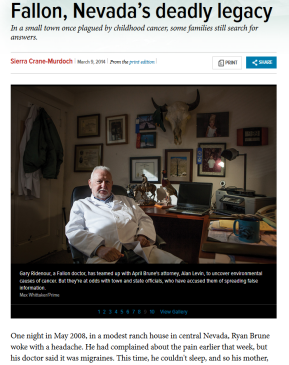

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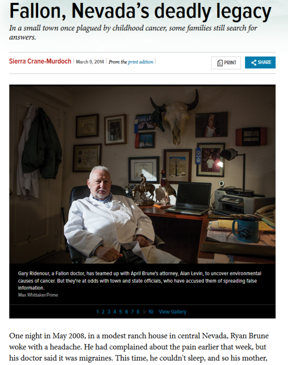
- Point data in Switzerland

EXCLUSIVE

Nineteen children living within 20 miles of the Sellafield nuclear plant have developed leukaemia, a cancer affecting their blood and bone marrow. In a few weeks' time their parents will begin proceedings to sue British Nuclear Fuels for compensation. If they win, it will make legal history. Four of these families have told their story exclusively to the Observer Magazine. Report by Alison Whyte and Annabel Ferriman. Photographs by Christopher Pillitz

Lynn and Ronald Marr with their son Ronald in the shadow of the nuclear plant at Sellafield, Cumbria. Young Ronald, now aged six, is suffering from acute lymphatic leukaemia

SELLAFIELD AND THE SUFFERING CHILDREN



Fallon, Nevada's deadly legacy

In a small town once plagued by childhood cancer, some families still search for answers.

Sierra Crane-Murdoch | March 9, 2014 | From the print edition | PRINT | SHARE

Gary Ridenour, a Fallon doctor, has teamed up with April Brune's attorney, Alan Levin, to uncover environmental causes of cancer. But they're at odds with town and state officials, who have accused them of spreading false information.
Max Whittaker/Prime

1 2 3 4 5 6 7 8 9 10 View Gallery

One night in May 2008, in a modest ranch house in central Nevada, Ryan Brune woke with a headache. He had complained about the pain earlier that week, but his doctor said it was migraines. This time, he couldn't sleep, and so his mother,

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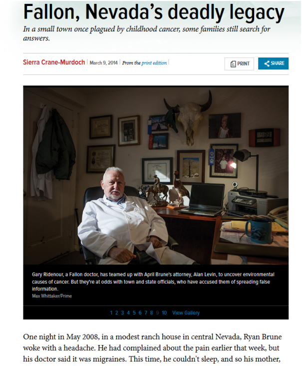
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LGCPs have some apparent advantages

- Bypass all the problems arisen when selecting arbitrary boundaries
- Step-wise risk function might be a strong assumption

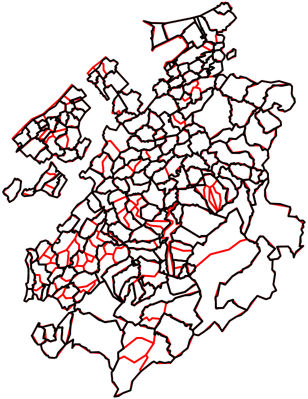

Figure. Municipality boundaries in the canton of Fribourg in 2001 (red) and 2015 (black)

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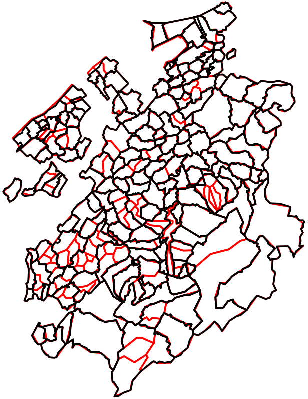

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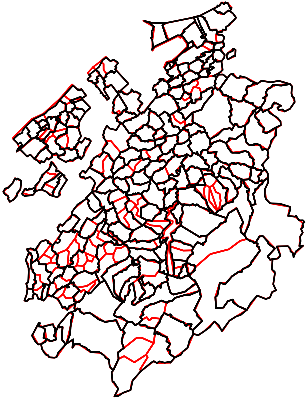

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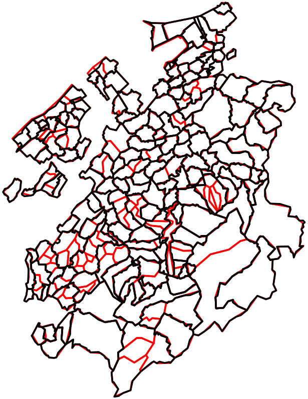

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Aim

Does LGCP on point data provide additional benefits over the BYM model on areal data when:

- **Aim 1**: Quantifying the risk in space
- **Aim 2**: Identify high-risk areas

Methods

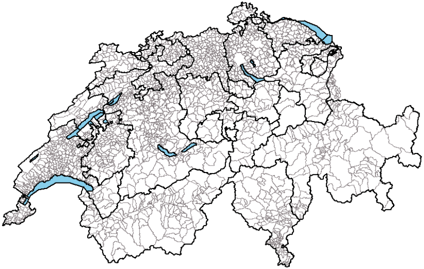
Data Availability

Cases

- Swiss Childhood Cancer Registry (SCCR)
- $> 90\%$ completeness[1]
- Precise locations

Population at risk

Cantons and municipalities in 2015



Geographical units in Switzerland

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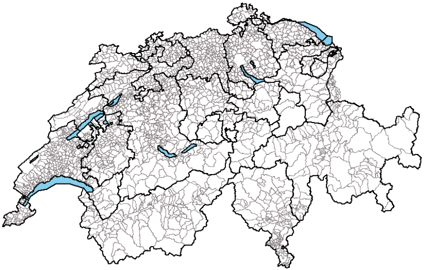

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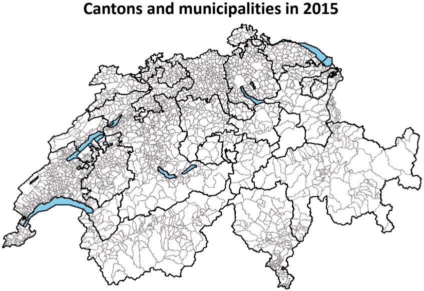
Geographical units in Switzerland

- 26 Cantons
- 2352 municipalities



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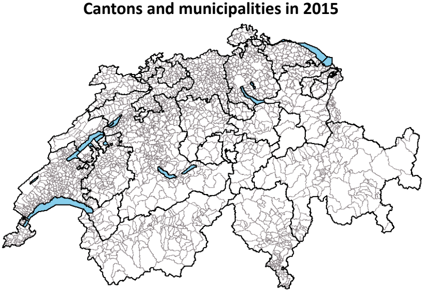


BYM model

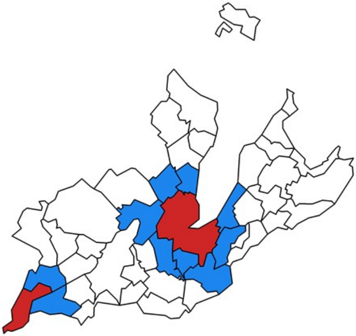
Let $\mathcal{W}$ an observation window, $A_1, ..., A_N$ a partition of $\mathcal{W}$, Y_i be the disease counts P_i the population and λ_i the risk in A_i:

$$Y_i | \lambda_i, P_i \sim \text{Poisson}(\lambda_i P_i)$$

$$\log(\mathbb{E}\, Y_i) = log(P_i) + \beta_0 + u_i + v_i$$

$$u_i | \mathbf{u}_{-i} \sim \mathcal{N}\Big(\frac{\sum_{j=1}^N w_{ij} u_j}{\sum_{j=1}^N w_{ij}}, \frac{1}{\tau_1 \sum_{j=1}^N w_{ij}}\Big)$$

$$v_i \sim \mathcal{N}(0, \tau_2^{-1})$$



LGCP model

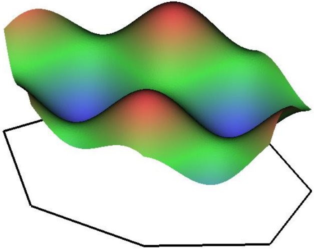
Let $\mathcal{W}$ an observation window and Ξ a point process with intensity $\lambda(s)$ on the s location:

$$\Xi|\lambda(s) \sim \text{Poisson}(\int_{\mathcal{W}} \lambda(s)ds)$$

$$\log(\lambda(s)) = log(\lambda_0(s)) + \beta_0 + u(s)$$

$$u(s) \sim \text{GF}(0, \boldsymbol{\Sigma}(h, \tau, \phi))$$

$$\kappa(h) = \tau^2 \rho_\nu(h/\phi), \rho_\nu(\cdot) \text{ Matern}$$



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- Inference for both models was conducted with Integrated Nested Laplace Approximation (INLA)

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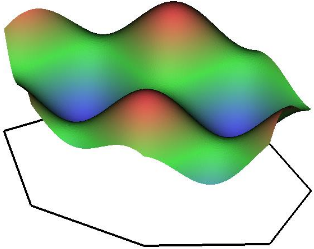

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Data simulation: Different scenarios

- Canton of Zurich
- $N = 205,242$ (15%) children
- Leukaemia incidence 1985-2015 ($n = 334$)

Radius	RR	times n	decay
1km	2	1	step function
5km	5	5	smooth function
10km	-	10	-

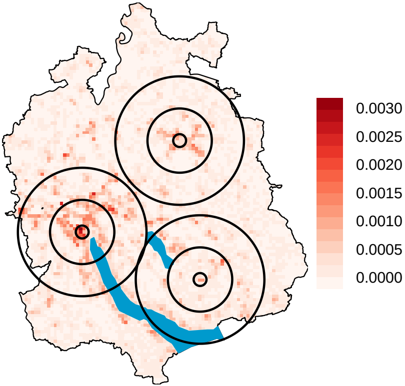
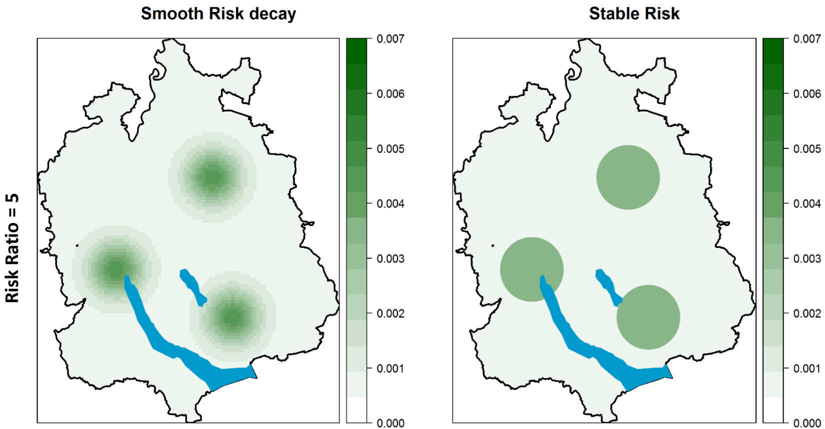


Figure: Population density and circles

Data Simulation: Example RR = 5 & radii = 5km



Data simulation: Simulation metrics

Aim 1: Quantify the risk in space

- Root mean integrated square error (RMISE)

$$\text{RMISE} = \left(\mathbb{E} \int_{\mathcal{W}} b(s)(log(\hat{\lambda}(s)) - log(\lambda(s)))^2 ds \right)^{1/2} =$$

$$\left(\mathbb{E} \sum_{g=1}^{G} b_g |D_g| (log(\hat{\lambda}_g) - log(\lambda_g))^2 \right)^{1/2}$$

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Aim 2: Identify high-risk areas

- Sensitivity, Specificity and area under the curve (AUC)

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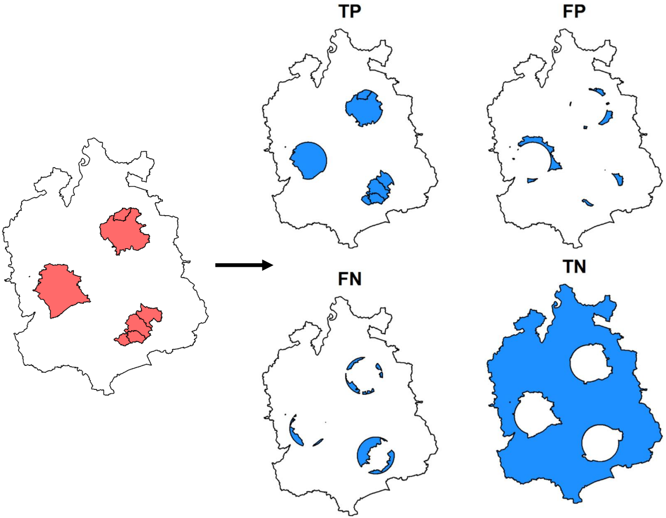
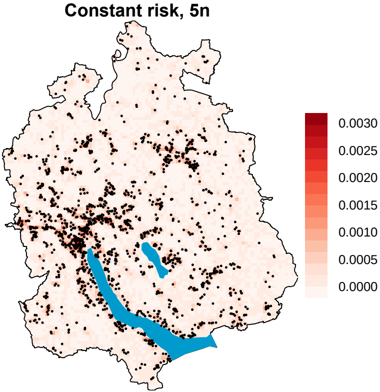
Data simulation: Sensitivity Specificity

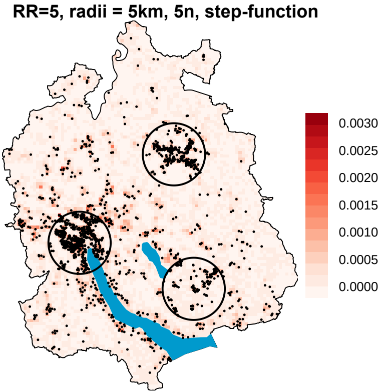
- Exceedance probability, $\Pr[\lambda_g > \frac{n}{N}] > \alpha$, $\alpha = 0, 0.05, 0.10, \ldots$



Results

Examples of simulated datasets

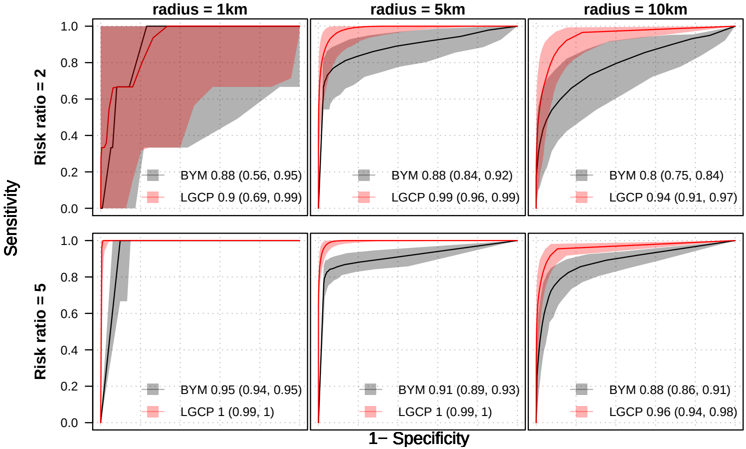




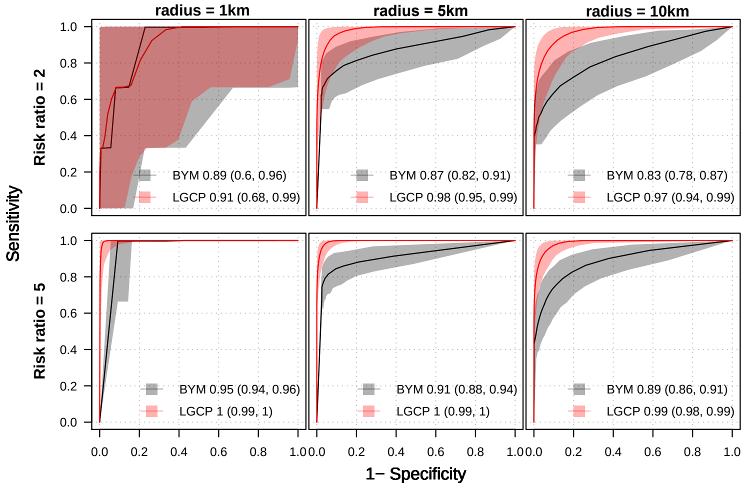
RMISE, $5n$

	BYM	LGCP
Step function		
Radius = 1km		
RR = 2	4.47 (3.17, 6.81)	6.62 (4.24, 9.88)
RR = 5	10.4 (8.77, 12.5)	14.8 (13.1, 17.1)
Radius = 5km		
RR = 2	11.6 (10.6, 13.1)	12.2 (10.8, 14.7)
RR = 5	22.8 (21.4, 24.5)	21.5 (19.6, 24.6)
Radius = 10km		
RR = 2	14.9 (14.3, 15.8)	12.1 (11, 14.4)
RR = 5	28.4 (27.3, 29.8)	22.3 (20.8, 24.6)
Smooth function		
Radius = 1km		
RR = 2	4.48 (3.1, 6.88)	6.51 (4.27, 9.9)
RR = 5	10.8 (8.82, 12.5)	14.8 (13, 16.8)
Radius = 5km		
RR = 2	10.4 (9.32, 12)	11 (9.33, 14.3)
RR = 5	19.2 (18, 20.6)	16.8 (14.8, 19.9)
Radius = 10km		
RR = 2	12.3 (11.5, 13.4)	10.1 (8.57, 12.7)
RR = 5	21.8 (21, 22.8)	13.9 (12.1, 17)

ROC-curves, Step-function, $5n$

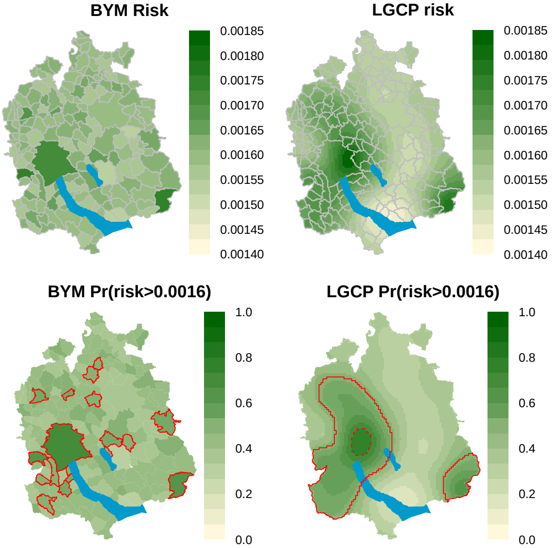


ROC-curves, Smooth-function, 5n



Example: Childhood leukaemia in Zurich

- $\Pr(\lambda(s) > \frac{n}{N}) > 0.50$ (red solid line)
- $\Pr(\lambda(s) > \frac{n}{N}) > 0.80$ (red dotted line)
- 95% CI $1.11(0.89, 1.38)$



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Our study suggests that this continuous domain models are preferable over the widely used BYM models.

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Prof. Haavard Rue *is a professor at the Computer, Electrical and Mathematical Science and Engineering Division – King Abdullah University of Science and Technology, Saudi Arabia*

«Bayesian quantile regression for discrete observations»

Wednesday, July 4, 2018 at 4:00 pm in room 220

INLA course in Zurich

http://www.zhrcourses.uzh.ch/en/programm/Bayesian-inference-using-R-INLA.html

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Zurich R Courses

- What is R?
- **Program 2018**
  - Introduction to R
  - Data Processing, Visualisation and Reporting with R
  - R4All: An introduction to the basics of R
  - Mixed (hierachical) Models in R
  - Categorical Data Analysis with R
  - Introduction to R programming
  - Shiny and Interactive Visualisation in R
  - R4All: Building on the basics of R
  - **Bayesian inference using R-INLA**
- Group Rates

Bayesian inference using R-INLA

Lecturers	• Dr. Haakon Bakka, CEMSE (King Abdullah University of Science and Technology) • Garyfallos Konstantinoudis (Institute of social and preventive medicine, University of Bern)
Certificate	Confirmation of participation
Target Audience	Advanced R users from all professional groups.
Costs	• CHF 600.- for members of UZH/ETH and associated institutes • CHF 800.- for alumni of UZH/ETH, members of other universities, the public sector and non-profit organizations • CHF 1200.- for companies Persons without current employment can register for the UZH/ETH fee upon → request .
Course language	English

Any questions?

Funded by:

Swiss cancer research (4012-08-2016, 3515-08-2014,3049-08-2012)

Swiss national science foundation (PZ00P3_147987)

Penalized complexity priors

- Occam's razor
  - Prefer simplicity, *base* model g
  - $x \sim \mathcal{N}(0, \tau I)$, $\tau = \infty$
- Measure of complexity (KLD from the *base* model)

$$\text{KLD}(f||g) = \int f(x) \log\left(\frac{f(x)}{g(x)}\right) dx$$

$$d(f||g) = \sqrt{2\text{KLD}(f||g)}$$

- Penalise complexity (constant decay rate penalisation)

$$\pi(\xi) = \lambda \exp(-\lambda d(\xi)) \left|\frac{\partial d(\xi)}{\partial \xi}\right|$$

- User-defined scaling; $\text{Prob}(Q(\xi) > U) = \alpha)$

Penalized complexity priors cont.

BYM model

- We considered a re-parametrisation:

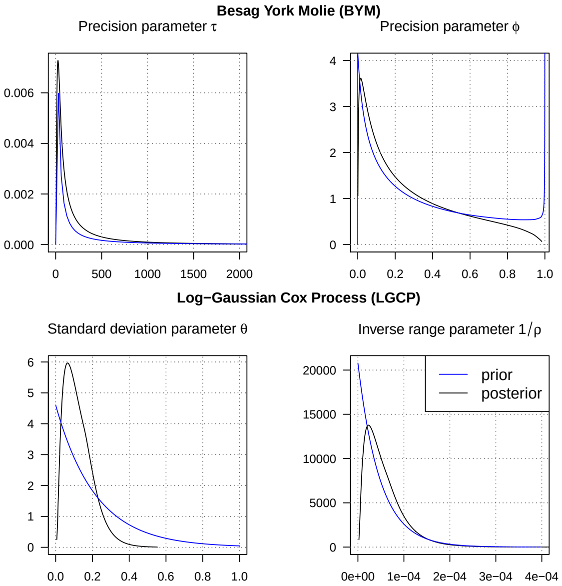
$$\log(Y_i) = log(P_i) + \beta_0 + \frac{1}{\sqrt{\tau}}\left(\sqrt{1-\phi}v_i\sqrt{\phi}u_i\right)$$

  ϕ is a mixing parameter and τ controls the marginal precision
- Prior specification independently
- base model: $\phi = 0$ or $\tau = \infty$
- $\Pr(\tau > 1) = 0.01$ and $\Pr(\phi < 0.5) = 0.5$

LGCP model

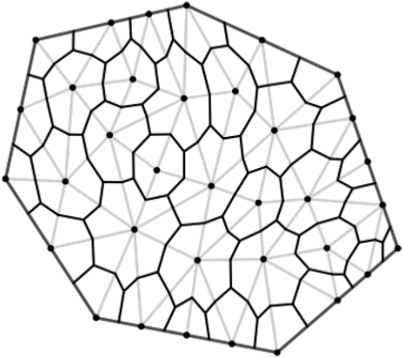
- Similar procedure
- $\Pr(\tau > 1) = 0.01$ and $\Pr(\phi < 30,000) = 0.5$

Example in ZH



LGCP and SPDE

- Simpson *Biometrika* 2016
- no more fine lattice but mesh
- likelihood and GF are separated
- the likelihood:



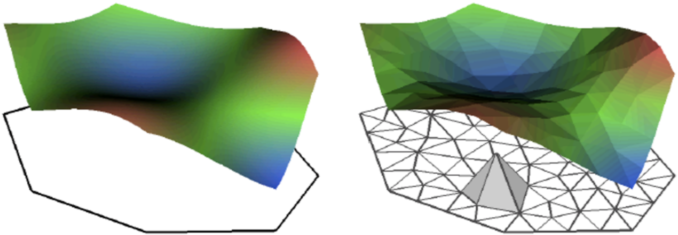
$$\pi(Y|u(s)) = \exp\left\{|\mathcal{W}| - \int_{\mathcal{W}} \lambda(s)ds\right\} \prod_i \lambda_i$$

Gaussian Field with SPDE

- Lindgren *J R Stat Soc Series B* 2011
- Stochastic partial differential equation (SPDE)
- Whittle *Biometrika* 1954:

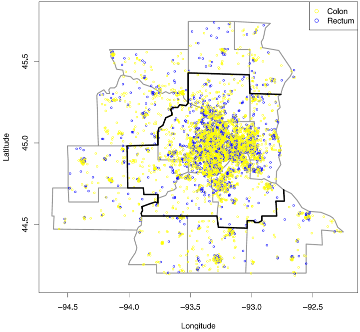
$$\tau(\kappa^2 - \triangle)^{\alpha/2} u(s) = W(s), \text{where } \kappa = \frac{\sqrt{8\nu}}{\phi}, \alpha = \nu + d/2$$

$$u(s) = \sum_i f_i(s) u_i$$

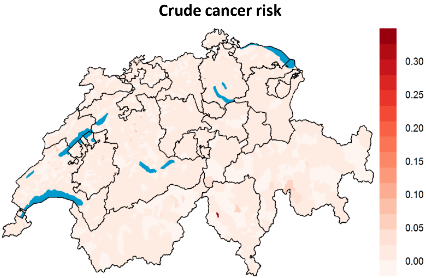


Types of data

- Areal data and Point data
- Besag York Mollie (BYM) model and Log Gaussian Cox Processes (LGCPs)



Liang *Ann Appl Stat* 2008



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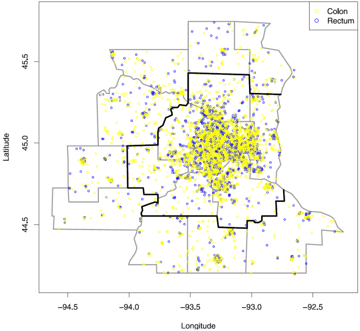

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